



# **HCHS/SOL Manual 2 Field Center Procedures for Visit 2**

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Study website - <http://www.csc.unc.edu/hchs/>

**HCHS/SOL Field Center Procedures for Visit 2  
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[Previous Manual, Date, Version]	Date(s) of Revisions; source	Approved by, Date	Revisions	Previous Page #s/Section changed	New Version of Manual	Distribution Date
Manual 2, version 1.0	7/2/2014	GH, SC	Content in all Chapters updated for Visit 2 Exam from Visit 1 basic manual	See tracked version	Manual 2, version 1.0	7/3/2014
Manual 2, version 1.0	8/29/14	GH, SC	Corrected Table 2 entries and specified convention for rounding of fractions in arm diameter measurements	Sections 11.2.3 & 11.2.4	Manual 2, version 1.0	7/29/14
Manual 2, version 1.0	10/10/14	GH, SC	Specify delay in scheduling for health conditions	3.1 – Participant Safety Screening	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/10/14	SC	Updated reference values to JNC 8 guidelines and modified per recommendations from the OSMB	20. Report BP Results to Participants	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/10/14	SC	Updated medication recording protocol per SC decision	8. Recording medications	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/17/14	GH, SC	Inserted safety questions for bioimpedence (10.3.2)	10 - Anthropometry	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/17/14	LA-S, GH, SC	Inserted hypoglycemia protocol	15. Oral Glucose Load	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/17/14	GH, SC	Inserted section on consideration of gender identity	16 - Interviews	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/22/14	GH, SC	Inserted reference to hypoglycemia protocol	19 – Participant Safety	Manual 2, version 1.0	11/11/14
Manual 2, version 1.0	10/22/14	SC	Updated list of assay results reported to participants	20.5.2 – Reporting Assay Results	Manual 2, version 1.1	11/11/14
Manual 2, version 1.1	11/4/2014	GH, SC	Administrative formatting to Sections 12 and 13	Sections 12 and 13	Manual 2, version 1.1	11/11/14
Manual 2, version 1.1	11/4/2014	GH, SC	Minor formatting changes with header/text spacing along with grammatical fixes	Sections 11, 15, 19	Manual 2, version 1.1	11/11/14
Manual 2, version 1.1	11/4/2014	GH, SC	Formatted Table 7 to fit onto one page	20.5.2	Manual 2, version 1.1	11/11/14
Manual 2, version 1.1	1/15/2015	GH, LA-S, SC	Oral glucose test eligibility and overview chart	15. Oral Glucose Load	Manual 2, version 1.1	6/05/15
Manual 2, version 1.1	1/15/2015	LA-S, GH, SC	Overview flow-charts of hyper/hypoglycemia safety	15.3.3 and Appendix 1	Manual 2, version 1.1	6/05/15
Manual 2, version 1.1	1/15/2015	SC	Heart rate values added as alert notifications	11.4. Recording the Omron Results, 20.4 Results Reporting Schedule, 20.5.1 Seated BP and Heart Rate, and 20.6 Conveying results to participants	Manual 2, version 1.1	6/05/15
Manual 2, version 1.1	1/27/2015	SC	Informed consent by proxy	5.5 Informed Consent by Proxy	Manual 2, version 1.1	6/04/15
Manual 2, version 1.1	1/27/2015	SC	Defining the need for consent by proxy	5.6 Defining the Need for ...Proxy	Manual 2, version 1.1	6/04/15
Manual 2, version 1.1	1/27/2015	SC	Identifying and recruiting alternate informants	16.7 Need for an Alternate Informant	Manual 2, version 1.1	6/04/15

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[Previous Manual, Date, Version]	Date(s) of Revisions; source	Approved by, Date	Revisions	Previous Page #s/Section changed	New Version of Manual	Distribution Date
1.1					1.1	
Manual 2, version 1.1	2/12/2015	SC	Relocation of participant in proximity to another FC	3.4 Contacting ppts./making appointments	Manual 2, version 1.1	6/04/15
Manual 2, version 1.1	2/12/2015	SC	FC examination eligibility of ppts. in passive follow-up	3.5 Contacting ppts./making appointments	Manual 2, version 1.1	6/04/15
Manual 2, version 1.1	3/11/2015	SC	Maximum desirable length of fasting time	14. Recommended duration of fasting	Manual 2, version 1.1	6/04/15
Manual 2, version 1.1	3/11/2015	SC	Delete alert values for total, LDL- and HDL-cholesterol	Table 7	Manual 2, version 2.0	6/04/15
Manual 2, version 2.0	4/16/2015	SC	Eligibility for OGTT: consult FC clinician if prior GI surgery uncertain	15.2, partial removal of stomach/small intestine or reduction surgery	Manual 2, version 2.0	6/04/15
Manual 2, version 2.0	5/01/2015	SC	Updates to informed consent status are recorded in CDART as a new occurrence of the ICT form.	Section 5.6 Informed consent tracking	Manual 2, version 2.0	6/04/15
Manual 2, version 2.0	5/13/2015	SC	Field center options in labeling urine specimens	Section 9. Collection of Biospecimen - Urine	Manual 2, version 2.0	6/04/15
Manual 2, version 2.0	6/15/2015	NA, CC	Update footer Section numbers for SC approved version on 5/13/2015	Footer sections numbers updated to show the correct section	Manual 2, version 2.0	6/15/2015
Manual 2, version 2.0	6/15/2015	GH, CC	Updates definition of adverse events and unanticipated problems, and their reporting schedule	Section 19.3	Manual 2, version 2.0	6/15/2015
Manual 2, version 2.0	7/23/15	GH	Selection of blood pressure cuff size; special situations / obese study participants	Section 11.2.4	Manual 2, version 2.1	6/15/2015
Manual 2, version 2.1	8/12/2015	SC	Identifies the set of interviews administered during a Visit 2 under consent by proxy	Section 5.5; Section 16, Table 4	Manual 2, version 2.1	8/19/2015
Manual 2, version 2.1	8/12/2015	SC	Fasting plasma glucose is measured with a POC glucose meter in all ppts. who fasted at least 8 hrs.	Section 15.1; Section 19.1	Manual 2, version 2.1	8/19/2015
Manual 2, version 2.1	8/24/2015	GH	Minimum fasting time specified as 8 hours	Section 3.2 – Scheduling participant meds.	Manual 2, version 2.1	-
Manual 2, version 2.1	8/24/2015	GH	Minimum fasting time specified as 8 hours	Section 14 – Determination of fasting time	Manual 2, version 2.1	-
Manual 2, version 2.1	8/24/2015	GH	Minimum fasting time specified as 8 hours	Section 15.5 – Administration of the OGTT	Manual 2, version 2.1	-
Manual 2, version 2.1	8/31/2015	NA	Final Formatting and TOC Updates	No changes, just format updates	Manual 2, version 2.1	-
Manual 2, version 2.1	10/13/2015	LAS	Nausea, GI discomfort added as exclusion from OGTT	Section 15.2	Manual 2, version 2.2	-
Manual 2, version 2.2	05/16/2016	GH	Updated Section 19.3 (adverse events and unanticipated problems) and Table 5	Section 19	Manual 2, version 2.2	-
Manual 2, version 2.2	07/15/2016	GH	Updated Section 15.3 (actions for high fasting glucose readings)	Section 15.3	Manual 2, version 2.3	-

Tracking Table of Revisions to HCHS/SOL MOP 2



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[Previous Manual, Date, Version]	Date(s) of Revisions; source	Approved by, Date	Revisions	Previous Page #s/Section changed	New Version of Manual	Distribution Date
Manual 2, version 2.3	8/5/2016	NA, GH	Informed consent update using new occurrence of ICT for in CDART	Section 6.2- Informed consent update	Manual 2, version 2.3	8/5/2016
Manual 2, version 2.3	10/20/2016	SC	Specification of split, abbreviated and home visit exams Administrative formatting	Section 1 Throughout document	Manual 2, version 2.4	11/16/2016
Manual 2, version 2.4	1/10/2017	NA, CC	Typo corrections, harmonization of tracked / clean copies Administrative formatting of tracking table of revisions	Section 1, Tables 1.0 and 1.1 Tracking table of revisions	Manual 2, version 2.5	1/10/2017
Manual 2, version 2.5	2/08/2017	SC	Introduced 'Evening exam visits and examination at host centers' as Appendix 2. Added an introductory paragraph to Section 1, page 1	Table of contents; Section 1, p. 1; Pagination and page break corrections; Appendix 2 (Section 20)	Manual 2, version 2.6	3/14/2017
Manual 2, ver. 2.6	5/11/2017	Update	Removed following sentence: If the calendar year is 2017, then schedule all appointments by September 1, 2017.	Section 2.1 p.2	Manual 2, ver. 2.6	
Manual 2, ver. 2.6	7/12/2017	SC	Remove selected laboratory assay values from report of study results according to length of time from venipuncture to specimen processing, and propose scripted statements to enclose with report	Section 1.3 (added sub-section 1.3.3)	Manual 2, ver. 2.7	7/19/2017
Manual 2, ver. 2.7	7/12/2017	SC	Updated the list of test results not reported to participants if the time from blood draw to specimen processing exceeds 2 hours.	Section 1.3.3, II, <i>ital. text</i>	Manual 2, ver. 2.7.1	
<b>Manual 2, ver 2.7</b>	<b>2/23/2018</b>	<b>SC</b>	<b>Updated information related to AFU reimbursement for study participants.</b>	<b>Section 5, page 1 of 3</b>	<b>Manual 2, ver 2.7.2</b>	<b>2/23/2018</b>

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**APPENDICES TO MANUAL 2**

**(Individual documents found on HCHS/SOL Investigator's website - refer to listing below)**

**Appendix 1 List of Study Forms**

**Appendix 2 Evening Examination Visits and Examination of Relocated HCHS/SOL  
Participants**

## 1. THE VISIT 2 EXAMINATION OF THE HCHS/SOL COHORT

This manual, entitled **Field Center Procedures for Visit 2** is one of a series of protocols and manuals of operation for the first re-examination of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) cohort. Because a number of procedures need to be described in detail for this study, more detailed manuals of operation containing full specifications and references have been organized into a set of protocol manuals. The study protocol as described in Manual 1 provides an overview of the background, aims, organization, and general objectives of the HCHS/SOL. Manual 2 provides an overview of the interviews and clinical measurements conducted as part of the second field center examination. The workstations are presented in the order in which they occur (i.e., reception, interviews, procedures, medical data review); the descriptions of the individual interviews and procedures are presented in alphabetical order. Table 1 (see below) lists the main components of the field center second examination and cross-references each procedure with its respective manual of operation.

Because high quality of data and a strict standardization of the examination and interview techniques across all field sites are essential it is important that HCHS/SOL field center personnel be fully familiar with this manual of procedures. To meet our scientific goals field center technicians must be trained and certified in the procedures described in this manual, and must remain standardized throughout the data collection phase. A complete knowledge of the procedures detailed in this manual is required so that patterns in the HCHS/SOL data can reflect differences between study participants and between groups of Hispanic background as opposed to differences between study technicians or deviations from study protocol. Strict and sustained adherence to study protocol by all HCHS/SOL personnel is required for the Study to be able to meet its obligations to the study participants, to the scientific community and to the funding agencies.

To the degree that this is applicable, the description of each interview/exam component in this manual includes a brief rationale for its use, operational procedures, an overview of training requirements and certification criteria, routine quality assurance measures, and data collection procedures.

At each HCHS/SOL study site, the re-examination of the HCHS/SOL cohort (Visit 2) is conducted on the premises of the HCHS/SOL Field Center, following the standardized procedures described in this manual. Under exceptional circumstances Visit 2 examinations may be split or conducted as a home examination. HCHS/SOL cohort members who are unable to take part in a Visit 2 exam during regular hours may be scheduled for an afternoon or evening examination at the field center. Each of these circumstances is described in Section 1 of this manual. The similarly unusual circumstance in which a study participant is examined at a host center different from the original field center is described in Appendix 2.

Table 1 Outline of HCHS/SOL Cohort Visit 2 Field Center Examination Visit

Standardized Visit 2 Examination Components	Manual of Procedure (MOP)	Form codes (English, Spanish)
Pre-visit screening and scheduling (eligibility)	2, 16	ELE
Participant safety screen	2, 16	PSE
<b>Fasting Block</b>		
Reception, itinerary checklist form,	2	CHK
Informed consent, medical releases	2	ICT
Updated personal and contact information	2	IDE
Participant safety update, and routing	2	PSE
Participant disability screen	2	PDE
Change clothes, urine specimen	2, 7	BIO
Anthropometry	2	ANT
Determination of fasting status and blood draw	7, 2	BIO
Phantom QC form for bio-specimens	2, 12	PHT
Determination of blood glucose levels – glucose load	7, 2	BIO
<b>Exams</b>		
Seated BP	2	SBP
Echocardiography	17	CHK
2-hour blood draw	7, 2	BIO
<b>Snack</b>		
<b>Interviews</b>		
Identifying Information and current address	2	IDE, IDS
Personal Medical History	2	MHE, MHS
Reproductive Medical History	2	RME, RMS
Pregnancy Complications	2	PCE, PCS
Socio-economic Status - Occupation	2	SEE, SES
Health Care	2	HCE, HCS
Chronic Stress	2	STE, STS
Family Cohesion	2	FCE, FCS
Social Support	2	SSE, SSS
Acculturation	2	ACE, ACS
Well Being, GAD7, CESD	2	WBE, WBS
Abbreviated medication use	2	MSE, MSS
Tobacco Use	2	TBE, TBS
Alcohol Use	2	ALE, ALS
Street clothes	2	--
Procedure and questionnaire administration tracking	2	CHK
Exit interview	2	EXE

### 1.1 Split Field Center Examinations

Examinations at the HCHS/SOL center may be scheduled as split exams if the study participant is unable to take part in a full examination, or split to accommodate circumstances not anticipated at the time the examination was scheduled. Split examinations must be completed no more than 30 days apart.

Under exceptional circumstances field center managers may authorize scheduling split examination beyond 30 days. Weather conditions, the unforeseen absence of key personnel, illnesses, and a participant’s inability to complete an examination within the time period specified by protocol represent such exceptional circumstances. The frequency of split examinations that occur more than 30 days apart must not exceed 5% of a field center’s examinations during one year.

An examination may be split if an alert condition requires that an exam visit be discontinued, and completion of the exam is scheduled once the medical condition prompting the alert is known to be resolved. Biospecimen collection may not be done more than once per participant. If an alert requires that the exam visit be stopped prior the venipuncture, no biospecimen should be collected at this time, and the full examination is repeated at a later date. If an exam visit is discontinued after biospecimen was collected, this original venipuncture and specimen processing information is entered into CDART and not repeated upon return (with the exception of the blood pressure for safety reasons), but not recorded in CDART.

On occasion individual interviews or examination components of a full examination may be missing, inadvertently or to accommodate various circumstances in the field. Completion of the missing component may be done while the participant is at the field center, or scheduled subsequently once flagged as missing in the data management report. Missing exam components must be completed within 90 days of the initial visit to maintain the temporal alignment in the baseline characterization of the HCHS/SOL participants.

When a study participant returns to the field center to complete an examination that was discontinued or split, s/he is asked to initial and date the informed consent signed during the first part of the examination to indicate consent for this portion of the examination. If the local IRB requires that a new informed consent be obtained to complete a split visit, the most recent informed consent supersedes an earlier version and should be reflected in the ICT form in CDART.

## **1.2 Abbreviated Examinations at Field Center**

If authorized by the field center principal investigator, HCHS/SOL cohort members who are unable or unwilling to take part in a full-length Visit 2 examination may be offered an abbreviated examination, with the “core” Visit 2 contents as shown in Table 1.1. Abbreviated examinations are conducted according to the standardized study procedures as specified in the HCHS/SOL manuals of operation. All Visit 2 quality assurance and quality control provisions apply. Abbreviated examinations conducted at the field may not be split. The contents of the abbreviated Visit 2 examination correspond to those of the Visit 2 Home Examination.

## **1.3 HCHS/SOL Examinations Conducted as Home Visits**

Home visits provide an opportunity to obtain important data on HCHS/SOL participants who are frail, disabled, cognitively impaired, those who provide dependent care for another person or are unable to come to a HCHS/SOL field center for another, legitimate reason. With approval by the field center principal investigator, study participants who meet the above criteria may be offered an examination at their place of residence if they are located within a distance that allows for arrival of biospecimen at the field center laboratory within 120 minutes from blood draw, as the maximum length of time specified in MOP 7 for biospecimen collection in the field. The examination at the participant’s home is an abbreviated Visit 2 which includes the examination components shown in Table 1.1. Home examination visits may also be conducted as split examinations that combine an abbreviated exam at the HCHS/SOL center focused on the collection of fasting biospecimen and physical examinations that require instrumentation, followed within 30 days by a home examination visit to acquire the remainder of the exam components listed in Table 1.1. If a home examination is required for a HCHS/SOL cohort member to take part in Visit 2 and processing of biospecimen within 120 minutes is not assured, a split exam that includes biospecimen collection at the field center should be attempted.

The interview and examination procedures at the home follow the field center protocol as closely as the physical environment permits. Two HCHS/SOL staff attend each home visit, one or both of whom are certified in HCHS/SOL's protocol for each of the data items to be acquired.

### **1.3.1 Scheduling and Setting Up A Home Examination**

#### *a. Setting up the Visit*

Cohort members eligible for a HCHS/SOL examination at home who are mobile are offered the option of an abbreviated examination at the HCHS/SOL field center instead of an examination at their place of residence. This offers greater participant safety and an exam environment that is standardized as well as more comfortable for the participant and HCHS/SOL personnel. The contents of a 'home examination' conducted at an HCHS/SOL field center do not differ from those conducted at a home, but field center facilities and equipment are used.

#### *b. Scheduling the Visit*

In scheduling the home visit with the participant HCHS/SOL staff considers the participant's routines and uninterrupted availability. The participant is reminded of the approximate time needed to complete the exam, the need for privacy, and for a quiet area with a table and two chairs. HCHS/SOL staff carefully explains the need for a private area and to avoid distractions during the examination period. This applies to interruptions by family members, children, pets, noise from TV, radio, stereo, or phone calls. If there is a pet in the home, the participant is asked whether the pet can be kept in a separate room during the testing (with the exception of service animals used by the participant). If the HCHS/SOL participant has identified a proxy or alternate informant, it is also determined in the course of scheduling whether the participant's proxy will be available during the home visit.

The scheduled visit, date, and time are confirmed by letter. The letter includes reference to the physical requirements for home testing, the informed consent video (if applicable), and the informed consent document (the latter at the discretion of the field center). HCHS/SOL staff calls the participant on the day before the scheduled examination, or the morning of the scheduled visit, to confirm the appointment. If needed, the examination time is adjusted. The participant is reminded of the need for a quiet space during testing.

HCHS/SOL personnel assembles the home examination materials on the day before the home visit. It is first determined whether biospecimens for this cohort exam were collected at the field center prior to the home visit, and the home examination kit is assembled accordingly. If biospecimen is to be collected at the home, MOP 7 procedures are followed to print the participant ID labels, to label the biospecimen collection tubes, and assemble the home examination kit. Unless the home exam follows a field center examination that collected anthropometry, sitting blood pressure and fasting biospecimen, the equipment required for the home visit includes: professional scale, home biospecimen collection kit and biospecimen collection supplies, small container with ice (for EDTA tubes), the OMRON blood pressure monitor, and a laptop computer equipped with 4G wireless internet access capability approved by the HCHS/SOL coordinating center as sufficient for data collection in CDART. Before departing for the home visit staff verifies that equipment and testing materials are complete, that the directions to the home are clear, and that adequate travel time has been allowed.

### *c. Staff Safety Considerations*

Home visits are made during daylight hours whenever possible. A map and explicit directions are secured before leaving the field center. Travel and home visits are done in pairs. Staff dress conservatively and wear the Study ID in a prominent place. Staff carries a letter of introduction, as well as a copy of the reminder letter or appointment card that the participant should have received earlier.

In the field, staff must remain aware of the surroundings and use common sense for personal safety. A written record of the HCHS/SOL visit destination and travel arrangements are left with the home field center, as well as the examiners' cell phone numbers. Purses are locked inside the trunk of the car before leaving (rather than doing this at the participant's home). Staff is encouraged to be cautious of pets, either the participant's or others, and to have car keys in hand when leaving the participant's home (not stand by the car to search for the keys). When directions to the home are obtained, ask whether there are safety concerns or pets (the participant's or others) to be aware of.

### *d. Liability Issues*

At each field center staff seeks counsel on the institutional requirements and the liability insurance policy that covers this field work. If paperwork is applicable for purposes of insurance, this is completed before leaving for the home visit.

## **1.3.2 Conducting The Home Visit Examination**

### *a. Rapport with the HCHS/SOL participant*

Appointments are met on time. If a situation arises that prevents staff from being on time, the participant (and the contact or proxy if applicable) are called and alerted to the possible delay. Appointments are rescheduled as a last resort. On arrival the examiners introduce themselves and show identification or copy of the appointment letter or card. Appropriate time is spent talking with the participant's family members to provide a transition from arrival to testing. The content and length of the examination are described, and time is taken to answer questions.

### *b. Examination Environment*

The environment is assessed for a suitable testing area and if necessary staff refers to the request for the use of a table (kitchen, card, desk, etc.), two straight chairs and adequate lighting. Care is taken to have an exam environment that is private and as quiet as possible, and that pets have been put in a separate room. All persons in the house are made aware that a quiet area and privacy are needed for testing. The participant is asked whether he/she would like to use the bathroom before beginning the testing, at which point the urine specimen is collected. A rest period or bathroom break can be offered about midpoint of the testing.

### *c. Informed Consent*

The informed consent is administered prior to setting up the examination area and proceeding to the examination, whether this applies to the study participant, the proxy or the informant. The informed consent DVD (and the informed consent forms at the field center's discretion) can be mailed to the study participant in advance of the home visit. One week is allowed for these materials to be reviewed prior to the home visit. To administer the informed consent HCHS/SOL staff follows the procedures for informed consent administration at the field center.

### *d. Examinations and Interviews*

The interviews and examinations are administered adhering to the standardized study protocol procedures, and the same quality assurance/quality control protocol applies. To protect confidentiality, selected portions of the personal medical history form (MHE/MHS) are omitted. When conducting a Visit 2 examination at the home collect only Sections A and B (items 1 through 23.f).

The interviews at the home are conducted using the HCHS/SOL CDART and include the standard versions of the data collection forms used at the field center. The materials and procedures used for biospecimen collection at a home are specified in MOP 7. This includes the protocol to be followed in transporting these specimens to the HCHS/SOL field center, and the prompt processing of the specimens once at the field center.

*e. Close-out of the Home Examination*

After completion of the interviews and examination the participant and proxy or informant are thanked, and asked whether they have questions. Staff mentions that a summary of the blood test results will be mailed in six to eight weeks to the person designated at the time informed consent was obtained. The cohort member’s continued participation in the HCHS/SOL follow-up calls (or the interview informant) is encouraged. A few minutes are spent in participant-centered conversation as a transition to the departure.

Table 1.1 Components of Abbreviated Visit Field Center Examination and Home Visit Examination

Visit 2 Examination Components	Abbreviated FC Exam	Home Visit Exam	Manual of Procedure (MOP)	Form codes (English, Spanish)
Pre-visit screening and scheduling	X	X	2, 16	ELE
Participant safety screen	X	X	2, 16	PSE
<b>Fasting Block</b>				
Reception, itinerary checklist form,	X	X	2	CHK
Informed consent, medical releases	X	X	2	ICT
Urine specimen	X	X	7, 2	BIO
Anthropometry	X	Weight only	2	ANT
Fasting status and blood draw	X	X	7, 2	BIO
<b>Exam</b>				
Seated BP	X	X	2	SBP
<b>Snack</b>				
<b>Interviews</b>				
Identifying Info. and current address	X	X	2	IDE, IDS
Personal Medical History	X	X <sup>§</sup>	2	MHE, MHS
Reproductive Medical History	X	X	2	RME, RMS
Pregnancy Complications	X	X	2	PCE, PCS
Abbreviated medication use	X	X	2	MSE, MSS
Tobacco Use	X	X	2	TBE, TBS
Alcohol Use	X	X	2	ALE, ALS
Procedure/questionnaire tracking	X	X	2	CHK
Exit interview	X	X	2	EXE

§ = When interview is conducted at the home, collect sections A and B only (items 1 through 23.f)

### 1.3.3 Reporting Study Results from Home Examinations

Because the length of time elapsed between the blood draw and specimen processing can affect certain laboratory assay values, SOL blinds or removes certain laboratory assay results from the study results reported to SOL participants according to the time to specimen processing. To reflect this, the following scripted statements are enclosed with the study results reported to SOL cohort members/their provider of medical care, when such results originate from a home visit.

I. Report of results from a SOL Visit 2 home visit – Blood drawn in the field was processed at the SOL field center within 2 hours of the venipuncture.

*Blood for the laboratory assays included in this reported was collected by SOL study personnel at the participant's home, and processed at the SOL field center within 2 hours of venipuncture. Because of the time elapsed we do not report the fasting glucose value.*

II. Report of results from a SOL Visit 2 home visit – Blood drawn in the field was processed at the SOL field center after more than 2 hours following venipuncture.

*The blood for the laboratory assays included in this reported was collected by SOL study personnel at the participant's home, and processed at the SOL field center after more than 2 hours of the venipuncture. Because of the time elapsed we do not report the test results for glucose, triglycerides, total cholesterol, LDL-cholesterol, nor HDL-cholesterol. For more complete results we are glad to offer a repeat test from blood drawn at the SOL field center.*

Blinding the specified assay values in the report to the SOL participant, and attaching a personalized version of the pertinent script shown above is done at the SOL field center. This implies that at the time of reporting study results to the SOL cohort members/their providers of care, field centers need to be aware of whether the Visit 2 examination was a home visit and also the length of time between venipuncture and blood processing.

## 1.4 Community Outreach

As detailed in Manual 14, it is a goal of the HCHS/SOL to improve the health of the Hispanic / Latino communities in general and in the HCHS/SOL study areas in particular. From the outset and prior to the initiation of field work, investigators and their associates at each HCHS/SOL field center established and maintained close links and cooperation with the community represented by the HCHS/SOL study area. Pre-existing connections with community leaders and associations are invigorated and new links established to inform the community of the goals and characteristics of the HCHS/SOL and to provide for consultation and interaction with the community in planning the implementation of the HCHS/SOL. During the study development phased the investigators seek to become aware of priorities and issues deemed to be sensitive by a study community or group, in order to reconcile such expectations with the goals of the study and its procedures. Cooperation, openness to feedback and education serve as the basis for successful recruitment and retention in the HCHS/SOL.RECRUITMENT

## 1.5 Recruitment and Examination Goals by Center

A total of 16,425 study participants were recruited at baseline (Visit 1) from four field centers located in The Bronx, New York; Chicago, Illinois; Miami, Florida; and San Diego, California from March 2008 through June 2011. The study sites and the cohort population are described in further detail in Manual 1 and in the NHLBI publication, *Hispanic Community Health Study–Study of Latinos Data Book: A Report to the Communities*. Each field center contributed 4,000 persons of Hispanic/Latino origin in the age range is 18-74, selected to obtain approximately 2,500 persons age 45-74, and approximately 1,500 persons age 18-44. The goal for the second examination (Visit 2) is to re-examine more than 80% (about 13,000) of those participants still living in the communities nearby each field centers at the time of the second exam. Note, all participants who have not withdrawn consent are eligible to be re-examined, including those currently lost to follow-up.

Recruitment for Visit 2 of the HCHS/SOL cohort will be optimized to each field center and the characteristics of its study community. The goal in the scheduling of appointments for this round of examinations is to see each participant again approximately 5-6 years after their baseline visit. In order to accomplish this timing, participants will be contacted by the AFU staff during the interview process or by separate call, and invitations to be re-examined will be offered to the three “waves” of the cohort in the order in which they were first seen at the centers. Recruitment screening and tracking forms for visit 2 will be entered locally into the central database for ongoing weekly feedback to each field center and periodic reports to the steering committee and OSMB. Manual 6 on Follow-up procedures contains an appendix dedicated to the Visit 2 recall for examinations.

## **2. CONTACTING PARTICIPANTS / MAKING THE CLINIC APPOINTMENT**

HCHS/SOL participants who meet the eligibility criteria (see ELE form) are scheduled for a field center examination by the field center recruitment team and/or by personnel at the field center who coordinate this process. Field centers exercise local options in contacting the individuals successfully recruited into the HCHS/SOL, using phone calls, home visits, and mailed materials in a sequence and combination considered to be optimal by each field center. Screening Call logs are used locally for the Visit 2 recruitment activities. The individuals being recalled for the second examination are recorded in the Eligibility Checklist (ELE form) which is also used to note the date of the second examination visit scheduled at the convenience of the study participant and availability at the field center. Updated records of recruited individuals are made available to field center personnel through periodic reports by the HCHS/SOL coordinating center for tracking and scheduling purposes. Each field center is responsible for entering information promptly into the study screening and recruitment forms so that updated lists used to schedule the field center examination visit can be produced locally. Attempts will be made to contact all participants, active or inactive, and the final outcome of that contact will be recorded on the ELE during the course of the 36-month examination cycle, so that standardized response rate for Visit 2 can be reported to the Steering Committee and the OSMB.

Before calling a participant, field center personnel must have the appropriate scheduling forms and worksheets used locally, the available clinic appointment dates/times, and all relevant scripts. Interviewers make the number of call attempts specified for each HCHS/SOL field center, tracking them on an exam scheduling worksheet. If informational materials have been mailed to the study participant prior to the call or left by the recruitment team during household visit, the interviewee is first reminded of the letter and brochure and the staff person reviews this information and answers questions about the study and its procedures, as required.

### **2.1 Participant Safety Screening**

Verification of eligibility for all study procedures and pre-screening to ensure safety are part of the visit scheduling procedures. For this purpose HCHS/SOL personnel use the Participant Safety Screening Form (PSE, PSS), supported by the web based HCHS/SOL CDART data entry system available through the staff person's laptop/desktop. Following an explanation of the HCHS/SOL procedures in Visit 2, the interviewer requests an opportunity to verify the individual's eligibility for the study procedures. The conditions reviewed during this interview (and listed on the form) include pregnancy, breast feeding, the participant's use of a pacemaker and defibrillator or other implanted electronic device. Study participants who are pregnant are asked to schedule an examination visit at three months after delivery, and to provide a date by which the HCHS/SOL can re-contact them for this purpose. Breast-feeding is not an impediment for the field center examination, nor a reason for rescheduling; field centers work with the nursing mother to accommodate her needs. The presence of implanted devices is recorded on the PSE form and the participant is told of the procedures to avoid, and that a sticker will be placed on his/her name tag to make the study technicians aware of this during the field center examination.

During this interview staff also inquires about special needs, such as any medical conditions that would affect the examination or the appointment time or the timely use of medications, difficulties in getting on or off an examination table, or impediments in hearing or reading. Arrangements for a

safe and comfortable examination visit are made, consulting with the Clinic Manager as appropriate. Participants should be reminded to bring all their medications to the field center. The HCHS/SOL Visit 2 examination is considered safe and does not include strenuous procedures. Study participants who report recent surgery or an illness that required hospitalization or prolonged bed rest are encouraged to schedule their HCHS/SOL exam once they feel well and have completed their convalescence. Two to 3 months should be allowed following an illness or significant surgery. If the study participant does not feel well at that time – or their health care provider advises them to do so – schedule the exam visit for a later date. A record is made each time to call the participant to make an appointment at the designated time. If the calendar year is 2017, then schedule all appointments by December 31, 2017.

## **2.2 Scheduling the Participant’s Medications on the Day of the Examination**

Participants who have conditions that require the daily use of pharmacologic agents are instructed to do the following on the day of their field center examination:

Antihypertensive medications should be taken according to the participant’s usual schedule for these medications. This is recommended to avoid changes in a participant’s usual blood pressure on the day of the examination and in order to avoid abrupt changes in blood pressure and possible hemodynamic events during the visit. Nitrates (anti-anginal medications) also should be taken on the day of the examination according to schedule.

There are no particular safety concerns associated with aspirin, anticoagulants and antiplatelet aggregation agents, although bruising and minimal bleeding may occur at the venipuncture site. Individuals who have diabetes and take oral hypoglycemic medications can withhold them until the last blood draw and their snack. Participants who take insulin should be asked to withhold the morning dose until the blood draw and snack. Participants who use insulin should be advised to check their capillary glucose level two hours after the snack.

Medications for cancer, HIV, autoimmune and neurological disorders should be taken as prescribed by the participant’s physician. Field centers make it possible for the participant to take these medications at the set times, and with food if so prescribed. If this is not practicable the participant is asked to consult with their physician.

The study participant is reminded that the blood tests and other examination procedures require fasting for at least 8 hours prior to drawing blood and that a snack is provided about two hours after the start of the field center examination. Fasting means no consumption of food or drinks (including alcohol), with the exception of water. Participants will be asked to not consume food or drinks after 10:00 p.m. prior to the clinic visit and to refrain from smoking for the same length of time, or for 10 hours prior to the scheduled time of arrival at the field center. The individual is asked whether there are medical reasons for him/her not to be fasting for this length of time and alternate arrangements are made if necessary after consultation with the a supervisor. Study participants are then told what the options for the snack are at the field center and asked whether the participant has any dietary needs that are not met by these choices.

Key scheduling tasks are to explain the clinic location; identify an appointment time; establish how participant prefers to get there; identify any special medical conditions; provide brief but complete instructions. The interviewer also mentions that a confirmation letter will be mailed with the

specifics of the appointment with instructions on how to prepare for the visit. Lastly, remaining questions are answered and (optionally) staff can mention that a reminder call will be made.

After a successful scheduling call, study personnel process the participant ID; name, address, email and phone number; appointment time and transportation preference; and any special instructions. The “final status” screening status is recorded on an exam scheduling worksheet.

### **2.3 Appointment Reminders and Instructions for the Clinic Examinations**

The instructions for the visit to the field center are specified on an information sheet prepared by each field center, and mailed to the participant soon after the appointment is made. The instructions include:

1. Appointment date and time.
2. Preparations:
  - a) Instructions on how to complete the 12-hour fast;
  - b) Instructions on proper hydration while maintaining the fast;
  - c) Instructions concerning restrictions on the use of tobacco and vigorous physical activity the morning prior to the visit;
  - d) Instructions on appropriate clothing to wear for the examinations.
3. Items to bring to the field center:
  - a) Eyeglasses for reading;
  - b) Name and address of primary care physician and/or clinic;
  - c) Name, address, email, and phone number of contact persons;
  - d) An identification card with their photo (workplace ID, driver’s license, etc.)
4. Overview of Clinic Operations:
  - a) A listing of the interviews and procedures for the examination (optional);
  - b) A reminder that a snack is provided during the exam;
  - c) Clinic hours and phone number for questions or rescheduling appointment.
5. Directions to the clinic (e.g., a map) and to parking facilities:
  - a) A reminder of the arrangements for parking and/or reimbursement.
6. Transportation, if applicable (some centers provide transportation and arrange for participant pick-up).

### **2.4 HCHS/SOL Study Participants Who Relocate**

**HCHS/SOL cohort members who relocate within convenient access to a different HCHS/SOL field center** are re-assigned to that center by the HCHS/SOL coordinating center, in consultation with the respective field centers. A new study participant ID is assigned that links to all prior consent and study records for the participant. Communications with the study participant to accomplish this transfer are in the purview of the original field center, and are then assumed by the participant’s new field center. The original field center is responsible for maintaining contact and for tracing all study participants who move away from the original study site, with the exception of those who relocate to another HCHS/SOL study site.

## **2.5 Eligibility for a HCHS/SOL Field Center Exam of Participants in Passive Follow-up**

HCHS/SOL cohort members may be in passive follow-up status because they completed fewer than the required subset of procedures and interviews during the HCHS/SOL baseline examination, or because they could not be located by study personnel nor “reported alive” by a contact, a proxy or other sources on two consecutive contact years. Participants who completed fewer than the required set of procedures and interviews during the HCHS/SOL baseline examination are not eligible for re-examination and are not included in the recruitment lists released by the coordinating center. Participants in passive follow-up status because they could not be located by study personnel nor “reported alive” on two consecutive contact years can be re-classified to full AFU status if contact is re-established.)

HCHS/SOL cohort members in passive follow-up status are eligible for recruitment to Visit 2 if their passive follow-up status reflects missed contacts (in person or reported alive by contact) on two or more consecutive years. They are not eligible for Visit 2 however if the passive follow-up status is due to an insufficient number of interviews and/or exam during the HCHS/SOL baseline examination. A listing distinguishing these reasons for passive follow-up status can be obtained from the HCHS/SOL coordinating center.

### **3. RECEPTION**

Reception is the first workstation for a participant's examination visit. The participant is welcomed, informed consent is obtained, participant questions are answered, demographic and tracking information are updated and fasting status is determined.

Prior to the participant's visit information on morbidity and special needs recorded on the screening form (PSE, PSS) are transferred to Participant Itinerary/Exam Checklist Form (see Appendix under this section heading). At the time of the participant's arrival at the reception station, staff displays the Participant Itinerary Form on the CDART entry screen monitor and confirms the identifying information on the form with the study participant. Staff confirms that special needs are noted Disability Screen and needed accommodations noted on the Participant Itinerary/Exam Checklist Form. Unless already indicated on the screening form, the participant is asked whether she/he is diabetic, and that Glucose Load is listed as 'No' if the latter is the case. The participant's language preference for the interviews to be conducted during the visit also is recorded on the itinerary sheet which is then printed and attached to the participant's labeled folder to accompany him/her throughout the examination visit.

As soon as the initial steps of welcome and reception mentioned above have been addressed and participants are comfortable, they are given the opportunity to read and review the informed consent as described below. No data collection can take place before informed consent has been obtained.

Once consenting procedures are complete (Section 4 of this manual) participants are then shown where to change into an examination gown/robe. They are reminded to remove pantyhose and constricting garments, to remove all jewelry, to place clothing and valuables in a secured locker, and to keep eye glasses with them. At this point the participant is reminded of the need to collect a urine specimen, by saying something like:

“As mentioned in the letter we sent you, we need to collect a urine sample. You may do that as you change clothes for the exam. If you wish to do it later, please notify us when you need to use the bathroom; we can take your urine specimen at any time.” The procedures for the collection of the urine specimen are described in Section 0 of this manual.

If during in the course of the reception procedures the participant appears to be acutely ill, staff asks the participant if s/he is not feeling well. If that is the case or if the participant has flu-like symptoms, the Field Center Manager is consulted to determine whether the exam should be rescheduled.

Staff is trained for the reception workstation by the Study Coordinator at each field center. Certification requirements include the training on general interviewing techniques, Informed Consent, the Informed Consent Tracking forms, and the data entry system. Although there is no formal certification process for staff at the reception workstation, personnel working at the reception workstation are observed by the local study coordinator for quality assurance and standardization.

## **4. INFORMED CONSENT**

Informed consent (see HCHS/SOL informed consent template in Appendix to this manual) is the first data collection form administered during the course of the Exam. Its core content complies with specifications from the National Heart, Lung, and Blood Institute and the HCHS/SOL Steering Committee. Its content and format may have been adapted to meet the specific requirements of each field center's Institutional Review Board.

The primary objective of re-administering the Informed Consent is to inform the participant of the procedures of the HCHS/SOL, protect the rights of the HCHS/SOL Study participants, meet local Institutional Review Board requirements, and to identify the participant's instructions for the type of data and biospecimens to be collected, their long term storage and disposition. The informed consent makes the study participant aware of the right to withdraw from the study, to not participate in a procedure, or to decline to answer question(s) without penalty. Also at this time the participant is asked for authorization for subsequent contacts by HCHS/SOL personnel, to access information in their medical records, and for instructions on distribution of the HCHS/SOL study results.

### **4.1 Administration**

The purpose of the HCHS/SOL and the measurements to be made are reviewed with the participant. Informational materials about HCHS/SOL, its goals, measurements and procedures are mailed to participants prior to their examination visit. The consent form is available in Spanish and English and bilingual HCHS/SOL staff is available for its review and administration. Early on in the visit the participant's preference to communicate in Spanish or English was recorded on the Itinerary Form for easy access during the remainder of the exam visit. Before proceeding assess whether the participant uses reading glasses or a hearing aid. Verify that this information is recorded on the Itinerary Form and review with the participant how to have the hearing aid / reading glasses conveniently available throughout the clinic visit.

After introducing the consent form to the participant in a private area ask whether s/he prefers to read the consent form or to have it read by the staff person. Record this preference on the Itinerary Form to make this information easily accessible to interviewers throughout the clinic visit to avoid repeated questions whether the participant is comfortable reading.

At field centers that mail the informed consent prior to the field center visit staff should be attentive to the possibility that participants may have had read (or had the form read to them) prior to their arrival. Under these circumstances questions for clarification should be solicited and the consent portion of the form must be filled out and signed in the presence of the staff person who serves as witness. This will be signed again during visit 2.

If the participant is visually handicapped or otherwise incapable of reading the study description and informed consent page, the narrative portion is read to him/her and then the participant is asked to sign the document. At all times, questions are encouraged and ample time is allowed for the person to read and sign the informed consent document.

The original Informed Consent document is filed in the participant's study folder. A copy of the informed consent is given to the participant if requested by the participant or required by the local Institutional Review Board.

## **4.2 Training and Certification**

Study coordinators are responsible for providing local staff training. Certification by the Study Coordinator is required. Quality assurance is provided at each field center by means of observation by the local study coordinator.

## **4.3 Data Collection**

The Informed Consent is a paper form. In some centers the form may be split into two forms The participant receives a COPY of the informed consent, at which point the field center has the option of providing a copy of the entire form, or of the signed consent pages. In all cases, the original signature page must be kept at the field center and stored in the participant's study folder.

## **4.4 Ability to Comprehend the Informed Consent**

Although the capacity to provide informed consent is required for the HCHS/SOL to be conducted in an ethical manner it can be challenging to identify individuals who may not have the ability to comprehend the information in the consent form. There are no nationally recognized standards for this purpose and somewhat different findings have emerged when some states (and courts) have taken up this issue. As a result, each field center follows the guidance of its local IRB on whether specific procedures are required for identification of such individuals.

Unless impairment is obvious, recognizing cognitive impairment in a participant is difficult (even for professionals), particularly since social skills can remain intact for participants who otherwise do not perform well on testing. As an added consideration, decision-making capacity is frequently task specific. As a result, depending on the type and extent of impairment, cognitively impaired individuals can remain fully capable of making a variety of decisions, including whether or not to participate in a study. Field center personnel need to be attentive to indicators of potential cognitive impairment, such as repetition (i.e., repeating questions/stories over the course of just a few minutes) and empty or poor responses (i.e., the participant who frequently responds with "I don't know"). Individuals who seem to always be looking to their spouse or a companion for answers to historical questions or medical history questions also warrant consideration for a reduced capacity to answer all HCHS/SOL questionnaires.

Unless an IRB specifies the procedures to use for vulnerable individuals there is need for the HCHS/SOL field centers to provide an environment that assists and supports participants in comprehending the informed consent. To ensure that participants understand the informed consent staff can ask the participant to explain back (in their own words) certain portions of the study. This can be introduced by stating that it is very important that the participant understand his/her rights and the process by which the HCHS/SOL project protects the confidentiality of the participant's information. If the responses from the participant suggest that he/she has difficulty comprehending the consent process or the form contents, the staff person administers the six-item Cognitive Screener, following the script and procedures described below. The participant's score on the 6-item screener will guide HCHS/SOL staff in deciding whether to recruit a Consent Proxy, and whether to alert a HCHS/SOL field center clinician to assess participant safety needs.

## 4.5 Informed Consent by Proxy

Cognitive deficits may affect the ability to provide informed consent and to accurately respond to interviews and questionnaires. Procedures are implemented to identify participants: (1) considered vulnerable due to diminished cognitive functioning, in particular reduced decision-making capacity to provide informed consent, and (2) with cognitive impairment sufficient to call into question their ability to provide accurate self-report. Those deemed to have diminished capacity to provide informed consent require consent from a proxy to participate in the HCHS/SOL study. In addition, access to a knowledgeable alternate informant who can assist with interviews and questionnaires is requested for participants falling into the second category, where self-report may be suspect. Staff should encourage the participant him/herself to respond to the questionnaire items unless the participant is unable to do so. Until a cohort member has participated in HCHS/SOL Visit 2 his/her informed consent of reference is the latest informed consent provided.

HCHS/SOL cohort members who take part in Visit 2 under a consent by proxy are offered all study procedures that are not preempted by a safety exclusion, and a subset of the interviews as selected by a group recently charged with this task. The set of interviews administered to the proxy, or to the participant with help from the proxy, is shown in Section 16, Table 4 (Revised August 12, 2015).

### Defining the Need for Consent by Proxy

A **proxy** is a person authorized to act on behalf of an adult not capable of giving consent. Although some variation exists by state, persons favored to serve as a proxy in order of priority are a Legally Authorized Representative, such as a Health Care Agent or Legal Guardian; a spouse; adult child; adult sibling; friend or other relative. An **alternate informant** is a person sufficiently familiar with the participant's daily activities to be able to provide information on the participant's performance. If sufficiently familiar with the participant's performance in the course of daily activities, a proxy may serve as an informant.

### Criteria for Recruiting a Proxy

Classifying decision-making capacity is challenging, and may be task-specific. Given the minimal risk associated with the HCHS/SOL Visit 2 procedures, conservative criteria are suggested as **triggers for requiring proxy consent**. These include (any of):

- Staff assessment, at the time of annual follow-up interview, the examination visit scheduling call, or at the time of in-person informed consent. Because no mental status screen will identify all cases of cognitive impairment, the need for a proxy will be informed by the judgment of the HCHS/SOL interviewers and with guidance from the study clinician (MD or RN).
- Impaired recall or some disorientation to time (a score <2 on the six-item cognitive screener, as detailed in Section 16.7.4).
- Disorientation to time (e.g., score = 0 on orientation items from six-item cognitive screener, as detailed in Section 16.7.4). A prior diagnosis of dementia (affirmative response to MHE questionnaire item on history of dementia) in an individual whom staff has determined to have potential cognitive difficulties. Note: A self-reported diagnosis of dementia/Alzheimer's Disease is not in itself a reason for requiring an alternate respondent.)

The need for a proxy may be ascertained prior to the field center examination; under these circumstances participation by proxy should be arranged in scheduling the participant's examination visit. If at the time of the annual follow-up call preceding the HCHS/SOL examination visit, or at the time of scheduling the examination visit it is determined that the participant requires proxy consent as described above, arrangements are made at that time to identify a proxy to accompany the

participant to the examination visit. Similarly, if at the time of the HCHS/SOL examination visit it is determined that the participant requires consent by proxy, arrangements are made to recruit and contact an alternate informant prior to the subsequent yearly contacts and interviews. Recruitment of the Exam Proxy

If recruitment of an exam proxy is necessary, the following script can be used: “We think that it might be helpful to have someone [come with you to the clinic/be with you while we complete your HCHS/SOL examination visit]. This person could assist you in making decisions about participation in the study. Do you agree to have someone [coming with you to the clinic/being with you during the exam]?”

If YES:

“This person should be someone who can provide consent for your participation in case you do not feel comfortable providing this consent without additional advice. Who would this person be?”

Record the name, street address, phone number and email address if available, and continue: “We ask you to tell [PROXY’S NAME] about your decision. In the next few days we will also contact [HIM/HER] to provide information about the exam.” Record the proxy’s contact information in the Contact Information Update (XXX) form. Confirm that the participant agrees to communicate with the proxy to request his/her engagement to assist the continued participation in HCHS/SOL of the study participant. The proxy is then contacted by HCHS/SOL staff a few days afterwards.

If NO:

Point out that having a trusted someone would help to make decisions about participation in the study. If the participant still does not agree, consult the supervisor or Principal Investigator.

#### **4.6 Administration of the Informed Consent by Proxy**

The HCHS/SOL informed consent by proxy (or the equivalent consentimiento por poder) are used to obtain informed consent for members of the HCHS/SOL cohort whose participation requires a proxy. It is important to identify the need for participation by proxy prior to the HCHS/SOL examination visit so that the participation of the proxy can be scheduled and the appropriate informed consent form be administered. If the need for a proxy becomes apparent only at the time of the HCHS/SOL examination the visit must be discontinued until an informed consent by proxy has been obtained. The disposition of data collected during the exam visit on a participant subsequently deemed to require a proxy/informed consent by proxy should be guided by consultation with the local IRB, and the HCHS/SOL coordinating center informed accordingly.5.6

##### **Informed Consent Tracking Form**

The Informed Consent Tracking form is an internal administrative form to monitor the level of consent given by study participants to participate in the HCHS/SOL and records all restrictions specified by the participant (see ICT, Appendix). This form is completed by study personnel, and not administered to participants.

The consent form administered prior to the second exam and signed by the participant during the visit is used to complete the informed consent tracking form (ICT). The ICT is NOT administered to participants and does not substitute for the official informed consent document that has been reviewed and dated by the field center IRBs. The purpose of the tracking form is to document electronically the level of consent at the second examination and will be the basis for tracking any changes (revisions) following the clinic visit to a participant’s original consent on (a) access to medical records, (b) the use

of genetic material for research, its long-term storage and opportunities for data sharing, (c) the use of other study data, (d) reporting the results to participant and/or to others designated for that purpose. At Visit 2 the continued participation in the study and the collection of additional data as described in the protocol and this manual is affirmed by the participant. The study is also granted continuing permission to obtain access to medical records for adjudication of events at follow up.

Any subsequent change in consent status is welcome during the post-visit period and is documented as soon as a participant requests that a change be made to his or her consent status. The change is recorded in the data management system (CDART) as a next occurrence of the ICT form. To do this, a next occurrence of the form is opened and only the item(s) being updated is/are changed; the other items are left blank.

At the discretion of each field center, as part of the informed consent process or following its completion, a schedule for reporting the participant's study results is reviewed with the participant. The participant is shown the summary of results that will be reviewed at the conclusion of the examination visit with the HCHS/SOL clinical staff, and told that a written summary report, including additional tests, will be mailed to the participant and his/her physician (or alternate) six to eight weeks after the field center exam. Participants are encouraged not to ask the staff for the results of their exams at individual stations to avoid distracting the technicians. The reporting of results is described in detail in Section 20 of this manual.

## **5. TRACKING AND FOLLOW-UP INFORMATION**

It is a goal of the HCHS/SOL to conduct annual interviews consisting of a brief questionnaire of all persons who participated in the baseline examination. Annual contacts are conducted by telephone or in person, and interview items include questions on health during the interim, visits to a provider of medical care, emergency room and hospital visits. The annual contact and data collection procedures are described in Manual 3 (Retention and Follow-up). To establish the ability for HCHS/SOL to maintain contact with its participants, during the examination visit study participants are asked to update and confirm their current address, phone number and email as well as those for individuals who can serve as contacts and their respective addresses, phone numbers and email.

Contact information is routinely updated annually, as required during the annual follow up interviews that occur both before and after visit 2. Field centers may reimburse study participants for costs incurred by the AFU interview phone call at a rate that is consistent with research practices and as approved by their local IRB.

The participant's address is a confidential data item recorded on the Personal Identifiers Form (IDE). Special confidentiality provisions apply to this form to ensure its protection as described in the Manual 13, Data Management. An additional use of the participant's address is its conversion to a code defined by longitude and latitude that will then be used for statistical analyses under procedures that safeguard the confidentiality of this information, for two primary purposes.

Field Center staff is trained in procedures for insuring confidentiality of participant information. Paper records are kept in secure storage and discarded when no longer needed using each institution's security protocol. The data entry and management system provides a high level of confidentiality for the machine readable information, since access to the system requires a password and all files are encrypted to prevent access to the data using other software. The Principal Investigators maintain data security and confidentiality in accordance with guidelines of the NIH and all investigators maintain data security and confidentiality in accordance with their Institutional Review Board agreement.

### **5.1 Procedures to Remove a Participant from the Study**

It is possible to remove a consented study participant for administrative reasons if the field center lead investigator notifies the coordinating center that one or more of the following conditions are true:

- (1) The participant's informed consent was invalid due to cognitive impairment, substance abuse, or equivalent
- (2) The informed consent was revoked by the participant, wishing a full withdrawal from the study and no further contact
- (3) Threatening or antisocial behavior by the participant towards the staff or other study participants

Administrative exclusion of an eligible participant recruited and/or examined by HCHS/SOL must be initiated or approved by the field center PI, and communicated to the coordinating center for adjustments to the field center's list of eligible enrollees, purging of the biospecimen repositories, adjustments to the collaborative database and analysis files, and to enable recognition of the former study participant by various study management tools.



## **5.2 Procedures to Document Changes to Participant's Informed Consent**

Consent to participate in a long term follow-up cohort study is a dynamic process. In the event that a study participant chooses to modify the scope of their consent to participate in the different elements, proper documentation of that change is required. To administratively capture those changes in the study database a new occurrence of the ICT needs to be entered in CDART. This new occurrence has blanks for all the elements. The field center staff making the change has to enter the date this change becomes effective in the form date and tab (jump) to the consent element(s) being changed from “yes” (allow) to “no” (dis-allow). Elements that have not changed will stay blank in the new occurrence of the ICT. After modifying the responses as needed the record is saved. If any aspect of consent is modified again by the participant at a later date, such as adding or removing a restriction, a new occurrence of the ICT should be completed in CDART following the procedure described above. Every time a change is made to the original scope of informed consent, field center staff must document the change by printing the corresponding ICT occurrence form and saving it in the participant file. (Refer to ICT QxQ for detail information on data entry).

## **6. PARTICIPANT FLOW AND ITINERARY**

The sequence of examination procedures (participant flow) includes fixed and flexible components which are organized to accommodate the collection of informed consent prior to any data collection, followed by the collection of a group measurements that must be obtained in the fasting state, followed by a glucose level screening test to determine whether the participant is eligible for a glucose load. If a glucose load is not administered, the fast is broken by a snack that corresponds to dietary preferences/needs identified during examination visit scheduling process. Alternatively, the time of administration of the glucose load is recorded on the itinerary /Clinic Exam Checklist Form as well as the clock time corresponding to the 2-hour target for the second blood draw. These times are recorded on the hard copy of the itinerary, and also into the study data management system (Clinic Exam Checklist, CHK) at the staff person's earliest convenience so that the information can be made available to the lab technician completing the Biospecimen Collection form (BIO).

Following this point, each participant's itinerary is structured exchanging procedures and sets of interviews to optimize participant and staff time. A verification of the completeness of data collection during the examination, of results that require review or notification as alert values, and the exit interview constitute the fixed set of steps that close out the examination visit at the field center. A CDART-based data inventory is run to prevent inadvertent omissions in data collection and that the clinically relevant study results available at this point are available for review with the participant. Modification of a fixed sequence is a matter of study protocol and requires Steering Committee approval.

At the field center's discretion, participant itineraries are prepared one day in advance according to the number of study participants scheduled and the available personnel. Such schedules are printed or displayed on a board for convenient consultation by staff during the examination, also at the discretion of the field center. Flexibility in restructuring such participant flow itineraries is desirable to accommodate last minute cancellations or delays that occur during the participant's progression through the sequence of examinations and interviews.

The sequence and timing of data acquisition documented on the Participant Itinerary Form serves several purposes: it reminds study personnel of a participant's special needs or medical conditions; it serves to monitor the amount of time it takes to complete each component of the examination; it provides staff with information about where the participant is in the process; it can be used to indicate the participant's pre-established sequence of procedures and interviews, and it serves to record unforeseen events. At some HCHS/SOL centers the start and end time of individual procedures and of blocks of interviews may be recorded by staff on the Participant Itinerary Form, as well as the completion of status of individual tasks, for purposes of QC and to monitor participant burden.

Participant comfort and safety are of a priority for the HCHS/SOL. Interviewers and technicians are attentive to signs of fatigue or physical and/or emotional discomfort. When any one of these conditions is observed, participants are offered the opportunity to rest. The termination of any interview or procedure is documented on the participant Itinerary Form.

## **7. RECORDING MEDICATIONS**

During Visit 2 the HCHS/SOL records medication usage in the four weeks preceding the examination date. Information on both prescription and over-the-counter medications is ascertained. To obtain this information, the participant is asked prior to the clinic visit to bring to the field center all prescription medications and over-the-counter preparations taken in the four-week period preceding the visit, or their containers. This request is mailed to the participant with the written instructions for the exam visit, and is re-stated during the appointment reminder call. At the time of the exam the cohort participants also are asked to report whether they take medications for specific conditions.

## **8. INITIAL BIOSPECIMEN COLLECTION – URINE**

A urine sample is collected from each participant (preferably) at the beginning of the clinical exam. After participants complete the Reception work station activities and are taken to change clothes, they are informed about the urine collection. The urine specimen is collected whenever the participant needs to void. If the participant has not voided by the time of the exit interview, the participant is asked to void at that time.

A specimen cup (labeled with the participant's ID), cup lid, and a Time Voided label are provided by the staff member working with the participant at that time. The participant is instructed to:

1. Void in the cup, filling it if possible, and place the lid securely on top of the container,
2. The participant or the HCHS/SOL staff record the time of voiding on the label, and
3. The specimen cup is returned to the staff member, OR
4. The sample container is placed in a refrigerator designated for urine samples. Scripted instructions (in English and Spanish) are provided in Appendix 5.

At the discretion of the HCHS/SOL field centers, bathrooms may be equipped with a wall clock and pencils for participants to use in recording the time of voiding on the label. The staff member verifies the participant has written the "time voided" on the label, and assesses the adequacy of the sample for processing. At least 6 mL of urine is required for processing. If insufficient, the participant is requested to void again in a clean container prior to leaving the field center. A note is made on the participant's Itinerary Sheet that a second sample is needed by the staff person who observes the placement of the participant's urine specimen in the refrigerator. The instructions for providing the urine sample are repeated to the participant at that time.

Labeled urine samples should be placed in the designated specimen refrigerator for storage prior to processing and as soon as possible after the specimen has been voided. This can be done either by the participant or a staff member, as determined by local option. Procedures are set up at each field center to verify that urine samples are not inadvertently left out at room temperature since urine may be left at room temperature more than 4 hours.

## **9. ANTHROPOMETRY**

Anthropometric measures include height, weight, waist and hip circumference and body fat. These measures are used to assess the relationship between overweight and risk of disease.

### **9.1 Equipment and Supplies**

The equipment and supplies necessary for body measurements are as follows:

- Tanita Body Composition Analyzer, TBF-300A
- Wall mounted stadiometer
- Measurement box for sitting height (one-meter box with a step)
- Gulick II 150 and 250 cm anthropometric tape
- Full length mirror
- Balance weight scale (available at all times as back up)
- Calibration weights (10 kg)

### **9.2 Staff**

It is preferable to have an examiner and recorder for each procedure. Technicians are trained to perform both roles. If necessary, a technician may perform the measurements and enter the data into the ANTA record in the data management system (DMS).

The examiner is responsible for positioning the participant, taking each measurement, and stating the measurement aloud to the recorder. The recorder keys the information into the data entry system and asks the examiner to confirm or re-measure any out-of-range messages identified by the data entry system. Otherwise, the examiner proceeds to the next measurement in the sequence established by the protocol. The participant remains on the instrument / the measuring device remains on the participant, until the recorder enters the measurement on the data entry screen.

#### **Anthropometry Form (ANTA)**

The ANT form records anthropometry measurements in three sections: ability to stand (A), height, weight, bio-impedance output values from the Tanita scale (B) , and waist circumference (C). As the technician progress through the examination procedures, they will record (or directly enter) results into the ANT form.

### **9.3 Examination Procedures**

For all measurements, participants should wear scrub suits or light, non-constricting clothing and slippers or socks, but participants must be barefoot when measuring weight and body composition with the Tanita scale.

#### **Standing Height**

Standing height is an assessment of maximum vertical size. Standing height is measured with a fixed (wall mounted) stadiometer with a vertical backboard and a moveable headboard. Have the participant move or remove hair ornaments, jewelry, buns, braids, and corn rolls from the top of the head in order to measure stature properly.

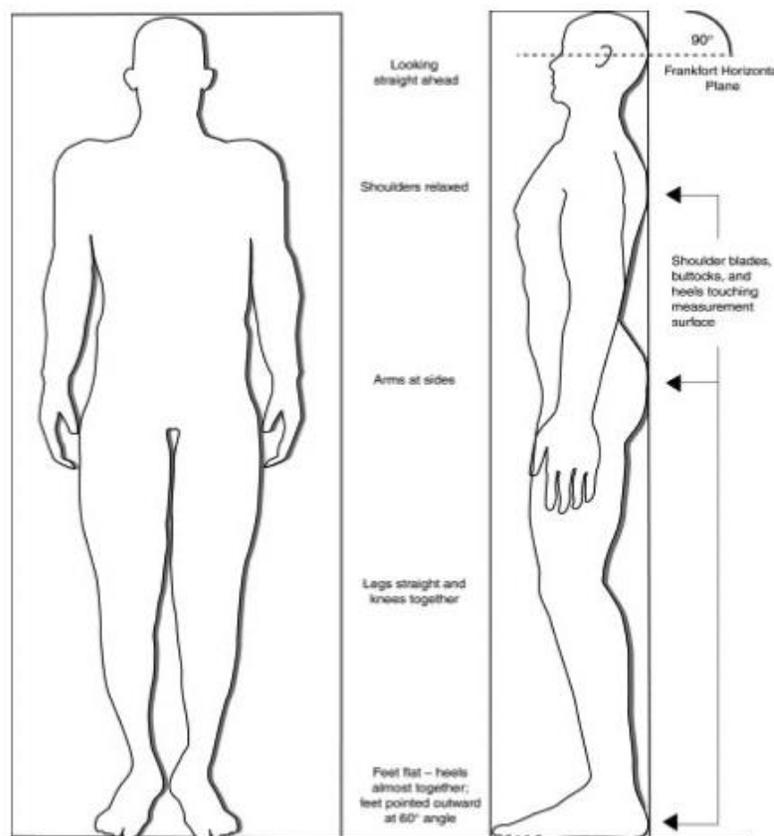
Have the participant stand on the floor (see Figure 1) with the heels of both feet together and the toes pointed slightly outward at approximately a 60° angle. Make sure the body weight is evenly distributed and both feet are flat on the floor. Check the position of the heels, the buttocks, shoulder

blades, and the back of the head for contact with the vertical backboard. Depending on the overall body conformation of the individual, all points may not touch. In such case, make sure the participant's trunk is vertical above the waist, and the arms and shoulders are relaxed.

Align the head in the Frankfort horizontal plane. The head is in the Frankfort plane when the horizontal line from the ear canal to the lower border of the orbit of the eye is parallel to the floor and perpendicular to the vertical backboard. Many people assume this position naturally, but for some it may be necessary to make a minor adjustment. If required, gently tilt the head up or down until proper alignment is achieved with eyes looking straight ahead. Once correctly positioned, lower the headboard and instruct the participant to take a deep breath and stand as tall as possible. A deep breath allows the spine to straighten, yielding a more consistent and reproducible stature measurement. Position the headboard firmly on top of the head with sufficient pressure to compress the hair. Then have the participant relax and step away from the stadiometer and record the participant's height on the computer system. The examiner should read the height at eye level to avoid parallax; a small stool may be required.

Some participants may have conditions that interfere with the specific procedure for measuring stature. One of the more common conditions is kyphosis. Kyphosis is a forward curvature of the spine that appears as a hump or crooked back condition. In these cases it is important to get the best measure possible according to the protocol. If a participant cannot stand erect or cannot stand on both feet, choose the appropriate code on the first section of the form (Section A. Q1 Determination of ability to stand).

Figure 1.  
Position for Standing Height

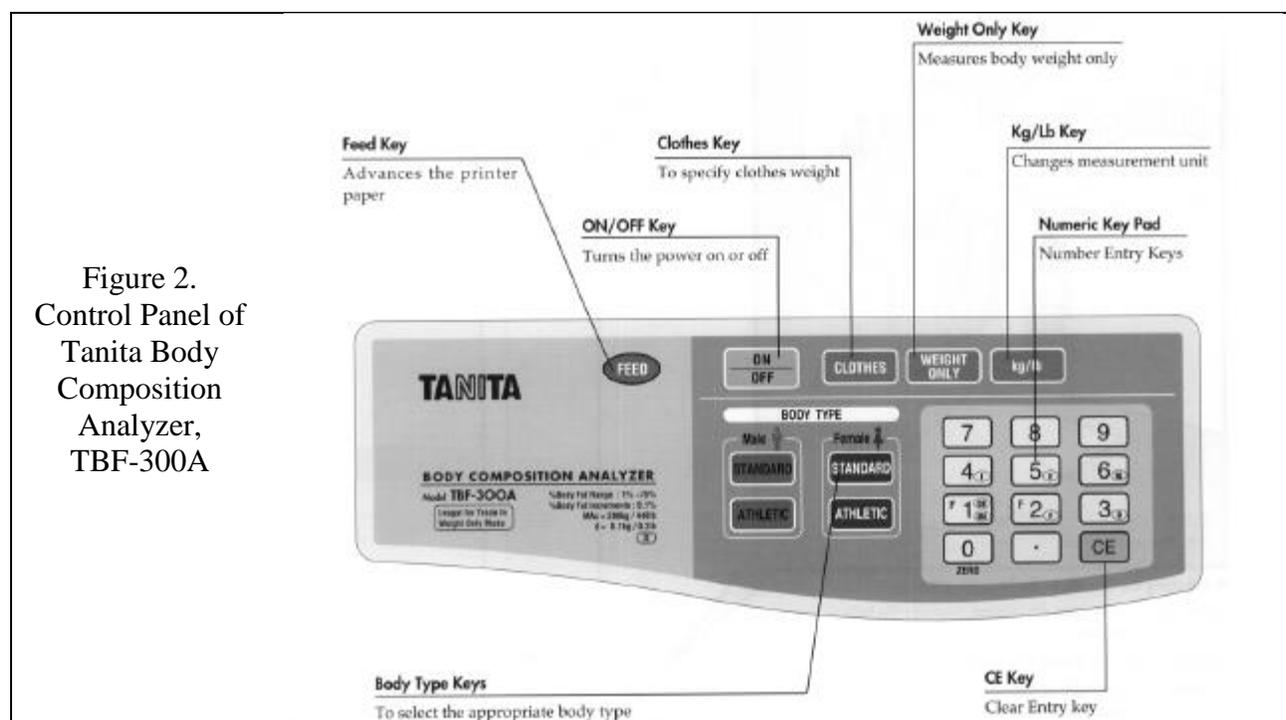


## Weight and Body Composition

Before taking any measurement on the digital scale, ask participants their weight and record it on the self-reported weight section of the form, rounding up to the nearest lb or kg. Participants may choose to report their weight in pounds (lb) or kilograms (kg) and the technician records the information on the form in the units provided by the respondent (section B, Q3a, 3b). Also ask the participant whether s/he has a pacemaker, a defibrillator or other internal electronic device. As an important safety precaution, if the answer is yes set the Tanita to the 'Weight Only' mode before a participant steps on the scale, or measure their weight on the balance scale. Also ask study participants whether they have an artificial joint, a metal plate, rod or other metal in the body. If that is the case, measure the weight in the "Weight Only" mode and record 99.9 for items 5 – 9 on the ANT form.

The participant's weight and body composition analysis are measured using the Tanita scale. This scale calculates the weight of the participant and using a bioelectrical impedance method provides percentage body fat, fat mass, lean body mass and total body water. All these measures are recorded on the HCHS/SOL Anthropometry Form in section B Q4 through Q9.

The control panel of the Tanita scale is depicted in Figure 2. A number of settings must be specified before using the scale for the first time. Once the settings are selected, these are recorded automatically and there is no need to make changes. Just press ON/OFF key to start.



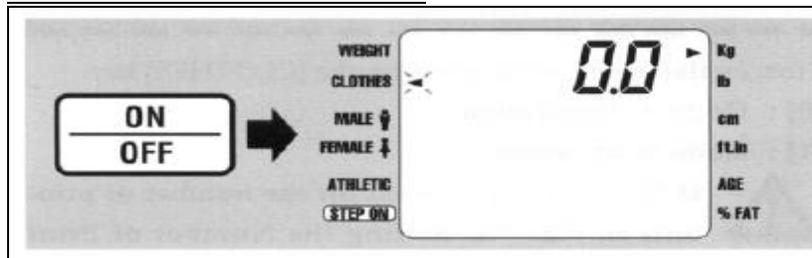
### a. Initial set up

1. Place the scale platform on a flat and level surface as possible, preferably not on carpet. Don't worry if balance bubble indicates it is not exactly level.
2. Connect the keyboard to the scale with the gray cord attached to the scale and plug it into the back of the keyboard in the socket marked "input."
3. Connect the keyboard to an electrical outlet using the black power cord and AC adapter. Plug the black cord into the socket on the back of the keyboard marked "DC5V."

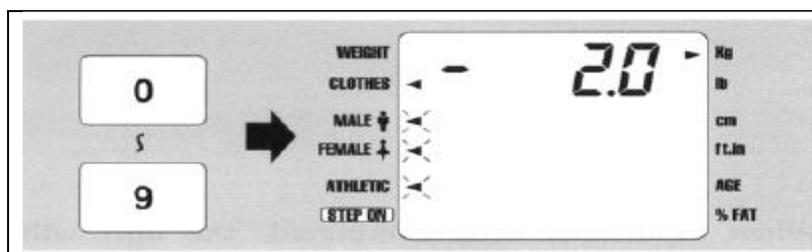
### b. Setting the number of print outs and printing language

Press and hold the 0 key, and press the ON/OFF key once. Release the 0 key after “Prt-1” is displayed on the screen. Select 0 (no print out). When no print out is selected there is no need to select the printing language. The panel will switch to the measurement screen.

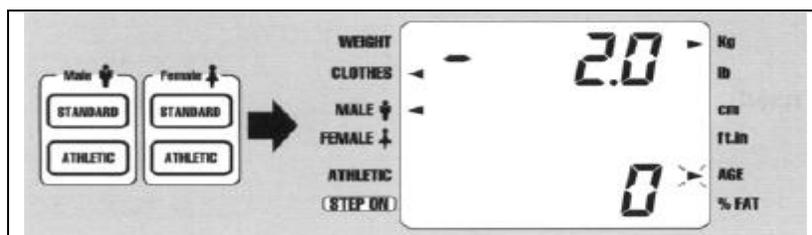
#### OPERATING INSTRUCTIONS



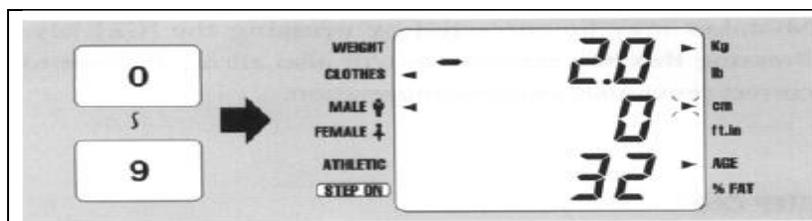
Press ON/OFF key to turn the machine on. Wait until 0.0 and an arrow appear on the screen. Check that the arrow points to “Kg”. If arrow point to “lb”, press the Kg/Lb key on the control panel and the arrow will shift to “Kg”



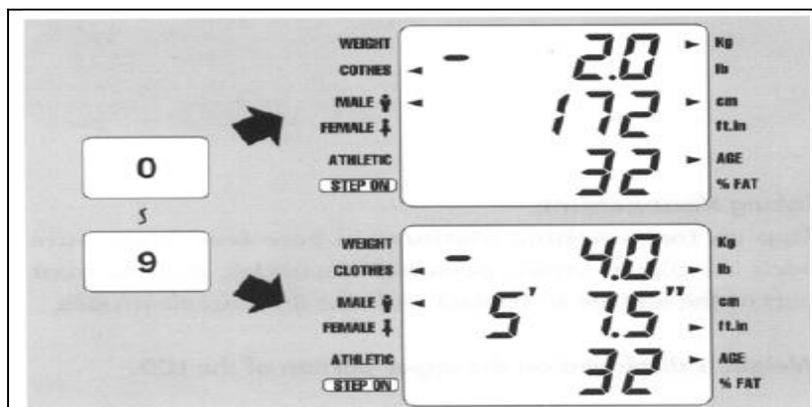
Enter Clothes weight: 1.0 kg using the numeric pad on the control panel



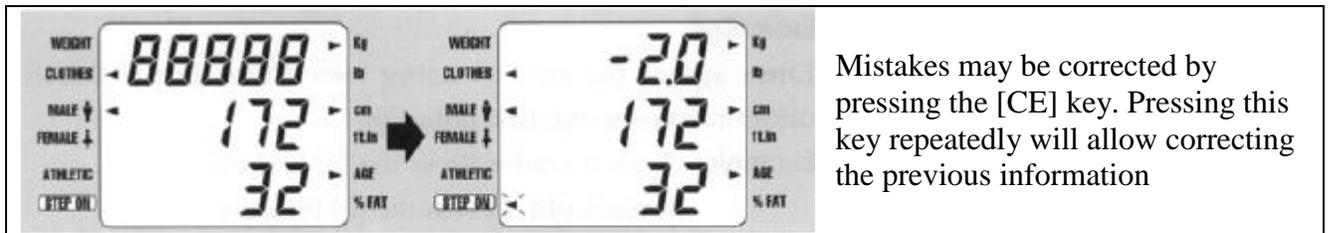
Select Gender and Body type: Standard Female or Standard Male



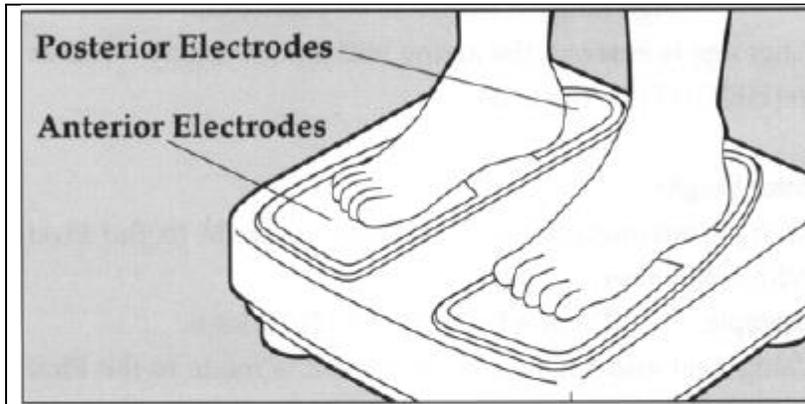
Enter age of participant using the numeric pad of the control panel. After age is entered, the arrow will direct you automatically to enter the height.



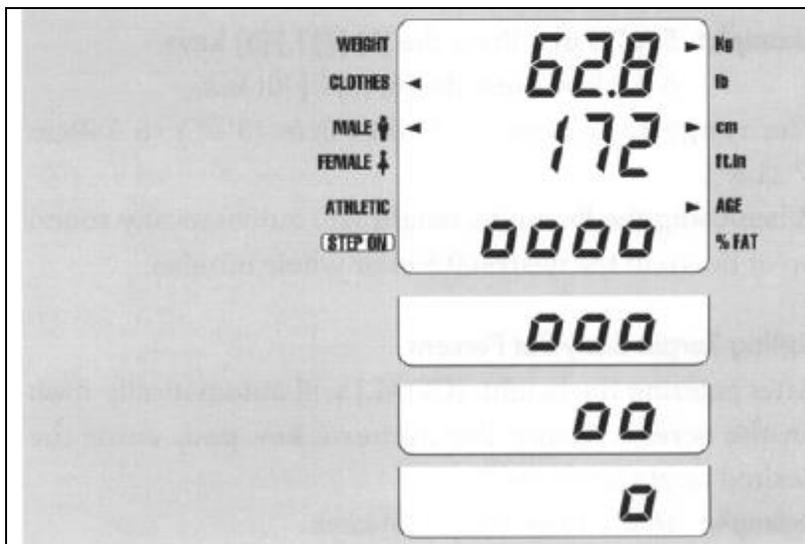
Enter height in cm. For example, for 172 cm, press the [1] [7] [2] keys.



Mistakes may be corrected by pressing the [CE] key. Pressing this key repeatedly will allow correcting the previous information



Wait until the screen displays “88888” and then ask the participant to step on the scale. Participants should be bare-foot. Each foot should be touching both the heel and toe plates, with weight evenly distributed on both feet.



Weight will be displayed on the upper section of the screen. After weight stabilizes, impedance measurement is taken. Bubbles “oooo” will appear on the bottom half of the screen as these measurements are being analyzed. Once body composition measurements are ready, the bubbles will disappear one by one. Record weight and each body composition measurement including impedance on the Anthropometry form. Ask the participant to step off the scale.

If the screen returns to ---- for weight, the participant weighs more than 440 lb. Record 999.9 for weight and 99.9 for % body fat on the data form.

If screen returns error messages **E-01** or **E-16** it means that the unit could not get a good reading, either because: 1) the participant stepped off the scales before the beep; or 2) the participant was wearing socks or has thick calluses on his/her feet. If the problem appears to be #1, just repeat the measurement procedure.

If the problem appears to be #2, place a drop or two of saline on each scale plate to help signal conduction. If the error messages appear again after adding saline, turn the unit off, turn the unit on, press **WEIGHT ONLY**, and only record a weight on the data form. Record **99.9** for % body fat on the data form.

Once measurements are completed, the machine will automatically return to the Gender and Body Type screen in about 10 seconds. Leave keyboard on. Wipe off plates on scale with antiseptic wipes. You can then measure the next participant.



**IMPORTANT SAFETY ALERT: PARTICIPANTS WITH A PACEMAKER, DEFIBRILLATOR OR OTHER INTERNAL ELECTRONIC DEVICE SHOULD BE MEASURED IN ‘WEIGHT ONLY’ MODE.**

If the participant is unsure about having an implanted electronic device, the scale should be placed in “Weight Only” mode (or the participant’s weight should be measured on the calibrated balance scale).

Do not weigh participants who have a cast that cannot easily be removed, or that the participant is uncomfortable removing, if larger than a finger splint. If a participant has a prosthetic limb, measure weight with limb in the “Weight Only” mode, make a note in the comment section of the form. If the study participant has an artificial joint, a metal plate, rod or other metal in the body, measure the weight in the “Weight Only” mode and record 99.9 for items 5 – 9 on the ANT form.

In the event of a power outage or if the scale is not functioning properly, use the balance scale as back-up and notify the project coordinator.

### **Waist Circumference**

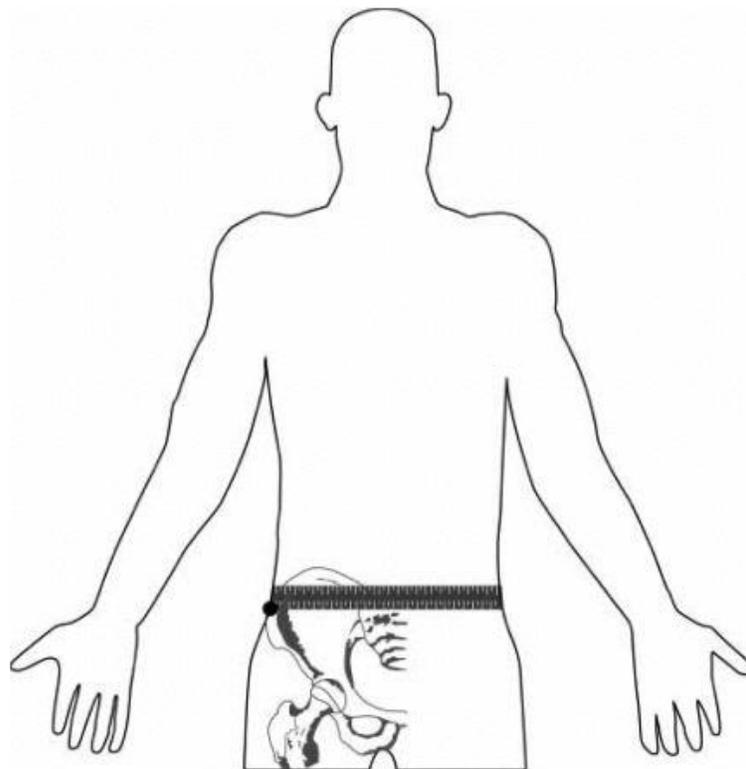
To define the level at which the waist or abdominal circumference is measured, you must first locate and mark a bony landmark, the lateral border of the ilium. Have the participant stand and hold their t-shirt above the waist. Lower the pants and underclothing of the participant slightly, and standing behind and to the right of the participant, palpate the hip area to locate the right ilium (see Figure 3). Draw a horizontal line just above the uppermost lateral border of the right ilium and then cross the line to indicate the mid-axillary line of the body. Standing on the participant’s right side, place the measuring tape around the trunk in a horizontal plane at the level marked on the right side of the trunk. Hold the zero end below the measurement value. Use the mirror on the wall to ensure correct horizontal alignment of the measuring tape. This is especially useful when measuring overweight participants or women with hourglass-shaped torsos. The recorder (if available) makes sure that the tape is parallel to the floor and that the tape is snug, without compressing the skin. Measurements are made at the end of a normal expiration and reported to the recorder to the nearest centimeter and entered in section C, Q10 of the ANT.

### **Hip Circumference**

Instruct the participant to stand erect but relaxed, with weight distributed equally over both feet. The hip girth is measured at the level of maximal protrusion of the gluteal muscles (hips). Verify this position by passing the tape above and below the observed maximum. Keep the anthropometric tape horizontal at this level and record the measurement to the nearest centimeter. The tape should be snug, but not tight enough to compress tissue. The measurement should be made from the participant’s right side. Only one measurement is made.

The greatest source of error for this measurement is due to not having the tape horizontal. Before making the measurement the observer verifies the position of the tape from both the front and back to assure its correct position and that the tape is horizontal. In the absence of a recorder the technician uses the wall mirror to confirm that the tape is horizontal.

Figure 3. Measuring Tape Position for Waist Circumference



#### 9.4 Quality Assurance/Quality Control

##### Calibration Procedures and Equipment Check

The Tanita scale is calibrated weekly or when moved. Calibrate the scale by pressing **WEIGHT ONLY** key. Make sure the arrow pointing to weight is in Kg units.

Place the calibration weight (10 Kg) in the middle of the scale, and record the weight indicated on the LED in the daily log. If the calibration weight is less than 8.5 kg or more than 11.5 kg, use the back-up scale, and notify the clinic coordinator to have the scale recalibrated by the manufacturer or by the appropriate institution personnel.

Wipe off plates on scale with antiseptic wipes.

Turn off scale by pressing the ON/OFF key. **The unit needs to be turned off after running in the “WEIGHT ONLY” mode before it can be used for body composition determinations.**

Examine anthropometry tapes on a weekly basis for sign of wear.

Each day check that headboard of the stadiometer moves up and down the track smoothly.

## **Training, Certification and Quality Control**

Field technicians or examiners are centrally trained in all anthropometric measures. Technicians who cannot attend the central training can be trained and certified locally by the clinic coordinator. Each technician performs a minimum of 5 observed procedures to receive certification, with a level of agreement of measurements relative to the supervisor as specified in the QA/QC manual.

Technicians are observed by the clinic coordinator twice monthly for the first month and then quarterly, to ensure standardization. The Supervisor Checklist is used to document these observations and deviations from the protocol are reviewed with the technicians. A minimum of 6 procedures every month is required in order to maintain certification.

Following a schedule set by the Quality Control Committee a sample of participants is automatically selected by the data management system software during data entry (see DMS users guide for a description) for repeat measurements by a different technician during the examination visit and recorded on the Anthropometry Quality Control form (AQCA). Inter-technician agreement is analyzed by the Quality Control Committee using the data entered into the AQCA and serves as a criterion for recertification. Retraining sessions are scheduled at the request of the Quality Control Committee when a lack of standardization is observed among the technicians.

## 10. SITTING BLOOD PRESSURE

### 10.1 Introduction, Equipment and Supplies

Because accurate blood pressure measurements are critical for the estimation of the national prevalence of high blood pressure for different age, ethnic and sex groups, it is important to use state-of-the-art measurement techniques that are comparable to other national datasets. For many years the “gold standard” blood pressure measuring device has been the mercury sphygmomanometer. However, because of the recent increase in awareness of the serious adverse health effects of mercury contamination in the environment, many institutions, including the National Institutes of Health, have banned or discouraged the continued use of mercury sphygmomanometers and thermometers. Further, the Environmental Protection Agency (EPA) and the American Hospital Association (AHA) have taken steps to eliminate mercury-containing waste by 2005. For these reasons, many institutions and clinics have switched to alternate sphygmomanometers such as aneroid or automated devices that do not contain mercury. In line with these developments and for the best repeatability of measurements, a tested, automatic sphygmomanometer (the OMRON HEM-907 XL) is used in HCHS/SOL. This model has been validated in 3 other studies, including CARDIA and NHANES. Field center technicians are responsible for verifying that all equipment and supplies are in the examination room.

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<u>Equipment</u>	<u>Supplies</u>
OMRON HEM -907XL	Wipes
sphygmomanometer	Alcohol
4 cuffs	Tissues
Gulick II tape measure	Water soluble ink pens
Foot stool	Gauze (4 x 4)
Room Thermometer	

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Figure 4 OMRON sphygmomanometer and 4 cuffs



OMRON HEM907XL – with four cuffs

## **The Sitting Blood Pressure (SBP) form**

The SBP form records arm measurements used to guide blood pressure cuff size selection and serial measurements of both blood pressure and pulse rate. The form is divided into five corresponding sections: (A) Arm Measurements and (B-E) the Average and First-Third Blood Pressure / Pulse Rate.

### **10.2 Blood Pressure Measurement Procedures**

The technician greets the participant and explains that his/her blood pressure will be measured next. To choose the appropriate cuff size the participant's arm will be measured first, followed by a period of quiet rest and three blood pressure measurements taken by a machine. The technician asks if the participant has questions, following which the participant is reminded that the results of the measurements will be provided at the end of the visit with a printed report.

#### **Selection of the Arm**

For the purpose of standardization, both pulse and blood pressure are measured in the right arm unless specific participant conditions prohibit the use of the right arm, or, if participants self-report any reason that the blood pressure procedure should not use the right arm. If the measurements cannot be taken in the right arm, they are taken in the left arm. Use of the right or left arm must be recorded on the SBP form in Item A.1. Measurements are not done on any arm that has rashes, small gauze/adhesive dressings, casts, are withered, puffy, have tubes, open sores, hematomas, wounds, arteriovenous (AV) shunt, or any other intravenous access device. Also, women who have had a unilateral radical mastectomy do not have their blood pressure measured in the arm on the same side as the mastectomy was performed. In all cases, if there is a problem with both arms, the blood pressure is not measured.

#### **Cuff Size Selection and Application**

It is important to select the appropriate size cuff that properly fits the participant's arm. The length and width of the bladder inside the cuff should encircle at least 80 percent and 40 percent of an arm respectively. The index lines on the cuff are not used in this study. Using a centimeter tape, determine the midpoint of the upper arm by measuring the length of the arm between the acromion and olecranon process (between the shoulder and elbow).

#### **Measurement of Arm Circumference**

Have the participant remove his/her upper garment or clear the upper arm area so that an unencumbered measurement may be made.

- i. Have the participant stand, with the right arm hanging and bending the elbow so that the forearm is horizontal (parallel) to the floor.
- ii. Measure arm length from the acromion (bony protuberance at the shoulder) to the olecranon (tip of the elbow), using the Gulick II anthropometric tape.
- iii. Mark the midpoint on the dorsal surface of the arm.
- iv. Have the participant relax arm alongside of the body.
- v. Draw the tape snugly around the arm at the midpoint mark. NOTE: Keep the tape horizontal. Tape should not indent the skin.
- vi. Measure and record the arm circumference on the SBP form in Item A.2.

Arm circumference measurements are recorded on the SBP form in centimeter increments (integers). Fractions of a centimeter of 0.5 cm or less are rounded down while fractions of a centimeter of 0.6 cm or greater are rounded up to the next integer value.

## Choosing the Correct Cuff Size

Table 2 (below) relates the measured arm circumference (first column) to the corresponding OMRON cuff size. Identify the measured arm circumference under column 1 to select the cuff size from column 2 associated with the arm circumference in column 1. (Example: If the arm circumference at midpoint is 36 cm, use the large adult cuff marked CL19.) The arm circumference is recorded on the SBP form in integers. To distinguish between the OMRON cuff sizes, the following arm circumference values are rounded down: 21.1 – 21.5 cm, 31.1-31.5 cm, and 41.1-41.5 cm. Arm circumference values of 21.6 – 21.9 cm, 31.6 - 31.9 cm, and 41.6-41.9 cm are rounded up. Record the cuff size on the SBP form in Item A.3.

Table 2.

<u>Arm Circumference (cm)</u>	<u>OMRON CUFF SIZE</u>
17.0 to 21.5	index 17- 22cm (CS19)
22.0 to 31.5	index 22-32cm (CR19)
32.0 to 41.5	index 32-42cm (CL19)
42.0 to 50.0+	index 42-50cm (CX19)

### Special Situations / Obese Study Participants.

The length and width of the cuff's bladder should encircle at least 80 percent of the length of the upper arm, and 40 percent of the width of the arm. If the upper arm is relatively short with a large circumference (>50 cm) it may be difficult to fit even a thigh cuff in a way that meets protocol. In this case an appropriately sized cuff is wrapped around the participant's forearm, supported at heart level. The cuff size should be selected according to the forearm diameter, measured at the (approximate) midpoint of the forearm's length. Note: when taking the blood pressure on the forearm reverse the cuff, so that the marker referring to the brachial artery is at the elbow.

**Record the use of the R/L forearm in item 1 of the SBP form (Other) and add a note log to this effect.**

Blood pressures measured on the forearm tend to overestimate the systolic and diastolic pressures, but they provide a good estimate of the systolic blood pressure in circumstances when a cuff is too small for an obese arm, which can lead to misclassification of an individual as hypertensive.

### Positioning the HCHS/SOL Participant and Placing the Cuff

Ask the participant to sit and rest quietly in the chair after adjusting it, if necessary, to allow participant's feet to rest flat on the floor when legs are in the uncrossed position. The technician then explains the next steps using the following script: "Before taking your first blood pressure reading, there will be a 5 minutes waiting period. When I inflate the cuff, it may feel tight and you will feel some pressure on your upper arm. While we are measuring your blood pressure, we ask you not to talk and I will not talk either because talking and moving changes your blood pressure. Do you have any questions?"

The right arm and back should be supported and the legs should be uncrossed with both feet flat on the floor. The right arm should be bared and unrestricted by clothing with the palm of the hand turned upward and the elbow slightly flexed.

The arm should be positioned so that the midpoint of the upper arm is at the level of the heart. The location of the heart is taken as the junction of the fourth intercostal space and the lower left sternal border. Small or short participants may have to raise their body to the correct position by changing the chair position up or down. If necessary, especially with short participants, place the participant's feet on the footstool provided to stabilize their feet in a flat position. Very tall participants may need to place their arm on a book or pillow to bring their upper arm to the correct position.

## Locating the Pulse Points

Figure 5: Locating the brachial pulse



**Locate the brachial artery by palpation** and mark the skin with a small dot, using a black pen. (The brachial artery is usually found just medial and superior to the cubital fossa posterior to the biceps muscle and slightly towards the body). For brachial artery palpitation, fingertips or thumb may be used.

## Wrapping the Blood Pressure Cuff around the Arm

Position the rubber bladder with the “art” label on the bottom of the cuff, just above the pen mark over the brachial artery pulse determined earlier at least 1” above the crease of the elbow. The cuff tubing should be at the outer (lateral) edge of the arm if the cuff is placed correctly.

For short or fat conical arms, if the cuff that matches the arm circumference or is too wide to fit on the upper arm with space above the brachial artery pulse point at the cubital fossa then choose the next smaller cuff size and enter the cuff size chosen on the SBP form in Item A.3.

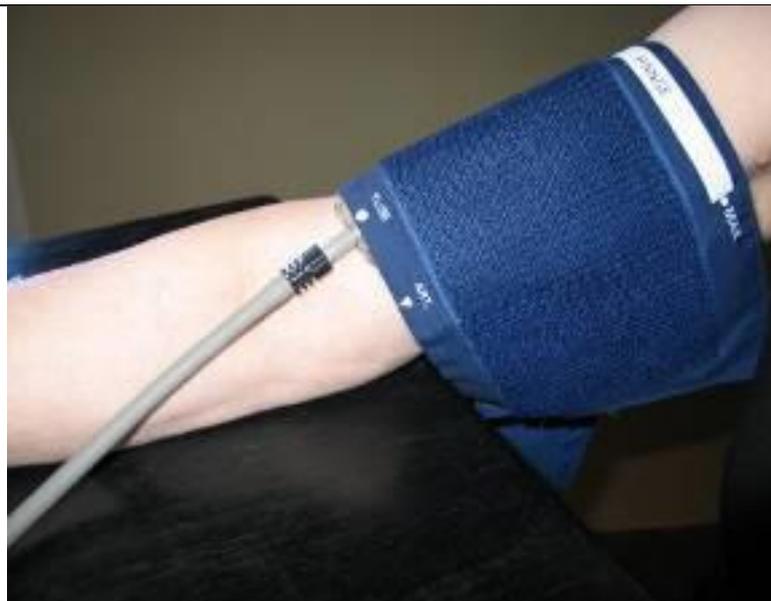


Figure 6:

Placing the cuff. Place the “art” marker on the inner part of the cuff directly over the brachial artery. The cuff should be wrapped in a circular manner. Do not wrap the cuff in any spiral direction. Check the fit of the cuff to ensure that it is secure but not tight. Figure 6 on the next page illustrates the cuff placement.

### 10.3 Procedure for the OMRON HEM-907XL

This protocol is written for use with the OMRON HEM-907XL automated blood pressure monitor. Special attention must be placed on assessment and maintenance of the instrument's accuracy as per the manual that accompanies the instrument. The design and operation of the OMRON HEM-907XL are based upon the combined principles of compression of the brachial artery under an elastic, inflatable cuff and estimation of the systolic and diastolic blood pressure levels by detection of oscillometric waves.

#### Setting up the OMRON

At a start of each session check that the monitor is attached to the AC adapter to the DC jack and plugged in (Figure 7) and AC sign (Figure 8) is visible in the lower window.

Figure 7

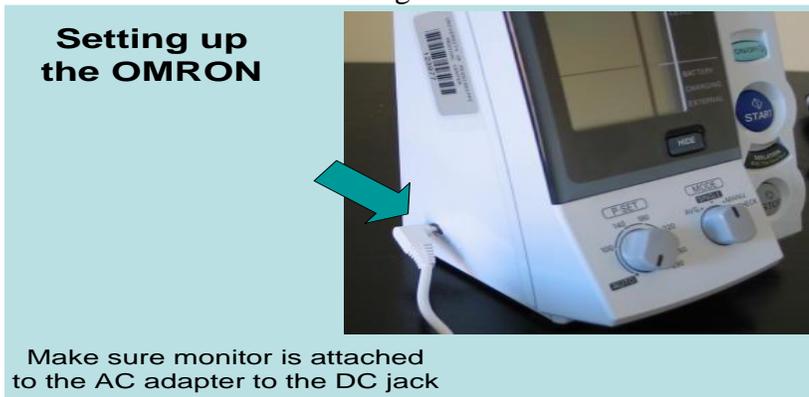


Figure 8



Figure 9



When the power is OFF, push the ON/OFF (power) button for more than three seconds while holding the START button simultaneously: F1 is displayed in the first window and three inflations (3) is displayed in the middle window (Figure 9). If needed push the DEFLATION (deflation control)/Measurement Result Display Switch Button to change the set value to 3 inflations.

Figure 10



Push the START button and F2 function is displayed in the first window and 0 waiting time is displayed in the middle window (Figure 10)

Figure 11



If needed push the DEFLATION (deflation control)/Measurement Result Display Switch Button and change the set value to 0 sec waiting time. Push the START button and F3 function is displayed in the first window and inflation interval 30 second time is displayed in the bottom window (Figure 11).

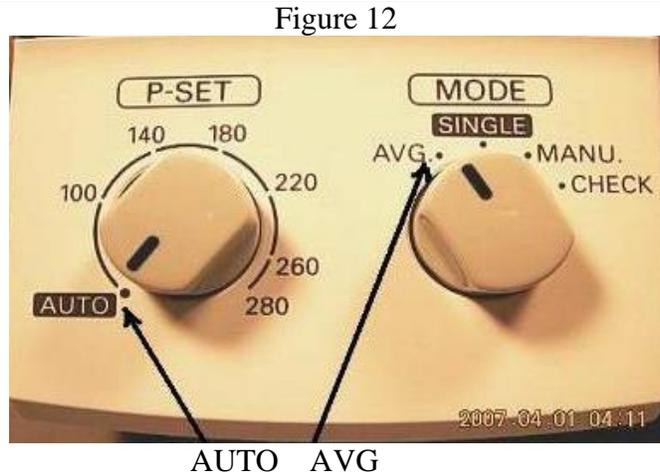
If needed push the DEFLATION (deflation control)/Measurement Result Display Switch Button and change the set value to 30 sec measurement interval.

Table 3 summarizes the needed setting for the exam

Function #	Items to set	Set value
F1	Number of inflations	3 times
F2	Waiting time to start the first inflation	0 sec
F3	Inflation interval	30 sec

## Measuring the Blood Pressure

Once these settings are validated the exam can start. Turn off the OMRON by pushing the ON/OFF button. To measure blood pressure in average mode, push the ON/OFF button to turn on the power. Set the MODE selection to AVG, set the P-SET (inflation level) knob to AUTO (Figure 12).



Next, connect the air tube to the cuff (Figure 13).



For all cuff sizes small, medium, large, and thigh connect the air tube to the main unit by attaching the air plug to the base of the air connector. Connect the cuff to the air tube attached to OMRON unit Wrap and secure the appropriate cuff to the participant's upper right arm as set out in section 12.2.7, above.

Record the time of blood pressure measurement in Item A.4, then push the START button to start the measurements. The cuff will inflate automatically and deflation will begin after the OMRON detects no oscillometric waves. The dial will show sequentially in the bottom panel of the LCD screen 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> measurements with 30 seconds between each listing (Figure 14).



After each inflation and deflation the systolic blood pressure, diastolic blood pressure and pulse rate will be displayed in the top, middle and bottom sections of the LCD screen.

After the first and second measurements are displayed there will be a preset 30 second interval before the beginning of the next measurement. During this time have the participant raise their cuffed arm above their heads as in Figure 15 below for the count of 5 and then return to the original resting position with the arm supported with the cubital fossa at heart level. Do not clench the fist. This action is to avoid venous congestion in the arm that may not have dissipated after inflation of the cuff – which in turn could increase the pressure recorded on subsequent measurements.

Figure 15



#### 10.4 Recording the OMRON Results

After all the inflations are finished, the average of the three systolic pressures, diastolic pressures and pulse rates is displayed. Record these average measures on the SBP form in Items B.5-B.7. Push the DEFLATION button to toggle to the first set of measures and record the 1<sup>st</sup> set on the SBP form in Items C.8-C.10. Repeat this process by pushing the DEFLATION button to display and record the 2<sup>nd</sup> and 3<sup>rd</sup> sets of measures on the SBP form in Items D.11-D.13 and Items E.14-E.16, respectively.

Average heart rate values that are 40 bpm or lower, or 100 bpm or greater, should be brought to the attention of the study clinician on site before participant leaves the field center. The study nurse, or the physician on call should evaluate the possible reasons for an abnormally high or low heart rate and refer the study participant for evaluation by their provider of care or to an Emergency Department, as deemed appropriate.

An average heart rate value of 40 bpm or lower, or 100 bpm or greater does not require that a seated blood pressure per HCHS/SOL protocol be repeated. A hemodynamic evaluation, including a seated blood pressure may be performed by a clinician on a participant who has a heart rate value of 40

bpm or lower, or 100 bpm or greater, but these measurements are not recorded as study data. If after evaluation by the study nurse or physician the participant is encouraged to proceed with the HCHS/SOL examination, the echocardiography sonographer should be alerted to the observed average heart rate value. If the echocardiography sonographer is the first study staff member to detect an abnormal heart rate, this should be brought to the attention of the study clinician on site, as described above.

Push the ON/OFF button. This terminates the exam and you are ready for the next participant

## **10.5 Reporting the Blood Pressure Values**

The participant's blood pressure values are not discussed at the blood pressure station nor during the measurement process. The technician will have informed the participant that the blood pressure values and other results will be printed out and discussed with the participant at the end of the visit. If pressed, the technician can add that the research protocol requires that results not be discussed during the examination. The OMRON display and the computer monitor should be turned away from the participant so that the blood pressure values being recorded are not easily visible.

The average systolic and diastolic blood values are reported to the study participant at the end of the field center examination and also as part of the consolidated report of study results that field centers send to the study participant (and his/her medical practitioner, if so instructed by the participant). In each case the average systolic and diastolic pressure values recorded on the form are retrieved by the data management system and displayed in the report, with the narrative statement that corresponds to that value and whether the participant has reported being on antihypertensive treatment. The blood pressure results are reviewed with the participant during the exit interview, at which time HCHS/SOL personnel explains the recommended follow-up for the pertinent blood pressure level according to the recommendations of the Report From the Panel Members Appointed to the Eighth Joint National Committee [JNC 8], (JAMA.2014;311(5):507-520).

As a participant safety procedure, if the average blood pressure is equal to or greater than 200 mmHg systolic or equal to or greater than 120 mmHg diastolic, the technician tells the participant that the procedure will be repeated as part of study protocol, removes the cuff and locates the brachial artery by palpation as shown in Figure 5 of this section, and repeats the blood pressure measurement steps. The resulting blood pressure values are recorded on the form and entered into the data entry system. If the average blood pressure still is equal to or greater than 200 mmHg systolic or equal to or greater than 120 mmHg diastolic, the technician closes out the data entry screen per protocol, interrupts the field center examination and notifies the supervisor of this immediate alert situation. With input from the supervisor or clinic manager, HCHS/SOL personnel then assist the participant in scheduling a visit to his/her provider of care during the same day, or arranges transportation to the nearest emergency room for a medical evaluation of the participant's blood pressure. Section 20 of this manual of operations describes the procedures used to report study results.

## **10.6 Equipment Maintenance**

Technicians maintain all blood pressure equipment used in their clinic. The following sections specifically state the steps that technicians follow to check equipment and maintain equipment used for the technician examination.

OMRON HEM-907XL: Weekly - wipe the monitor with a soft, damp cloth diluted with disinfectant alcohol, or diluted detergent. Complete cleaning by wiping the monitor with a soft, dry cloth.

Blood Pressure Cuffs: Check the inflation cuff for cleanliness, and wipe between each use with disinfectant wipes.

## 10.7 Inspection and Validation of the OMRON Sphygmomanometer

### Daily Check points

1. Check function settings on the OMRON machine (0 waiting, 3 inflations, 30 seconds interval between inflations)
2. Check Mode and P-setting on OMRON unit
3. Make sure that the AC adapter cord of the OMRON unit is securely plugged in (it has a tendency to get disconnected from the unit).
4. Check the OMRON unit AC adapter cord and tubing for cracks.
5. Clean all the equipment.

### Quarterly Validation of the OMRON Sphygmomanometer

Each OMRON unit is checked every 3 months as described in this section. The results of the calibration checks are recorded on the OMRON calibration log (together with the unit number, the date and the technician ID) and sent to the HCHS Coordinating Center for inclusion in the quality control reports. A copy of the calibration log is found in Appendix 4.

### Equipment Required for Accuracy Check

The calibration equipment is the Pressure-Vacuum Meter (Shown in Figure 16. Netech DigiMano Digital Pressure/ Vacuum Meter model 2000 for a range of 0 to 300 mmHg). The following adaptors are used and are kept at the field center: **Y tubing** – with 2 arms and an inflation bulb attached to the middle arm of the Y tubing; **Y- adapter** with appropriate male/female connectors Adaptors for tubing connection; OMRON cuff with short tubing attached. Once a year each DigiMano device is shipped to the manufacturer for calibration. Completion of this check by Netech is reported to the Quality Control Committee.

Figure 16



## Testing protocol

The following sequence of steps detail the OMRON accuracy testing protocol.

1. Inspect the OMRON sphygmomanometer for signs of damage to the case, and wall mount bracket if applicable.
2. Inspect the tubing for holes or cracks, which would allow air to leak out. Cracking is commonly found around the connection points to the sphygmomanometer, and cuff. If cracking is seen the tubing is replaced from that point by trimming the damaged area with scissors and reconnecting the tubing. In extreme cases, the entire tubing is replaced.
3. Inspect the cuff(s) for signs of wear and tear to the outer cloth casing and Velcro fabric. Also, inflate the unit (with the cuff connected to the OMRON and wrapped around a rigid cylinder and the OMRON MODE knob set on CHECK) enough to determine if the bladder within the cuff is leak- proof. If leaks or damage are noted to the cuff or bladder, it should be replaced.
4. Disconnect the cuff from the long adaptor tubing that stays connected to the OMRON sphygmomanometer.
5. Connect one upper arm of the Y adaptor to the short tubing from the cuff and attach the other upper arm to the long tubing attached to the OMRON.
6. Connect the bottom arm of the **Y adapter** to one arm of the **Y tubing**.
7. Connect other end of the **Y tubing** to the pressure-vacuum meter.
8. Turn the pressure-vacuum meter on. Use the accompanying AC adapter if necessary.
9. Following manufacturer's instructions, select "mm Hg" as the type of unit to be tested.
10. Zero the pressure-vacuum meter per manufacturer's instruction.
11. Pump up the aneroid unit to 280 mm Hg. Release the pressure slowly and observe the changing OMRON LED mm Hg for a smooth descent along the range to 20 mm Hg
12. Again, pump the aneroid unit to above 250 mm Hg (but less than 300 mmHg) using the bulb and tighten the valve as tightly as possible
13. Check to see if the aneroid unit is within  $\pm 3$  mm Hg of the readout on the pressure-vacuum meter.
14. Continue to compare the readout of the OMRON unit to the pressure-vacuum meter approximately every 20 mm Hg along the entire range – down to 30mm Hg. Variations greater than  $\pm 3$  mm Hg requires the OMRON unit be removed from service and repaired or replaced.
15. Record the results of the calibration checks on the OMRON calibration log (together with the unit number, the date and the technician ID) and send the log to the HCHS Coordinating Center. A copy of the calibration log is found in Appendix 4.

## 10.8 Glossary and References

Systolic blood pressure is defined as the highest arterial blood pressure of a cardiac cycle occurring immediately after contraction of the left ventricle of the heart.

Diastolic blood pressure the lowest arterial blood pressure of a cardiac cycle occurring during the passive rhythmical expansion or dilation of the cavities of the heart during which they fill with blood.

Auscultatory method detects sounds of pulsatile blood flow in the artery using a stethoscope held over the artery just below an inflated blood pressure cuff. As the blood pressure cuff gradually deflated, pulsatile blood flow is re-established and accompanied by sounds that can be detected by the stethoscope. The pulsatile sound corresponds to a reading of a mercury column (mercury sphygmomanometer) or a dial (aneroid) device connected to the blood pressure cuff.

Oscillometric method uses a transducer to measure the oscillations of pressure in the blood pressure cuff corresponding to the pulsatile blood flow in the artery under the cuff. The oscillometric method is used by all automated blood pressure machine.

**11. Not Used in Visit 2**

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**12. Not Used in Visit 2**

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#### 14. DURATION OF FASTING, BIOSPECIMEN COLLECTION AND PROCESSING

Blood specimen samples are collected at the HCHS/SOL visit to perform selected laboratory tests and for long term storage of biospecimen. The collection and processing of the biospecimens are performed according to a common, standardized protocol detailed in Manual 7. Centrally trained and certified HCHS/SOL personnel draw, label and processed the blood samples and process spot urine samples.

At the time of scheduling the examination visit study participant is reminded that the blood tests and other examination procedures require fasting for at least 8 hours prior to drawing blood, and that a snack is provided about two hours after the start of the field center examination. Fasting means no consumption of food or drinks (including alcohol), with the exception of water. Participants will be asked to not consume food or drinks after 10:00 p.m. prior to the clinic visit and to refrain from smoking for the same length of time, or for 8 hours prior to the scheduled time of arrival at the field center. All participants are asked whether there are medical reasons for him/her not to be fasting for this length of time and alternate arrangements are made if necessary after consultation with the a supervisor. Study participants also are asked whether they have diabetes/are being treated for diabetes in order to limit the duration of fasting if the latter is the case. To enhance their safety, HCHS/SOL participants who have diabetes are offered the early morning appointments at the time of scheduling their examination visit.

**Maximum Desirable of Fasting Time.** Both for participant safety and to protect the quality of the assays performed in the HCHS/SOL the recommended maximum length of fasting time is as follows.

- a. For **participants known to have diabetes or being treated with glucose-lowering medications**, the recommended maximum fasting time is 12 hrs. During visit scheduling it is ascertained whether a participant has diabetes or is being treated with glucose-lowering medications, and based on this information appointments are made for participants who have diabetes so that length of fasting time not exceed 12 hours on arrival at the HCHS/SOL field center. The duration of fasting also is ascertained at reception so that a venipuncture can be arranged to fall within the maximum desirable fasting time.

If a HCHS/SOL participant who has diabetes is estimated to have 12 hours of fasting time or longer on arrival at the field center, staff verifies whether the participant is comfortable and asymptomatic, and proceeds to a glucose meter determination and fasting blood draw once informed consent has been obtained. A snack is offered following the blood draw.

- b. For **participants who are not known to have diabetes/are not taking glucose-lowering medications** the maximum desirable fasting time is 16 hours, at which time the HCHS/SOL field center personnel offers the participant the option to reschedule a fasting blood draw.

The HCHS/SOL Central Laboratory performs the tests on the blood and urine and aliquots of serum, plasma, and urine prepared at the field centers are stored at the Central Laboratory. A list of the tests performed is located in Table 7 of this manual and in Appendix 1 of Manual 7. Assay results of demonstrated value for medical diagnosis or treatment are reported to the study participant, as described in Section 20 of this manual.

## 15. ORAL GLUCOSE LOAD

### 15.1 Overview

HCHS/SOL participants who are not diabetic and are otherwise eligible are invited to do a glucose tolerance test to measure how their body breaks down sugar. After the fasting blood sample is taken the participant is asked to drink a liquid containing 75 grams of glucose and another blood sample is taken two hours after the participants begins to drink the glucola solution, to determine how much of that glucose 'load' remains in circulation in the blood. The participant should neither drink nor eat following the glucose administration, until the 2-hour blood draw. At that point the participant is given a snack or light meal. The procedure, the staff training and certification, as well as the supplies used are detailed in HCHS/SOL Manual 7.

Among other eligibility criteria, an oral glucose tolerance test (OGTT) is performed only if the fasting plasma glucose (FPG) is <150 mg/dL (see section 15.2, below). Accordingly, FPG is measured with a POC glucose meter on those eligible for an oral glucose tolerance test, as specified below. For participant safety reasons, FPG is measured with the POC glucose meter on all participants who fasted at least 8 hours (whether or not they are eligible for the OGTT). If the FPG >200 mg/dL or <50 mg/dL, safety precautions are implemented without delay as described in sections 15.1 and 15.2 of this manual.

### 15.2 Eligibility and Safety Exclusions

For safety reasons, before an oral glucose load is administered certain conditions are ruled out by the laboratory technician based on answers to safety questions A3-A5 on the Biospecimen Collection form. An oral glucose is NOT administered under the following circumstances:

1. If the participant has diabetes/is being treated for diabetes, or is taking a medication used to treat diabetes.
2. If participant is on kidney dialysis.
3. If participant has had partial removal of the stomach or small intestine. Note: if the participant is uncertain about having had gastric reduction surgery (such as for weight loss), by-pass surgery, or a partial removal of the stomach or small intestine, the field center clinician should be consulted to determine whether the participant can safely ingest the glucose load.
4. If the participant has consumed food less than 8 hours prior to the time of the blood draw.
5. The participant feels nausea or has gastrointestinal discomfort

If none of the above conditions apply, the technician proceeds with the fasting blood draw and performs a glucose meter reading. To ensure that only participants with a fasting glucose level less than 150 mg/dL receive an oral glucose load, a glucose meter check is made using blood from one of the tubes drawn during Venipuncture (tube #5). A SureStepPro Glucose Meter is used for this purpose, with instructions for this procedure provided in Manual 7. As an important precaution a HCHS/SOL staff person should be designated to keep the glucose meter calibrated, to periodically make sure that the glucose measuring strips are not expired, and to confirm that all staff performing this measurement cover the entire area of the testing strip tip with the drop of blood.

The procedure to check the fasting blood glucose using the glucose meter is described in Manual 7. The following decision rules apply in determining whether an oral glucose load is to be administered. An overview chart of these decision rules should be displayed in the laboratory area where it is easily accessible to the HCHS/SOL staff persons performing the glucose meter tests.

1. If FPG <150 mg/dL, the participant has fasted for at least 8 hours and does not have diabetes, proceed with the OGTT and the rest of the examination.
2. If the FPG  $\geq$  150 mg/dL, do not proceed with the OGTT. Explain to the participant that his/her fasting blood glucose level is high and recommend that this be checked by the provider of health care at the participant's next appointment. Enter result on the form (for report to be discussed during exit interview).

3. If the FPG 200-399 mg/dL proceed as follows:
  - a. Ascertain signs/symptoms of hyperglycemia (e.g., thirst, dizziness, headaches, hunger, blurred vision, nausea, confusion, abdominal pain, or vomiting).
    - If symptoms(s) are present alert the HCHS/SOL Center health professional who may refer to the ER or make a same-day appoint with the participant's provider of care.
  - b. Measure urine for ketones.
    - If the urine dipstick indicates large or moderate ketones, refer to the emergency room.
    - If the urine dipstick is negative, trace or small for ketones, refer to the participant's health care provider or a referral physician, for evaluation within a week.
4. If the FPG  $\geq$  400 mg/dL **STOP** the examination and refer to the emergency room or make same-day appointment with participant's provider of care (regardless of the presence of symptoms).

If blood was drawn before the examination visit is stopped (as is typically the case before a glucose meter test), the blood and urine specimens are processed according to the study protocol (Manual 7) and shipped to the Central Laboratory on a regular schedule.

The glucose reading from the glucose meter is recorded on Item A.6 of the biospecimen form (BIO) and the decision to proceed with a glucose load is recorded on the Itinerary Form, together with the target time for the two-hour blood draw. A timer is set in the laboratory area to remind the technician of the pre-set times for each participant's two-hour Venipuncture and the information on the Itinerary Form is periodically keyed into the DES version of this form, to enable the DES to display alerts to the study personnel for the individual participant's two-hour target times.

## Overview of Oral Glucose Test Eligibility and Safety Exclusions

### HCHS/SOL Visit 2 Oral Glucose Load Eligibility and Safety Protocol

#### a. Determine Eligibility (*Biospecimen Collection Form, Items A3-A5*)

- i. Participant has diabetes/is taking glucose-lowering medications, or
- ii. Participant is on kidney dialysis, or
- iii. Participant had partial removal of stomach or small intestines, or
- iv. Participant consumed food less than 8 hours ago (schedule a fasting blood draw)

Not Eligible  
for an Oral  
Glucose  
Tolerance Test  
(OGTT)

#### b. If Eligible (none of the above): Glucose meter check of fasting blood glucose (FPG) from Tube #5

- If FPG 70-149 mg/dL** → Proceed with OGTT  
**If FPG 150-199 mg/dL** → Withhold OGTT; recommend checking FPG by provider of care  
**If FPG 200-399 mg/dL** → Withhold OGTT and:

- i. Assess signs/symptoms<sup>†</sup>.

<sup>†</sup> *Thirst, dizziness, headaches, hunger, blurred vision, nausea, confusion, abdominal pain, or vomiting*

If **symptom(s) present** alert the HCHS/SOL Center health professional who may refer to the ER or make a same-day appointment with participant's provider of care

- ii. Check urine for ketones:
  - a. **If ketones moderate or large** → refer to the ER;
  - b. If ketones negative, trace or small → refer to health care provider for evaluation within 1 week

**If FPG  $\geq$ 400 mg/dL** → **Stop the HCHS/SOL examination** visit. Refer to the ER or make same-day appointment with participant's provider of care

The above chart is displayed in locations conveniently accessible to HCHS/SOL field center personnel in charge of fasting glucose meter assessments and/or participant safety.

### 15.3 Glucose Monitoring Safety Protocol – Responding to High or Low Fasting Blood Glucose

Following the fasting blood draw, the blood glucose level is monitored on all participants who are eligible for a glucose load test (see Section 15.2). The glucose meter reading may indicate that the participant has fasting hypoglycemia (low blood glucose) or hyperglycemia (elevated blood glucose). The procedures to follow in each case are described in this section.

The first step in responding to a low or high blood glucose reading on the glucose monitor is to repeat the measurement, verifying that the drop of blood covers the full area of the testing strip tip. Further actions depend on whether the participant has diabetes or not. Thus, the next step is to confirm whether the participant has diabetes, and if so, whether insulin and/or oral medications for diabetes were taken on the day of the Visit 2 exam or the night before the HCHS/SOL examination visit.

#### **Low blood glucose readings in participants without diabetes or pre-diabetes [*who are not taking hypoglycemic medications*]**

- A. Participants with fasting glucose between 70 and 149 mg/dL  
No action is required; the participant may have an OGTT.
- B. Participants with fasting glucose between 50 and 69 mg/dL
  - 1. Repeat the glucose meter measurement immediately using a new drop of blood from Tube #5.
  - 2. Assess participant comfort. Symptoms may include irritability, pale or cold skin, cold sweat, tremor, rapid heart rate, headache, nausea, vomiting or dizziness. If there are no signs or symptoms proceed with OGTT and provide snack with protein following the 2-hour blood draw.
  - 3. If any of the above signs or symptoms are present alert the HCHS/SOL Center health professional for observation.
- C. Participants with fasting glucose <50 mg/dL

1. Repeat the glucose meter measurement (use a new drop of blood from Tube #5)
2. If value is confirmed alert the HCHS/SOL Center health professional
3. Assess participant comfort. Symptoms may include irritability, pale or cold skin, cold sweat, tremor, rapid heart rate, headache, nausea, vomiting or dizziness.
  - a. If participant is **Free of Symptoms** (see above) proceed with the OGTT
    - i. After drinking the Glucola assess participant comfort every 30 minutes
    - ii. Provide snack with protein or early lunch following the 2-hour blood draw
  - b. If participant **has any Symptoms** (see above), withhold the OGTT and:
    - i. Provide candy with sugar to dissolve 2-3 pieces in the mouth
    - ii. Within 15 minutes perform a glucose meter measurement from a finger stick.
    - iii. If FPG <70 mg/dL at this point, provide 2-3 pieces candy with sugar to dissolve in the mouth
    - iv. If nausea /dizziness persist call 911, and follow the Institution's safety protocol and incident event instructions
    - v. If FPG is now between 70 and 100 mg/dL and participant does not have nausea, offer 4oz of fruit juice or half a can of soda (not diet soda)
    - vi. If the participant feels well after 3,b.v (above), offer a snack with protein or an early lunch and assess whether participant is comfortable proceeding with the exam visit.

**Low blood glucose readings in participants with diabetes, or taking any hypoglycemic medications.**

- A. Participants whose fasting blood glucose is 70-149 mg/dL without signs or symptoms.  
Symptoms of hypoglycemia that are common in persons with diabetes (especially those who take insulin alone or in combination with oral medications) include: irritability, pale or cold skin, cold sweats, headache, blurred vision, tingling around the mouth or tongue, rapid heart rate, sleepiness, weakness, difficulty concentrating or speaking well, nausea or dizziness. The level of consciousness may deteriorate quickly.
- B. Participants with fasting glucose 50-69 mg/dL without signs or symptoms (see above)
  1. Offer 4oz of fruit juice or half a can of soda (not diet soda)
    - a. Within 15 minutes perform a glucose meter measurement from capillary blood (finger stick). The participant may prefer to use own glucose meter
    - b. If FPG is still below 70 mg/dL, repeat 1 (offer juice or soda)
  2. Once FPG is >70 mg/dL offer a snack and/or early lunch, assess whether participant is comfortable proceeding with the exam visit, and check on participant every 30-40 minutes.
- C. Participants with fasting glucose <70 mg/dL with symptoms (see above), OR <50 mg/dL (with or without symptoms)

1. Give participant 4oz of fruit juice or half a can of regular (not diet) soda; if participant feels nausea or dizziness offer 2-3 pieces of pure sugar candy. If the participant carries glucagon and prefers it, she/he may self-administer glucagon
2. Within 15 minutes perform a glucose meter measurement from capillary blood (finger stick). The participant may prefer to use own glucose meter.
  - a. If FPG still <80 mg/dL repeat 1 (offer fruit juice or regular soda); if participant feels nausea or dizziness offer 2-3 pieces of pure sugar candy.
  - b. Within 15 minutes perform capillary blood glucose measurement (finger stick).
3. If after 3 rounds of juice/soda/candy the PG is <80 mg/dL place a call to 911 and follow the Institution's safety protocol and incident event instructions
4. If after administration of juice, soda or candy PG >80 mg/dL offer a snack with protein and/or an early lunch, and assess whether the participant is comfortable proceeding with the exam visit, and check on participant every 30-40 minutes. Advise the participant to inform his/her provider of care of this episode.

### **15.3.3 High blood glucose readings in participants without diabetes or pre-diabetes**

#### A. Participants with fasting glucose 150-199 mg/dL

Participant is not eligible for OGTT; recommend checking FPG at next visit with a provider of care

#### B. Participants with fasting glucose 200-399 mg/dL

Assess signs/symptoms: Thirst, dizziness, headaches, hunger, blurred vision, nausea, confusion, abdominal pain, or vomiting.

- a. If no symptoms present: Alert the HCHS/SOL Center health professional and recommend that participant make an appointment with provider of care within one month.
- b. If symptom(s) present: If symptoms(s) are present alert the HCHS/SOL Center health professional who may refer to the ER or make same-day appoint with participant's provider of care.
- c. Check urine for ketones:
  - i. If ketones negative, trace or small: Refer to health care provider for evaluation within 1 week
  - ii. If ketones moderate or large: Discontinue the HCHS/SOL exam and refer to the ER.

#### C. Participants with fasting glucose >400 mg/dL

Stop the HCHS/SOL examination visit. Refer to the ER or make same-day appointment with the participant's provider of care

### **15.3.4 High blood glucose readings in participants with diabetes, or taking hypoglycemic medications.**

If the fasting blood glucose is elevated in a participant who has diabetes (or is taking a hypoglycemic medication) the steps to follow are as shown above for participants who do not have diabetes. Symptoms and urine ketones should be checked if fasting glucose levels are above 200 mg/dL. Note that trace or small urine ketones in a person who is asymptomatic may be a sign of prolonged fasting, prolonged but stable hyperglycemia, recent alcohol intake, or chronic poor caloric intake.

If the participant is able to safely ingest liquids or food, it is recommended that the participant take his/her medications and have breakfast after the blood draw. Glucose levels should be re-checked 30 min or 1 hour later. If the participant has fever, nausea or abdominal pain, or is otherwise unable to tolerate water or food, a medical referral is recommended.

### **15.3.5 Overview of safety procedures based on glucose readings in HCHS/SOL participants**

The above safety procedures have been summarized in a flow-chart format. These charts are displayed in locations conveniently accessible to HCHS/SOL field center personnel in charge of fasting glucose meter assessments and/or participant safety.

## **15.4 Follow-up with Participants Referred to Medical Care**

If a study participant is referred to an emergency room or to another source of medical care because of an FPG  $\geq$  400 mg/dL or an FPG 200-399 mg/dL accompanied by positive ketones in the urine or by symptoms, field center personnel explain the urgent need to seek medical care and assist the participant in making an appointment if this is helpful. It is also mentioned to the study participant that HCHS/SOL personnel will contact him/her within 48 hours as a courtesy follow up. During this follow-up call field center personnel confirm that the participant has seen a doctor, or has understood the need to seek medical care.

If the field center examination was interrupted because of the above-mentioned results of the glucose meter test, the participant is scheduled at a later date to complete the examination. Within 3 months after the initial visit the participant is contacted and asked whether she/he has seen a doctor for the high blood sugar detected at the first visit. If the participant has not seen a physician he/she is again encouraged to do so (but no clinic visit is scheduled). If the participant reports having seen a physician or having been tested for diabetes, field center personnel ask if the participant feels well enough to schedule the continuation of the HCHS/SOL examination visits and proceed according to the response.

At the time of the exam continuation visit study personnel verify whether a blood draw and urine collection were completed during the initial (interrupted) visit. If that is the case no additional blood or urine specimens are obtained at the continuation visit. A glucose meter test is not required by protocol at the time of the continuation visit, but one can be performed if the study participant requests it or as a safety precaution at the discretion of study personnel. If fasting glucose is measured, the exam stopping rules listed in Section 19.6 apply. The result of this glucose meter test is not recorded in the DES.

If blood was not drawn at the time of the initial visit, this is done as part of the continuation visit. Similarly, urine is collected if not done at the initial visit. Manual 7 procedures are followed for

these procedures during the continuation visit. If the participant reports a diagnosis of diabetes or to be in treatment for high blood sugar an oral glucose load is not administered and a glucose meter test is not required by protocol. If requested by the participant a glucose meter reading can be done; its result is not recorded in the DES and the standard stopping rules apply (see Section 15.1 of this manual).

### **15.5 Administration of the Oral Glucose Load**

An oral glucose load is not administered to a participant who has diabetes or is being treated for diabetes, a participant who is on kidney dialysis, anyone who has had partial removal of the stomach or small intestine, not to a participant who has consumed food less than 8 hours prior to the time of the blood draw. The preferred means of serving the glucola drink to the participant is to remove the cap and serve the bottle with a straw. If requested by the participant, the contents can also be poured into a paper cup and served with or without a straw. Participants are instructed to consume the contents of the container in less than 5 minutes. Most individuals consume the full amount in 3 to 5 minutes quite easily.

The timing for the 2 hour post load venipuncture begins as soon as the participant starts to drink the glucose solution. The time the participant *began* drinking the glucola is recorded in Item 25 of the Biospecimen Collection Form and the time the participant should have the 2 hour post load venipuncture is then recorded on the Itinerary Form/Clinic Exam Check List.

Study participants are encouraged to drink the full amount of glucola; otherwise they will not get the full benefit of the test. If the individual does not consume the full amount of glucola, the technician measures the residual amount and records it in Item 23 of the Biospecimen Collection Form. The measurement of the residual glucola is not necessary if only a few drops are left. If the residual amount is 145 ml or more, the 2 hour blood draw is NOT performed, and Item 24 of the Biospecimen Collection Form is completed accordingly. Based on the experience in many epidemiologic studies in the U.S. and elsewhere, this should be a very uncommon event.

### **15.6 Two Hour Post Glucose Load Blood Draw**

The two hour blood sample is obtained for measurement of glucose two hours after the start of the test. The blood sample is drawn as close to the two hour time as possible. The phlebotomist records that the post-load blood glucose sample was drawn, and the actual time it was drawn (items 24 and 26 of the Biospecimen Collection Form).

Every scheduling effort is made to allow participants to go to the venipuncture work station for the 2 hour blood sample. The Clinic Check List needs to be checked frequently as a guide to scheduling interviews and procedures, especially towards the end of the examination. In a complex field center examination such as the HCHS/SOL, it is likely that some participants will be busy with other parts of the examination. If the participant is available within a 10 minute window of the scheduled 2 hour post-load venipuncture, the overlapping interview or procedure does not need to be rescheduled or interrupted. However if the 2 hour blood sample is due and the participant cannot come to the venipuncture work station within the 10 minute window, the phlebotomist, if possible, goes to the participant to obtain the sample at the examination or interview station.

## **15.7 Snack**

Study participants should neither drink nor eat anything in the period between the glucose administration and the 2-hour blood draw. After the post-load venipuncture, participants are given the regular snack. Study participants will have been asked at the reception station whether on advice of their physician they can postpone taking the medications they usually take first thing in the morning until they have their 2 hour post-load Venipuncture. If that is the case, this will be noted on the Clinic Visit Check List and participants are then assisted in retrieving their medications during the snack break.

The snack should consist of simple and complex carbohydrates, protein and fat (example, 8-12 oz of juice, and two or three slices of bread with cheese (or a sandwich). It can be anticipated that after participants will be hungry after the prolonged fasting. Coffee or tea is optional at this point.

## **15.8 Side Effects and their Documentation**

Based on many previous studies similar to HCHS/SOL, side effects are quite infrequent, and vomiting was reported only on 0.1 percent of tests. Participants may temporarily experience fullness, or on occasion transient, mild nausea. Diarrhea is not a side effect of the glucose load test. If vomiting has occurred, a 2-hour blood draw should not be done, and the reason for the incomplete test recorded in Item 23 of the BIO form. If a participant complains of any discomfort during the test, this should be reported to the Study Coordinator or the Study Nurse and documented on the field center's Incident Log.

## **15.9 Emergencies**

If syncope/loss of consciousness occurs after an oral glucose test, hypoglycemia should be presumed until ruled out. Field center staff attends to the participant while the medical staff responsible for emergencies is contacted as well as the field center manager. Field centers keep on hand orange juice or equivalent, sugar-containing beverages at all times. If recognized promptly by clinic staff hypoglycemia should be easily treated with orange juice or a similar sugar containing beverage. Severe hypoglycemic reactions are a medical emergency and the participant should be transported immediately to an emergency care facility. Readiness for emergencies and the procedures to follow under these circumstances are described in this manual under Participant Safety (Section 19)

## 16. INTERVIEWS

Interviewing is a collaboration between the HCHS/SOL staff and the study participant to collect study data, using standardized techniques common to each examination site, that are unchanged for the duration of the Visit 2 cohort re-examination. This section of Manual 2 presents a general description of interviewing in the Visit 2 examination of the HCHS/SOL.

Interviews in the HCHS/SOL are administered in English or Spanish – at the preference of the study participant – by trained and certified personnel who are bilingual. Participants need not be consistent in their use of Spanish or English between forms; for each form the language of administration will be recorded in the database for quality assurance purposes. Interviews conducted at the HCHS/SOL field center are administered using the HCHS/SOL Data Entry and Management System (DES) which supports the interviewer with automatic skip pattern implementation auto-fill features, and provides quality assurance features such as on-entry editing. The most important factor influencing the study participant’s satisfaction and the quality of the interview data is the interviewer, his/her skills and adherence to the study protocol.

Table 4 Questionnaire Interview Portion of Visit 2 Examination (Revised August 12, 2015)

Standardized Visit 2 Questionnaires	Form codes (English, Spanish)	Interviews Administered to Participants	Interviews Administered to Proxy Ppts.
Eligibility Screen	ELE	X	X
Disability Screen	PDE, PDS	X	X
Identifying Information and current address	IDE, IDS	X	X
Biospecimen Collection & Screening Qx	BIO	X	X
Personal Medical History	MHE, MHS	X	Items 1 to 23f
Reproductive Medical History	RME, RMS	X	-
Pregnancy Complications	PCE, PCS	X	-
Socio-economic Status - Occupation	SEE, SES	X	X
Health Care	HCE, HCS	X	-
Chronic Stress	STE, STS	X	-
Family Cohesion	FCE, FCS	X	-
Social Support	SSE, SSS	X	-
Acculturation	ACE, ACS	X	-
Well Being, GAD7, CESD	WBE, WBS	X	-
Abbreviated medication use	MSE, MSS	X	X
Tobacco Use	TBE, TBS	X	X
Alcohol Use	ALE, ALS	X	X
Participant Feedback	PFE, PFS	X	X
Exit interview	EXE	X	X

### 16.1 Characteristics of a Good Interview

Interviews are friendly but businesslike. At the beginning of each encounter the interviewer makes introductions and verifies the participant's name. Participants are always thanked at the conclusion of interview sessions. Interview areas should be as quiet and private as possible. Although this is often out of the control of the interviewer, participants should be accommodated to have their interviews take place at a time when these conditions are possible.

Interviews are the structured, one-sided transfer of information, not a conversation. The pacing of questions is based on the comfort and comprehension of the participant with each interview; it may vary as the content, complexity or period of recall of the person or subject matter changes. During an interview, questions from the participant are answered with neutral, nonjudgmental responses and

questions to the participant are limited to probes to clarify or resolve incomplete, ambiguous or inconsistent responses. Repeating a question is most appropriate when the participant does not appear to understand the intent or meaning of the question. Gently stressing the portion of the question which was not understood when the question is repeated (e.g., "has a doctor ever") is often more efficacious than rereading it in exactly the same manner.

## **16.2 Characteristics of a Good Interviewer**

Interviewers are responsible for being fully familiar with the questions, response categories and skip patterns of each interview. At the beginning of an interview the study participants may wish to be reassured that of the confidentiality of each response/measurement. Interviewers use a conversational tone and establish a pace consistent with the interest and ability of the participant. A good interviewer projects the importance of the interview to the participant and attempts to gain his/her confidence, while remaining impartial and nonjudgmental. For example, a verbal response (or body language when the interview is being conducted in person) which indicates positive feedback is inappropriate, even in the light of participant reports of behavioral modifications which in a clinical setting would result in praise and encouragement. Participant confidence in the confidentiality of each response/measurement is established.

### **Communication Traps and Obstacles to Standardization**

Communication traps include: (1) anticipating or answering questions directed to the participant with the interviewer's own thoughts; (2) hearing what one expects to hear; or (3) being drawn into a conversation. The likely sensitivity of a question is often as much a perceptual problem of the interviewer as it is the participant. Questions thought to be "sensitive" should be asked in a neutral manner which does not differ from the normal professional flow of the interview.

The most frequent obstacles to the administration of a standardized interview are: (1) a perceived conflict by the interviewer between the need to standardize the question with the desire to obtain the truth; (2) a conflict between the interviewer's desire to achieve rapport with the participant and adherence to standardization; (3) inadequate training of the interviewer; and (4) inadequate training of the respondent.

## **16.3 Interviewer Bias**

The use of standardized interviewing techniques is employed to reduce one of the many potential sources of misclassification; i.e., interviewer bias, a *systematic* difference between responses obtained by different interviewers. Although introductory scripts may be modified to respond to different situations an interviewer may encounter, administration of each question exactly as written and use of standardized definitions or explanations are critically important to avoid bias.

## **16.4 Conducting the Interview**

Interviewers must keep in mind that the interviewee is not familiar with the questions, their sequence and response categories. Many interviews require the interviewer to "train" the respondent, mostly using verbal instructions and at times using response cards handed to the study participant. For example, responses may follow a series of patterned questions, e.g., a doctor diagnosed condition, age at onset, and age at treatment during the participant's lifetime or may require the selection of the most appropriate category from a series of descriptors, e.g., almost never, sometimes, often and almost always. Unless a response card is used, these instructions should be repeated until it is clear

that the respondent understands them, and then subsequently offered only as needed. When the pattern of questions in a form changes to another repeated sequence of responses the interviewer should assist the study participant in making this transition.

The most important technique for conducting a rigorously standardized interview is to read the question in the exact words and in the exact sequence as printed in the questionnaire. With experience the interviewer can memorize specific questions. This helps in maintaining eye contact with the study participant, but care must be taken to avoid changing the wording of the question(s) that are not being read. The review of taped interviews assists in maintaining standardization in that it can alert interviewers who inadvertently change the wording of a question. Every question must be asked, even if the participant appears to have provided the information in the answer to another question. If based on a previous answer a question is asked out of the printed sequence, a skip pattern instruction is printed on the form (and presented on the monitor screen).

Reading the transition statements exactly as they are worded is equally important in maintaining standardization. The transition statements are designed to inform the participant about the nature of a question or a series of questions, to define a term, establish a time frame or describe what is being asked in the question.

Response styles of an interviewer influence the willingness of the participant to respond to questions and the quality of the response. Inappropriate styles include those that are evaluative or judgmental, interpretive or pedantic. Interrupting responses for reasons other than to focus or channel the participant's answer should be avoided.

Appropriate styles of interviewing include providing neutral noises to reassure, pacify or reduce the intensity of the respondent's feelings. These include general clucking or an understanding murmur, as well as nondirective or understanding statements such as a repetition of what the respondent has just said (in contrast to paraphrasing). These are intended to reassure that participant or show interest without intruding on the flow of the response.

Probing is appropriate to seek further information, provoke further discussion along a certain line of thought or explanation, or to present a question to the respondent. In general, and unless specifically countermanded in the QxQ instructions of the interview, probing is appropriate when an answer is unclear, incomplete, inconsistent or no response is given. The best and most frequently employed probe is silence. In a silent probe, the interviewer pauses or hesitates and looks to the participant for an answer. What appears to be dead time to the interviewer may allow the participant to review a lifetime of events. Other types of probing include repetition of the original question, channeling ("tell me more about ..."), clarification ("when did your doctor tell you that?"), elaboration/continuation ("what happened next?"), encouragement ("I see, um, uhuh") and completion ("anything else?"; "can you tell me anything more about that?").

The most effective, spoken probes are neutral, such as:

"How do you mean that?" instead of "Why?"

"Can you tell me more about this?"

"Can you give me an example?" or "Can you explain that in a little more detail?"

"How are you using that term?"

"If you had to choose, which would you say?"

"What else can you tell me about that?" instead of "Anything else?"

In using probes, as for other interviewing techniques, do not interrupt; do not give the impression you are not listening; do not paraphrase the respondent's words and do not suggest an answer.

## **16.5 Administration of the Interviews**

HCHS/SOL questionnaires are interviewer-administered, using a specialized data entry and management system. The data entry and management system used by HCHS/SOL is designed to enhance data accuracy and security, while minimizing the burden for the participant and staff. The system displays screens that resemble the paper forms. The interviewer reads the items from the screen and keys the response into the computer. As data are entered, they are edited by the system. Values failing the edit checks cause an error message to be displayed prompting the interviewer to confirm the value, correct it, or flag it as in need of further investigation.

Questionnaires are available in both English and Spanish versions. Questionnaires for which no existing Spanish translations are available were translated by the Research Triangle Institute (RTI), with expertise in multilingual instrument development for large-scale surveys. New as well as existing translations were reviewed by members of the HCHS/SOL Translation and Validation Subcommittee with representation from the four field centers, the coordinating center and the project office who are bilingual and represent the four regions of origin for the study (Mexican, Cuban, Puerto-Rican, and Central/South American). Several of the translated questionnaires were tested by focus groups were conducted at each field center including community volunteers representing the various countries of origin at each site. The final translations were certified by RTI prior to release for programming at the coordinating center.

## **16.6 Consideration of Gender and Cross-gender Identity in Conducting Interviews**

### **Overview**

The gender identity of the HCHS/SOL cohort member is important in interacting with the study participant, and in the administration of questionnaires with sex-specific information, i.e., Medical History (MHE/MHS – Men's health), Reproductive and Medical History (RME/RMS), Pregnancy Complications (PCE/PCS), and selected questions on screening/preventive services in the Health Care Use interview (HCE/HCS). The cohort members' gender/sex is recorded in the HCHS/SOL database as classified at the HCHS/SOL baseline examination, but they may self-identify with a different sex/gender at Visit 2. Error in assigning or recording a sex to a participant at baseline may account for some instances, but others may correspond to transgender/transsexual study participants whose sexual identity at the time of this examination visit must be considered.

HCHS/SOL staff must be able to distinguish the terms self (sexual)-identity and sexual preference, as well as transgender and transsexual. Gender identity is how the person defines his/her gender, which may or not correspond to the person's biologic sex, and how that person identifies with that sex (e.g., "I am a man", "I feel I am a man", "I am a woman", etc.) or identify with the opposite sex (e.g., "I was born a man, but I feel I am a woman", etc.). Sexual preference is the sex that person feels attracted to, independent of sexual identity. For example, a woman may self-identify as a woman and may feel attracted to men (heterosexual), to women (lesbian or homosexual) or both (bisexual). Questions about sexual preference are not asked in HCHS/SOL, and it is not in the

purview of HCHS/SOL staff to do so. What is pertinent to our interaction with the participants and to the administration of the HCHS/SOL interviews is awareness of sexual identity. To accomplish this, prior to each interview that contains information specific to one sex or gender the HCHS/SOL interviewer will use a script that makes reference to the nature of the questions that follow, and ask the participant if he/she agrees to proceed. Instructions are provided below for the pertinent forms. Three of these forms have to be administered in a predetermined sequence:

- i. Demographics Pre-fill for Visit 2 (DEM) and Personal Identifiers (IDE/IDS). Each of these forms contains pre-filled information from the HCHS/SOL database, to be confirmed at reception immediately following the participant's welcome and the administration of the informed consent. Personal information and that on contacts is updated on these forms, as required.
- ii. The Pregnancy Complications (PCE/PCS) interview always follows the administration of Reproductive and Medical History (RME/RMS).

### **Consideration of Gender and Sex for Specific Visit 2 Interviews**

Personal Identifiers form (IDE/IDS) and Demographics Pre-fill for Visit 2 (DEM). At Visit 1 the HCHS/SOL participant's gender was assigned from observation by HCHS/SOL staff, and recorded on the Personal Information (PIE/PIS) form. HCHS/SOL personnel were instructed to enquire about a participant's gender if gender classification was not self-evident. In Visit 2 that gender classification is prepopulated to several forms, and also drives the automated skip-patterns in Visit 2 interviews. It is therefore important to verify the participant's gender as recorded at Visit 1, as part of the verification of the participant's name, address, phone and social security number at the outset of the Visit 2 examination.

Since the personal information being verified is confidential, this interview is conducted in a private setting, without family members or friends who may accompany the cohort member. The Personal Identifiers form (IDE/IDS) should be opened in CDART as part of the verification of the personal identifiers prepopulated on the Visit 2 Personal Identifiers Form (IDE/IDS), as well as the Demographics Pre-fill for Visit 2 (DEM) to display the participant's gender (item A.1) and the Date of Birth (A.2) for verification against a photo ID (if the latter option is exercised by the field center). At this time HCHS/SOL staff verifies the agreement between the gender recorded in item A.1 of the DEM and the participant's appearance. If the participant's gender is not evident, or is discrepant with the participant's physical appearance HCHS/SOL staff can ask for guidance (e.g. *"I see that our records from your first HCHS/SOL examination list you as Ms/Mr. <\_\_Name\_\_>. We seem to have listed you as a <man/woman>; did we make a mistake?"*).

Allow the participant to confirm his/her name and to indicate whether his/her gender or sex was mis-specified at Visit 1. If the participant clearly indicates that his/her gender is different from what is displayed on the Demographics Pre-fill for Visit 2 (DEM), the staff person should make the corresponding change to item A.1 of the DEM form. This will re-set the participant's gender for purposes of the Visit 2 examination, and will be reflected in the gender/sex-specific skip patterns in

the Reproductive and Medical History form (RME/RMS). These forms need to be saved and closed for the Visit 2 data collection to proceed.

Personal Medical History (MHE/MHS). Proceed through sections A through E of the form, which are gender neutral. Close the MHE/MHS interview for women after question 36.b, and in transitioning to section F for men read the script on the form:

*The next set of questions is about men's health including urinary and prostate problems. The prostate is a gland located just below the bladder. Can I proceed to ask these questions? If the participant declines the MHE/MHS interview is closed without further questions.*

Health Care Use interview (HCE/HCS). The header portion of the form includes a pre-populated field for participant gender (item 0.c), drawn from the HCHS/SOL database. This information drives the skip patterns built into CDART for this form. If there is an evident discrepancy between the participant's biologic sex attributes or dress and the pre-populated information displayed in item 0.c, ask the participant:

*I see that our records from your first HCHS/SOL examination visit list you as Ms/Mr. <\_\_Name\_\_>; did we make a mistake? We seem to have listed you as a <man/woman>.*

Allow the participant to confirm his/her name, to indicate whether his/her gender or sex was mis-specified at Visit 1, or to confirm the pre-filled information. Set up a Note Log for item 0.c to record any information provided by the participant to update, or to provide context for the sex/gender designation shown in item 0.c (such as 'I feel like a man' or 'I was born a man but I am a woman'). Do not attempt to change the gender field (item 0.c) in the form header.

Regardless of any apparent discrepancies between the perceived gender of the participant and the information displayed in item 0.c, introduce the HCE/HCS interview with the following script:

*Next I will ask questions about health care, the type of care you may have received recently and where you received care. Some of these questions refer to different medical care given to women and to men. Can I proceed to ask these questions? Follow the participant's guidance if they direct the interviewer to questions specific to one or the other gender.*

Reproductive and Medical History (RME/RMS). This interview is presented to all participants who have been identified as women at the HCHS/SOL Visit 1 and to those who identify themselves as women at Visit 2. Introduce the interview with the following script:

*This next interview includes questions for women about your menstrual periods and pregnancies, and about hormones that you may have used or are using. Can I proceed to ask these questions?*

*[If yes] Some questions I ask may make you feel uncomfortable, and may include questions you may not feel like answering. Please take your time to think through your answers. We want to understand these aspects of women's health, and at the same time we want you to feel respected and comfortable. Your answers are important to us, and your participation in the study is extremely valuable.*

Pregnancy Complications (PCE/PCS). This interview always follows the administration of Reproductive and Medical History (RME/RMS).

### **Interaction with the Transgender/Transsexual Participant**

Because of their rapport with HCHS/SOL staff participants may feel comfortable disclosing their sexual identity, or may have done so already. If sexual identity that is not obvious is disclosed in the setting of the interviews mentioned above it is important to follow the participant's direction on whether he/she is able to answer the questions for the intended sex (health/health care or reproductive questions for women, or health/health care-related questions for men). If the participant is not certain or uncomfortable about answering such questions (as specified in the introductory script to the forms listed above), set the form to 'permanently missing' or identify the pertinent items of the interview as permanently missing. The response to the scripted questions should guide the HCHS/SOL interviewer in making this decision, which requires that the participant feel comfortable and respected, and that the interviewer be relaxed and maintain a neutral, professional attitude. No assumptions should be made about the applicability of individual study forms or questions from a participant's name, appearance or dress.

### **16.7 Need for an Alternate Informant**

Cognitive deficits may affect the ability to accurately respond to interviews and questionnaires. Access to a knowledgeable informant who can assist with interviews and questionnaires is requested for participants whose self-reported information may be suspect. An Alternate Informant is a person sufficiently familiar with the participant's daily activities to be able to provide information on the participant's performance. If sufficiently familiar with the participant's performance in the course of daily activities, a proxy participant (see Section 5) may serve as an informant.

Unless impairment is obvious, recognizing diminished cognitive ability in a participant is difficult, particularly since social skills can remain intact for participants who otherwise do not perform well during interviews. Cognitive abilities are frequently task specific. As a result, depending on the type and extent of impairment cognitively impaired individuals can remain fully capable of making a variety of decisions, including whether or not to participate in a study, although they may subsequently exhibit some difficulties during an interview. Field center personnel need to be attentive to indicators of potential cognitive impairment in the course of interviews, such as repetition (i.e., repeating questions/stories over the course of just a few minutes) and empty or poor responses (i.e., the participant who frequently responds with "I don't know"). Individuals who repeatedly wish to engage their spouse or a companion for answers to historical questions or their medical history also may exhibit a reduced capacity to answer all HCHS/SOL questionnaires.

## **Standardized Assessments to Assist Staff in Defining the Need for an Informant**

Because of the complexity of assessing impairments in cognitive domains, a standardized instrument is used to assess disorientation to time and impaired memory as a screening tool for participant safety and the need for consent by proxy and/or a (proxy) informant. This tool is the Six-item Cognitive Screener, previously used in the HCHS/SOL as part of the neurocognitive assessment (NEE/NES forms) in Visit 1. It is important to note that the Six-item Cognitive Screener (SIS) is not a diagnostic tool and that the HCHS/SOL personnel do not make diagnoses. The SIS is used to assist HCHS/SOL staff to identify cognitive impairment if deemed necessary, and to assist the study participant accordingly. The results of the SIS are recoded in the HCHS/SOL database but are not reported as a HCHS/SOL study result to the participant. If the study participant's performance on the SIS prompts HCHS/SOL staff to notify the field center clinician for consultation, the latter may include the SIS test results as part of a referral to the participant's health care provider if this is warranted in the opinion of the field center clinician.

### **Administration of the Six-item Cognitive Screener.**

If HCHS/SOL staff has doubts about the study participant's capacity to provide informed consent, or the participant appears to experience difficulty during the exam visit, a trained HCHS/SOL staff person administers the Six-item Cognitive Screener using the SIB form. HCHS/SOL staff can use the following script:

“Before we continue I would like to ask you some questions that will help us to decide the best way to conduct the HCHS/SOL visit. Specifically, I will ask you to use your memory. I am going to name three objects. Please wait until I say all three words, then repeat them. Remember what they are because I am going to ask you to name them again in a few minutes. Please repeat these words for me: BLUE – PEAR – SOFA.” (Interviewer may repeat names 3 times if necessary but repetition not scored.) The interview then continues with items 1-3 (“What year is this?”; “What month is this?”; “What is the day of the week?”) and proceeds to ask: “What were the three objects I asked you to remember?” See the six-item screener (SIB) question-by-question instructions for administration of this form.

### **Criteria for Recruiting an Alternate Informant**

Classifying decision-making capacity is challenging, and may be task specific. Given the minimal risk associated with the HCHS/SOL Visit 2 procedures, conservative criteria are suggested as **triggers for requiring an alternate informant**. These include (any of):

- Staff assessment, at the time of annual follow-up interview, the examination visit scheduling call, or at the time of in-person informed consent. Because no mental status screen will identify all cases of cognitive impairment, the need for an alternate informant will be informed by the judgment of the HCHS/SOL interviewers.
- Impaired memory (e.g., score <2 on memory items from six-item cognitive screener).
- Disorientation to time (e.g., score < 2 on orientation items from six-item cognitive screener).
- A prior diagnosis of dementia in an individual whom staff has determined to have potential cognitive difficulties. (Affirmative response to MHE questionnaire item on history of dementia). Note: A self-reported diagnosis of dementia/Alzheimer's Disease is not in itself a reason for requiring an alternate respondent.)

The need for an informant will most often be ascertained during an annual telephone interview with the HCHS/SOL participant. The procedures to be followed during a telephone interview are consistent with those described in this manual for the field center setting. The procedures followed during telephone interviews are specified in Manual 3 (Retention and Follow-up). If at the time of the annual follow-up call preceding the HCHS/SOL examination visit, or at the time of scheduling the examination visit it is determined that the participant likely requires proxy consent and participation by proxy as described above, arrangements are made at that time to identify a proxy to accompany the participant to the examination visit. Similarly, if at the time of the HCHS/SOL examination visit it is determined that the participant requires an alternate informant, arrangements are made to identify and contact the alternate informant prior to the subsequent yearly contacts and interviews.

### **Scoring of the SIS to identify the need for an alternate informant or proxy participant**

Computation of the six-item screener score is done by the HCHS/SOL data management system (CDART) will score the SIS, to avoid possible error introduced by manual scoring. The six-item screener questions are scored as follows:

- a) Introduction of the SIS. If the participant fails to repeat all three words correctly after three attempts, this portion of the test (i.e., recall of the three words) is discontinued and the interviewer marks Item 0c on the SIS form as "Incorrect" (option 4). Items 4 – 6 of the SIS are marked 'Not attempted/Refusal' (option 4). While there is no SIS score under these circumstances, an alternate informant or proxy participant should be identified for future interviews of the participant.
- b) Scoring the SIS (items 1-6 on the SIS form). One (1) point is assigned to a correct response and 0 points for an incorrect response. The total SIS score = sum of the correct responses (range = 0 to 6).
- c) "Not attempted/refusal" responses. Not attempted/refusal are treated as missing for the purpose of identifying an alternate informant or proxy for subsequent interviews of the HCHS/SOL participant.

A pro-rated total score (which takes into account the number SIS of items attempted) is calculated when up no more than one item is missing.

- d) The orientation items on the SIS (questions 1 – 3) are treated as a sub-scale and a score also is calculated for the orientation items, with range 0 to 3 as well.

Unless a physical impairment affects the administration of the SIS, the following SIS scores recommend that an alternate informant or proxy participant be recruited:

- i. SIS not attempted, with item 0c marked as "Incorrect" (see above), or
- ii. SIS total score  $\leq 2$  (a pro-rated total score is used if 1 SIS item is missing), or
- iii. The orientation subscale (items 1 - 3) score = 0. This value ("0") is chosen as a conservative score considering that the SIS is administered over the telephone, by interviewers whose training does not include psychometric instruction.
- iv. Interviews that fall into gaps in the above schema, e.g., SIS refusal or refusing multiple items on the SIS, are subject to impressions by the interviewer in determining whether an alternate informant or proxy participant is needed.

## **Recruitment of the Alternate Informant**

If recruitment of an alternate informant is necessary, the following script can be used: “We think that it might be helpful to have someone [come with you to the clinic/be with you while we complete your HCHS/SOL examination visit]. This person could assist you in your participation in the study. Do you agree to have someone [coming with you to the clinic/being with you during the exam]?”

If YES:

“This person should be someone who can answer questions for you during an interview in case you do not feel comfortable providing the answers. Who would this person be?” Verify whether this is one of the participant’s contacts and record/update the name, street address, phone number and email address if available, and continue: “We ask you to tell [ALTERNATE INFORMANT’S NAME] about your decision. In the next few days we will also contact [HIM/HER] to provide information about the exam.” Record the informant’s contact information in the Contact Information Update form. Confirm that the participant agrees to communicate with the informant to request his/her engagement to assist the continued participation in HCHS/SOL of the study participant. The alternate or proxy is then contacted by HCHS/SOL staff a few days afterwards.

If NO:

Point out that having a trusted someone would help to make decisions about participation in the study. If the participant still does not agree, consult the supervisor or Principal Investigator.

## **16.8 Quality Assurance of Interviews**

The quality of data collected during interviews is supported by quality assurance procedures. All interviewer-administered interviews are based on the reading of written questionnaires, supported by a Manual of Operations and question by question (QxQ) instructions for each form. Interviewers are trained and certified in interviewing techniques, in the subject matter, terminology, and flow of each data collection form. Certification requires attendance at the (web-based) central training workshop at the beginning of the study, local practice, and the successful completion of three taped interviews on surrogate, age and sex appropriate participants.

Monitoring of the interviewing skills of each interviewer through direct observation by the supervisor is conducted quarterly, as described in Manual 12 – Quality Control. Interviewers who experience difficulty in maintaining their skills are retrained. Interviewers are re-certified at least once a year by the interviewer supervisor listening to interviews the staff member conducts with actual participants, and reviewing the contents of the respective for form. Field centers report their certification activities to the coordinating center for the central repository of certification status. The Coordinating Center informs study coordinators when the interviewer certification status is about to lapse.

A round robin review of taped interviews is organized by the coordinating center on an annual schedule. One field center's supervisor reviews another center's taped interviews with the help of the certification check list (see Manual 12 – Quality Control).

## **17. DATA INVENTORY AND REPORT PREPARATION**

The data inventory is done after all interviews and examination procedures have been completed and prior to the Exit Interview. At the field center's discretion, this can be done while the study participant changes into street clothes. Because participant data are collected by various means during the course of the exam, the objective of this inventory is to verify that all data items have been collected before the participant leaves the study center. In order to perform the data inventory, the Form Inventory Report found on the "Reports" tab of the study Data Management System (CDART-DMS) is run. The HCHS/SOL participant ID is entered and the application lists the set of completed forms and procedures, noting ones that are missing. Manual 13 includes details about running reports and use of the study data management system and reporting tools in general. As part of this forms inventory the "end of visit" report of study results is personalized and printed for review with the participant during the exit interview. All materials need for the exit interview are assembled and placed in the participant's folder at this time.

## **18. EXIT INTERVIEW**

The end of visit debriefing provides an opportunity to ask for feed-back about the visit and to identify aspects that the participant may have perceived as stressful or unpleasant. It also provides an opportunity to strengthen rapport with the study participant and to seek commitment for a continued, long-term association with the HCHS/SOL.

The “end of visit” study results are reviewed with the study participant and results identified for confirmation or referrals to a provider of medical care are discussed. The schedule of notification for the full set of study results also is reviewed at this time. These materials are shown in Section 18 of this manual. Lastly, the participant is asked whether he/she has any remaining questions about the study, the results to be received, or any concerns.

## **19. PARTICIPANT SAFETY**

The safety of the HCHS/SOL participants is protected by specific measures taken in the design or conduct of the examination for their safety; by the mechanisms established for handling potential emergencies; the routine notification of participants and their physicians regarding the results of the examination, and procedures used by study personnel to review all potentially medically important results and make the appropriate referrals.

To ensure participant safety the use of a pacemaker or defibrillator and reported physician diagnosis of diabetes are ascertained (for safety in the bioimpedance measurement and oral glucose tolerance testing, respectively). The presence of these conditions is ascertained at various stages ranging from recruitment, scheduling, and the examination process. Safety information may be ascertained early on to plan the exam visit and/or at the field center prior to administration of the procedure. As a result, updated, revised or contradictory information on self-reported exclusionary conditions can occur, due to the time elapsed since recruitment or in response to an interview with differently trained field center staff. Internally inconsistent information has to be resolved – and documented – to verify that participant safety precautions have been met.

The master record used in HCHS/SOL to document and monitor safety is the Participant Safety Screening Form (PSEA). Although some exclusion conditions are also recorded on other study forms as well as on a check list, the Participant Safety Screening Form (PSEA) serves as the summary record of safety items in the HCHS/SOL database and is the register by which the Study monitors compliance with the safety protocol. Thus, if the study participant or an authorized HCHS/SOL clinic staff person updates information provided previously (such as prior to the blood draw), the PSEA form must be updated. This is done by (a) changing the pertinent response on the PSEA in the DMS, and (b) by adding a note log to that item with a brief explanation for this action and the staff person's HCHS/SOL ID.

### **19.1 Measures to Protect the Participant**

Examination procedures which convey potential, small risk to participants include the venipuncture, and the administration of an oral glucose tolerance test. Precautions are taken to exclude individual who have conditions or characteristics that expose them to greater than minimal risk in the context of these procedures, as detailed below. At the time a participant's examination at the HCHS/SOL field center is scheduled, conditions and circumstances that can convey risk in the context of examination procedure are ascertained and recorded. Pregnant women are asked to reschedule their examination and characteristics identified as safety exclusions for individual procedures are considered in setting up a participant's examination itinerary. Safety exclusions are also ascertained prior to specific exclusions, as detailed below.

The Participant Safety Screening form (PSE/PSS ver. B) must be completed before a participant can proceed through the HCHS/SOL baseline examination. The form can be completed on paper or in the HCHS/SOL DMS. A completed copy of the Participant Safety Screening form, whether completed on paper or a printed copy of the form completed in the DMS, accompanies the HCHS/SOL participant throughout the course of the baseline examination. The PSE/PSS form must be available to the technician who performs an examination procedure.

Early in the exam visit a lead staff person reviews the safety exclusions reported by the participant and confirms the reported condition with the participant prior to excluding him/her from a test or

procedure. At that point the HCHS/SOL staff person confirms that the exclusion conditions are noted on the PSE/PSS form. The participant's Exam Itinerary Checklist is marked according to any positive responses to questions on the PSE/PSS, and the study participant is informed of the exams and procedures she/he should not do.

Verification is the responsibility of the technician performing the procedure.

The technician may re-ask the pertinent safety exclusion question, and may confirm with the study participant an exclusionary condition noted on the Safety Screening form (as Yes). If the condition is denied, or deemed to have been recorded in error, the technician may override the previously recorded response/exclusion if authorized to do so. Otherwise the technician asks for input of a supervisor.

To modify a previous entry on the PSE/PSS form the extant entry is crossed out on the paper form and the appropriate entry is marked, adding the initials of the technician (and reference to the supervisor if pertinent) as well as a brief note to document the occurrence. The latter will be keyed as a note log in the DMS for the item in question. Items on the PSE/PSS that are changed from 'No' to 'Yes' by a technician after asking the safety question prior to a test or procedure are recorded on the PSE/PSS for following the same procedure.

The HCHS/SOL staff person conducting the Exit Interview reviews the procedures performed and verifies the agreement with the exclusion conditions noted on the PSE/PSS form. Any discrepancies between exclusion conditions recorded on the PSE/PSS form and a test performed are reviewed with the Study Coordinator, the Study Physician or Nurse. The participant's wellbeing and safety must be addressed before the participant leaves the premises. If a procedure was conducted despite an exclusion condition, the Study Coordinator, Study Physician, or Field Center PI will notify the participant and if pertinent, consult with the participant whether they wish to have their physician informed of what happened.

The possibility of hypoglycemia with a 12-hour fast is diminished by routine inquiry about reasons which should exempt the participant from fasting during the scheduling of the examination visit. Other medical conditions or dietary restrictions which may be incompatible with the snack provided in the clinic are also ascertained. Hematomas or prolonged bleeding resulting from venipuncture. are usually avoided if well-trained technicians follow the procedures for blood drawing and take the precautions described in HCHS/SOL Manual 7. Occasionally, bleeding persists after Venipuncture, in which case procedures described in Manual 7 are followed. Participants may experience syncope during the venipuncture. Methods for handling major and minor emergencies are described below.

For persons with conditions which require emergency and immediate referrals, such as cardiac events, angina pain, or blood pressures  $\geq 200/120$  mm Hg (see below), the HCHS/SOL clinician is consulted immediately, the clinic exam is terminated as soon as the condition is observed, and another appointment rescheduled as appropriate.

## **19.2 Procedures for Handling Emergencies**

While all life threatening emergencies (e.g., acute MI) require immediate evaluation of the participant at an acute care facility, some emergency measures may be required in the clinic before departure. In addition, there are minor emergencies (hypotension, fainting, etc.) which may require treatment on the premises only. Although most emergencies are of the less severe nature, HCHS/SOL Field Center clinics are prepared for both types.

### **Major emergencies**

In a serious event the primary concern of the clinic staff is to implement pre-established procedures to get the participant to the nearest medical facility. All HCHS/SOL clinics are located within a few city blocks of a large, general, acute-care hospital. A staff person with certification in basic life support is on duty and physically present at every clinic session. Needed life support procedures are continued until emergency care arrives or the participant is transported to a hospital. Each HCHS/SOL field center, depending on its location and staffing patterns, has specific emergency procedures, which define:

1. Who is in charge during the emergency.
2. Who is to administer treatments.
3. Who is to be notified.
4. What action clinic staff is to take.
5. Which reports are to be filed.

Each field center clinic is required to have access to either a physician, a physician assistant or a registered nurse at all times during which participants are interviewed and examined. Each field center has in addition to trained personnel and emergency equipment, posted in conspicuous places (e.g., the reception area): phone numbers of police and fire stations; ambulance services; and specific phone numbers or codes to alert medical teams, if applicable.

In each participant's record, the name and phone number of his/her physician or usual source of health care and the home and work telephone numbers of one or more contact persons should be available. Emergency situations are coordinated by the staff person designated a priori, or by a physician if present. Each center has a designated physician on call. If not physically present in clinic, he or she is within immediate reach by phone or paging system and within a short distance to the clinic. The physician roster is posted in the field center and in the office of the nurse/clinician so that the name of the responsible physician is readily accessible. However, in no case is emergency referral and/or care deferred while staff is attempting to locate a clinic doctor.

All emergencies, whether serious or minor, are documented. This requires filling out an institutionally-approved form identifying the type of emergency. This is done by the person in charge at the time, and all reports are co-signed by a clinic physician and are filed at each clinic.

### **Minor emergencies**

The most common minor emergency is simple syncope (fainting) and near syncope. These events may occur during venipuncture. The management of simple syncope or near syncope follows the procedures detailed in Manual 7.

Many syncopal episodes can be prevented if clinic staff is alert to early signs. In any situation in which syncope is likely, e.g., after the venipuncture, staff verifies that the participant does not look or feel faint. If the participant looks faint or feels faint in the venipuncture area:

1. Have the person remain in the chair and sit with head between the knees or recline if the appropriate chair is used at the field center.
2. Crush an ampule of smelling salts and wave it under the participant's nose for a few seconds;
3. Provide the participant with a basin and a towel if he/she feels nauseous;
4. Have the participant stay in the chair until he/she feels better and the color returns.

If the participant continues to feel sick, recline the chair, place a cold wet towel on the back of the person's neck, and notify the supervisor. If a participant faints, he/she is cautiously lowered to the supine position on the floor and one attendant immediately calls for an in-house nurse/clinician to assist the patient. The remaining attendant raises the patient's legs above the plane of the body to increase venous return. Prior to this, the staff member momentarily palpates for a carotid pulse and checks to be sure the subject is breathing. If life support measures are needed, the procedures outlined above are followed.

Hypoglycemia (blood glucose < 50 mg/dL with or without symptoms) refers to abnormally low blood glucose level and occurs when there is an imbalance between the dose of hypoglycemic medications (in a treated diabetic) or the blood sugar level (in any person) and the person's food intake and activity level. Symptoms of hypoglycemia associated to the blood glucose range of 30-50 mg/dL are not very prominent in persons without diabetes. The most common are hunger (yawning) and a mild headache. Symptoms associated with blood glucose lower than 30 mg/dL may include irritability, pallor and cold sweat.

Individuals with diabetes with hypoglycemia may complain of headache, blurred vision, tingling around the mouth or tongue, tachycardia, sleepiness, weakness, feeling like they cannot concentrate or cannot speak well, nausea and dizziness. Signs of hypoglycemia range from cold sweats, shaking, slurred speech, incoherent thoughts, and passing out. Persons with history of poorly controlled diabetes, or Type 1 diabetes may not develop any symptoms or signs of hypoglycemia and suddenly pass out. Some may have visible sweat and pallor yet state "I feel fine".

Prolonged hypoglycemia may precipitate angina pectoris or seizures. *It is important to remember that symptoms of hypoglycemia are variable and may be partially masked in older participants.* If a person displays any of these symptoms after ingesting the glucola and is able to take food orally, 8oz of orange juice containing additional sugar should be given immediately and the clinic nurse or physician notified as soon as possible. If orange juice or sugar in other forms is administered a two hour blood draw is not done. This is recorded, as detailed in MOP 7. If a hypoglycemic reaction has occurred the person is evaluated by clinical staff prior to leaving the field center.

If an episode of hypoglycemia has occurred, capillary blood glucose should be rechecked within 15 minutes. Capillary blood glucose needs to be rechecked 15 minutes after every oral glucose replacement, until it is  $\geq 100$  mg/dL, and the participant is symptom-free. If  $\geq 100$  mg/dL, no further oral replacement will be necessary unless the participant complains of hypoglycemia or hypoglycemic symptoms. At checkout, blood glucose levels will be checked again. If capillary blood glucose is  $\leq 80$  mg/dL, provide juice and crackers before the participant leaves the premises, and advise to proceed with lunch as soon as possible.

If participant loses consciousness after an oral glucose test, hypoglycemia should be presumed until ruled out. **Severe hypoglycemic reactions are a medical emergency** and the person should be transported immediately to an emergency care facility. Should a participant with hypoglycemia become stuporous or non-responsive, oral replacement with glucose should not be administered in order to avoid aspiration. Glucagon intramuscularly or intravenous dextrose should be administered, and the participant needs to be immediately transferred to the nearest ER. If Glucagon or dextrose are not available, oral glucose gel can be placed on the inside of the cheeks, and immediate transfer to the ER should proceed.

**The Role of Diabetes.** Persons without diabetes or without chronic, debilitating diseases (including cancer, HIV/AIDS, liver or kidney disease, malnutrition) tend to tolerate blood glucose levels under 50 mg/dL for a longer time than persons with diabetes. Patients with diabetes (especially those with Type 1 diabetes) may have impaired hormonal responses and not be able to counteract hypoglycemia quickly. Some patients with diabetes have had elevated glucose levels for such a long time that they may experience symptoms of hypoglycemia when their blood glucose level is within normal range, but below the habitual range of their blood glucose levels. Patients with long-term diabetes (e.g. longer than 15 years) may have neuropathy (nerve damage) and experience hypoglycemia unawareness, in that they may have seriously low blood glucose levels and not perceive it. Patients with hypoglycemia unawareness are at a high risk of experiencing severe central nervous system depression (e.g. loss of consciousness, seizures, coma) if hypoglycemia is not treated promptly.

#### Emergency Equipment

A basic first aid kit is maintained at each field center. The kit contains a reference guide of its contents, and is checked every year and immediately after each use. At each field center the Study Coordinator identifies a person responsible for its maintenance.

### **19.3 Procedures to Define and Report Adverse Events and Unanticipated Problems**

As NIH-supported research that involves human subjects the HCHS/SOL study protocol includes procedures for identifying, monitoring, and reporting all adverse events (AEs, both serious (SAE) and non-serious (MAE) events), as well as Unanticipated Problems (UPs). Identification and reporting of UPs and AEs follow a uniform policy based on the FDA/Office for Human Research Protections (OHRP) regulations and guidance for definitions and timelines (<http://www.hhs.gov/ohrp/policy/advevtguid.html>).

#### **Adverse Events and Unanticipated Problems - Definition and Reporting in HCHS/SOL**

To comply with OHRP guidelines we define an adverse event as an adverse change in health or unfavorable medical occurrence that occurs in a person who participates in HCHS/SOL, which may or may not be caused by participation in the study. Adverse events include both physical and psychological harms, temporally associated with the individual's participation in the research, whether or not considered related to the subject's participation in the research. Pre-existing conditions detected as a result of participation in HCHS/SOL, its tests and examination protocols do not by themselves constitute an adverse event. Adverse events and problems that are not foreseen or mentioned in the study protocol or the informed consent are considered unanticipated. If an unanticipated problem suggests that the research places the participant at increased risk (as defined below) the unanticipated problem must be reported to the local Institutional Review Board (IRB), and to the study sponsor (NHLBI) as described below.

Adverse events and unanticipated problems must be addressed promptly according to institutional safety guidelines and the HCHS/SOL study protocol, to quickly resolve any safety concerns or participant

discomfort. The supervisor, medical director and/or principal investigator are notified according to the perceived severity of the event and the event's perceived relation to participation in the study.

### **Definition and Classification of AEs in HCHS/SOL**

#### *a. Serious (as opposed to minor or non-serious)*

An adverse event is serious (SAE) if it affected a pregnant study participant, a fetus or a newborn, or if it results in any of the following outcomes:

1. Death
2. A threat to life
3. Requires (inpatient) hospitalization, operationally defined as 24 hours or more
4. Likely causes persistent or significant disability or incapacity
5. Likely associated with a congenital anomaly or birth defect
6. Requires treatment to prevent one of the outcomes listed above, other than for pre-existing conditions detected as a result of participation in HCHS/SOL, its tests and examination protocol.

*The majority of the adverse events classified as SAEs in HCHS/SOL meet this criterion because the event required (inpatient) hospitalization, i.e., 24 hours or more from admission to discharge.*

#### *b. Expected (vs. unexpected) AEs*

An adverse event is unexpected if the risk information is not mentioned in the consent form, if the possibility of experiencing this AE is not mentioned in the study protocol, or if the AE is not reasonably expected to be related to study procedures. The study procedures in HCHS/SOL are deemed to be safe. Serious adverse events (SAEs) are therefore unanticipated and unexpected, whether study related or otherwise.

#### *c. Study-related, possibly study-related, or not study-related*

- **Related AE** – An adverse event which is related to the use of a device, procedure or an ingested substance in a way that supports a reasonable possibility (such as strong temporal relationship) that the adverse event may have been caused by the device, procedure or intervention used in HCHS/SOL.
- **Possibly Related AE** – An adverse event which is possibly study-related is one that may have been caused by a procedure, device, or ingested substance, with insufficient information to determine the likelihood of this possibility.
- **Unrelated AE** – An adverse event that has no apparent relationship to the study.

Note: Many of the AEs that occur in the course of participation in a study such as HCHS/SOL are not related to the research procedures or the setting the research takes place in.

It can be difficult to determine with certainty whether a particular AE is related or possibly related to participation in research. This often requires an assessment of how likely an AE is related to participation in HCHS/SOL, ranging from definitely related to definitely unrelated, and classified into one of three options shown above.

### **Definition and Classification of Unanticipated Problems in HCHS/SOL**

OHRP considers unanticipated problems (UP) to include any incident, experience, or outcome that meets all of the following criteria:

- a. Unexpected;

- b. Related or possibly related to participation in the research; and
- c. Suggesting that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

The large majority of adverse events are unanticipated. Unanticipated problems can include unforeseen incidents, experiences or outcomes; if they also are related or possibly related to participation in HCHS/SOL and indicate that they place the study participant or others at a greater risk of harm they qualify as a UP and HCHS/SOL personnel must act on them as described below.

In SOL all serious adverse events (SAEs) are considered to be unanticipated and unexpected, whether they are study-related, possibly study-related, or not study-related. In contrast, not all unanticipated problems (UPs) are SAEs.

### Reporting of Adverse Events and Information Flow

If a study participant experiences an adverse event or unanticipated problem, the first priority for HCHS/SOL staff is to attend to the participant’s safety. While a staff person always remains with the participant, the field center medical staff is notified, and if warranted, 911 is called. Once the participant’s safety and comfort have been addressed and the situation is not considered emergent, reports are prepared to notify the Institutional Review Board (IRB) according to each IRB’s guidelines, and all AEs and UPs are promptly recorded in the HCHS/SOL DMS (CDART). Events are recorded in CDART using the pertinent form for a Serious Adverse Event (SAE), a Minor (not serious) Adverse Event (MAE), or an Unanticipated Problem (using the UPR form). Each time a SAE or UP is entered in CDART the HCHS/SOL staff person completing this task should promptly notify HCHSAdministration by email that such a form has been entered (note: HCHSAdministration is an alias for [HCHSAdministration@unc.edu](mailto:HCHSAdministration@unc.edu)).

Completion of a SAE, UPR, or MAE form in CDART results in a review of the report by the HCHS/SOL Coordinating Center and a report of the event to the NHLBI according to schedules shown in Table 19.1. No direct notification of an adverse event or UP to NHLBI is required of the field center. Adverse events not considered serious and anticipated problems are summarized periodically by the Coordinating Center for the NHLBI, the OSMB, and the Steering Committee. The reporting schedule of AEs and UPs in HCHS/SOL is presented in Table 5 (below).

<b>Table 5. Types of unanticipated problems and adverse events, and required actions by the HCHS/SOL Staff and Timing</b>						
	<b>HCHS/SOL Field Center</b>			<b>Coordinating Center</b>	<b>HCHS/SOL Operations Committee</b>	<b>HCHS/SOL Steering Committee</b>
<b>1) Unanticipated Problem (UP)</b>						
<b>Response</b>	Address any ppt. safety issues; inform medical director and PI	Record UP in HCHS/SOL DMS (CDART), notify HCHSAdministration	Report UP to IRB	Notify NHLBI via the CC	Review study procedures; propose revisions if warranted	Review report of AE and study procedures; modify protocol if required
<b>Time / Schedule</b>	Immediate	48 hrs	72 hrs	Within 7 calendar days	Within 14 calendar days	Within 30 calendar days
<b>2) Serious Adverse Event (SAE)</b>						

<b>Response</b>	Address any ppt. safety issues; inform medical director and PI	Record SAE in HCHS/SOL DMS (CDART), notify HCHSAdministration	Report SAE to IRB	Notify NHLBI via the CC	Review study procedures; propose revisions if warranted	Review report of AE and study procedures; modify protocol if required
<b>Time / Schedule</b>	Immediate	48 hrs.	72 hrs.	Within 7 calendar days	Within 14 calendar days	Within 30 calendar days
<b>3) Minor Averse Event (MAE)</b>						
<b>Response</b>	Address any ppt. safety / comfort issues	Record AE in the HCHS/SOL DMS (CDART)	Report AE to IRB	Notify NHLBI via the CC	Review study procedures with experts; propose revisions if required	Review report of AE and study procedures; modify protocol if required
<b>Time / Schedule</b>	Immediate	48 hrs.	Within 7 calendar days	Quarterly	Within 30 calendar days	Quarterly
<b>4) Anticipated Problem, not an AE</b>						
<b>Response</b>	Address any ppt. comfort issues	Not reported (not recorded in CDART)	Report to IRB not required per OHR	Report to NHLBI not required	N.A.	N.A.
<b>Time / Schedule</b>	Immediate	N.A.	N.A.	N.A.	N.A.	N.A.

## 19.4 Conditions Ascertained at the Time of Scheduling Field Center Visit

1. Pregnancy (re-schedule)
2. Medications that need to be taken on schedule

## 19.5 Exclusions from Study Procedures

### Exclusion from Any Study Component

SBP  $\geq$  200 or DBP  $>$ 120 (Stop exam visit, arrange for urgent care; if technician unaware, this alert condition is triggered on entry into DES)

### Exclusion from Bioimpedence Estimation

Cardiac pacemakers (or automatic implanted cardiac defibrillator (AICD), if in doubt)

### Exclusions from the Oral Glucose Test and response to Glucose Meter Testing

#### A. Do not perform the OGTT (if):

1. If the participant has diabetes/is being treated for diabetes (lab technician checks Itinerary Form; asks if not marked on form).
2. If participant is on kidney dialysis. (lab technician asks; script needed)
3. If participant has had partial removal of the stomach or small intestine. (lab technician asks; script needed)

B. Check fasting plasma/blood glucose (FPG/FBG) using the glucose meter.

1. If FPG <150 mg/dL, and the participant does not have diabetes, proceed with the OGTT and the rest of the examination.
2. If the FPG  $\geq$  150 mg/dL, do not proceed with the OGTT. Explain according to script and enter result on the form (for report to be discussed during exit interview).
3. If the FPG 200-399 mg/dL proceed as follows:
  - a. Ascertain symptoms of hyperglycemia (follow script on thirst, frequent urination, dizziness, active infection, or blurred vision).
    - If symptoms(s) present refer to the emergency room.
  - b. Measure urine for ketones.
    - If the urine dipstick is positive for ketones, refer to the emergency room.
    - If the urine dipstick is negative for ketones, refer to the participant's health care provider, or a referral physician to be evaluated within a week.
4. If the FPG  $\geq$  400 mg/dL **STOP** the examination and refer to the emergency room (regardless of the presence of symptoms).

## **19.6 Stopping Rules for Interviews and Procedures**

### **Participant Safety/Alert Thresholds on Study Measurements**

If a participant feels unwell or if an alert value is met on a study measurement the participant is referred to health care and the remainder of the field center examination may be deferred, according to the action levels identified in previous sections of this manual. If the health care referral is an alert value or if the examination is discontinued field center personnel explain the urgent need to seek medical care and assist the participant in making an appointment if this is helpful. The study participant is also told that HCHS/SOL personnel will contact him/her within 48 hours as a courtesy follow up. During this follow-up call field center personnel confirm that the participant has seen a doctor, or has understood the need to seek medical care.

Within 3 months after the initial visit the participant is contacted to complete the examination. Section 15.2 of this manual describes the procedures by which to follow up on an examination that was deferred because of an elevated blood glucose. A similar process is followed to schedule a continuation visit for field center examinations interrupted because of an elevated blood pressure, a major acute abnormality detected on an electrocardiogram, or similar alert referrals. On re-contacting the participant HCHS/SOL personnel ask whether she/he has seen a doctor for the condition that prompted the referral. If the participant has not seen a physician he/she is again encouraged to do so (but no clinic visit is scheduled). If the participant reports having seen a physician field center personnel ask if the participant feels well enough to schedule the continuation of the HCHS/SOL examination visits and proceed according to the response.

### **Fatigue/Discomfort**

Interviewers and technicians observe participants for signs of fatigue or physical and/or emotional discomfort. When any one of these conditions are observed, participants are offered the opportunity to discontinue the interview or procedure, and are given an opportunity to rest before being taken to the next work station. If in the course of the field center visit a participant seems to exhibit anxiety when instructed to perform tasks or shows a pattern of repetition or empty responses during interviews and/or seeks assistance from others during interviews, the staff person uses a break between procedures to bring this to the attention of the supervisor. The supervisor can decide whether the participant should be asked to complete the longer interviews that remain on the participant's schedule. Persons incapable of completing the full field center exam are invited to change back into their street clothes and participate in the exit review and reschedule the clinic exam on another day.

## **19.7 Mental Health Emergency Procedures**

In the course of the HCHS/SOL field center activities there are a number of circumstances that require training and judgment on the part of staff, consultation regarding clinical decision making, and filing of incident reports. They include medical emergencies, participants who may be suicidal, participants who may be homicidal, participants who appear intoxicated, indications that it may be necessary to file a child abuse report, and circumstances when it may be necessary to file an elder or dependent adult abuse report.

While several of these situations will not be directly assessed in HCHS/SOL, procedures are in place at the HCHS/SOL field center for the eventuality that any of these issues arise during the course of the study. Each of these instances must be handled with caution and sensitivity, in a way that ensures

that the appropriate clinical decisions are made. Information regarding each of these separate circumstances is presented below.

HCHS/SOL field centers have personnel trained to respond to physical and medical emergencies, and certified according to their institutional policies. As mentioned above, contact and locator information for medical emergencies and physical threats are displayed throughout the field center. In all emergencies and crises study personnel contact the supervisor, consultant or security personnel according to the circumstances. If the situation is associated with potential harm to a study participant, action is taken and resolved prior to the participant's departure from the premises. An incident report is filed and documented within 24 hours of an incident in order to provide a record of the actions taken by the staff and supervisors. The study principal investigator is informed of the incident and of any action taken by the study personnel.

#### Participant Appears Intoxicated

Participants who arrive at the field center potentially intoxicated are asked not to participate in the research procedures at that time. The clinic manager is notified of any suspicion of intoxication. The interviewer or clinician will explain to the participant why he or she will be excluded from the procedures and why s/he should leave the research premises (i.e. that s/he appears to be intoxicated, smells like alcohol, is staggering). To protect the participant from possible injury, interviewers and/or clinicians must make sure that the client does not drive home, either by calling a taxi or calling the police to escort him/her home. Intoxication must be documented as an incident report.

#### Participant Threatens to Harm Another Person

Although clinical determinations about the lethality of a person's homicidal ideations are quite inaccurate the following basic rules to follow are suggested:

- If the participant has a plan and a means for carrying out the threat, lethality is considered to be high.
- If the intended victim is in immediate danger, it may be necessary to contact the intended victim and warn him or her of the threat. It is also necessary to contact police and attempt to have the participant placed on a 72-hour hold. Contact \_\_\_\_\_ to help you make this determination.
- If the participant indicates that s/he has not formulated a plan, it may only be necessary to establish a contract with the participant to prevent the attack. This decision must be made in consultation with \_\_\_\_\_.

## 19.8 Procedure for Reporting Child Maltreatment

Law mandates the report of *any suspicion* of child maltreatment, including abuse and neglect. Failure to report is a felony. Mandated reporters are protected under the law from civil suit, should the report prove to be false. This protects those who are carrying out the law from being sued for false reports.

If study personnel discover information that leads to a concern about child maltreatment (refer to definitions below), several steps are important.

First, consult the Field Center Manager. You will most likely need to ask follow up questions.

Second, if you and your supervisor feel the information warrants a report: the law, [Florida Statue Chapter 39], states, “Each report of known or suspected child abuse, abandonment, or neglect pursuant to this section shall be made immediately to the department’s central abuse hotline on the single statewide toll-free telephone number.”

Third, it is in the best interest of the child and the family if the family does the reporting. If appropriate, the supervisor can determine how to talk with the family about the need for reporting, and the family can be offered the following options.

- The best is for the family to call. Staff is responsible for making sure that they do so, however. Therefore, staff may offer to be in the room with them.
- Most families find it very difficult to self-report. Therefore, another very good option is for staff to call the hotline with the family in the room.
- Staff can also let the family know that if they don’t want to call in that way, staff will be making the call and ask them if there are things they want to make sure you inform DCF about (especially efforts they are making to ameliorate the maltreatment).

Other important issues when calling in an abuse report:

1. Call in the morning – DCF has strict timelines for investigations; a call in the morning makes it more likely that the case is addressed at a time when staff can be reached.
2. Ask to be either the “first point of contact” or “a point of contact.” If you are the first point of contact, they will contact you first, before contacting the family or child. This may be important if you are worried about retribution to the child or other issues. Asking to be a point of contact allows you to give the information you would like to make sure that DCF has. This is an important step to remember.

Statutory definitions of child abuse are kept in at a field center, conveniently retrievable by the supervisors and staff.

## **20. REPORT OF STUDY RESULTS, MEDICAL REFERRALS AND NOTIFICATIONS**

HCHS/SOL is committed to serve its study participants and their communities by returning as much scientific information that has applicability and translational value as is possible. In the same spirit, all study results that have value in the context of medical diagnosis or treatment are reported to the study participants, in ways that are consistent with current guidelines endorsed by professional societies and governmental agencies. Laboratory tests and examinations performed by HCHS/SOL that are of research value only and not directly relevant in the context of current guidelines are not reported, to avoid burden to the study participants and their medical practitioners. As part of the informed consent process, study examinees are told that they are participating in a research study which is guided by a research protocol. They are informed that the HCHS/SOL procedures are not identical to those performed in a regular clinical examination, and that only study results that are of known value to medical practitioners are returned. The type of result returned and the reporting schedule are described in this section.

### **20.1 Procedures for Medical Referrals and Notification of Results**

Although HCHS/SOL does not diagnose or treat any medical condition, the participant's safety is of paramount concern. Therefore, data collected during the examination that could indicate the need for referral for medical care are reviewed with the participant prior to the completion of the examination. The type of study result to be reported to the study participant and the schedule of notification also are reviewed at this time.

### **20.2 Reporting of Results to HCHS/SOL Participants**

In its feedback to the participants, the study relies on established guidelines and other evidence-based documentation that practitioners in the community refer to. Values or measurement results that exceed the thresholds underwritten by treatment guidelines are identified for the participant with a recommendation for review and or confirmation in consultation with their provider of medical care. The study defines these notifications as a referral, although such notifications emphasize to the study participant and his/her provider of care that the results originate from a research protocol and cannot be equated to a clinical evaluation.

### **20.3 Medically Relevant Information**

Medically relevant information is provided to the study participants and their providers of medical care, if so authorized by the study participant. If consent to provide this information to the person's physician was given as part of the informed consent process, copies of the reports of study results are sent to the participant's physician. No study information is shared with other persons or entities, except with the written authorization of the participant, or as required by law. Copies of prototype reports are shown in the Appendix.

Procedures are in place throughout HCHS/SOL to identify clinically relevant values in the study data that are so abnormal as to be considered an "alert value." This applies to measurements performed at the field centers and to study data processed at the Central Laboratory and the Echocardiography Center. Alert values trigger a rapid notification process described below. Study results that exceed the study guidelines are identified to the study participant as requiring consultation with their provider of medical care for purposes of confirmation. Lastly,

measurements and assay results that are within normal ranges according to the guidelines in use in HCHS/SOL are reported in a consolidated summary report to the participant once all information has converged at the collaborative database. This report includes any results previously reported to the study participant on an expedited schedule (such as “alert values”).

Consequently, medical information is provided to participants (and physicians) at the following points:

- (1) During the exit interview at the conclusion of the field center examination, at the time a staff member gives the participant a printed "clinic visit report." This “clinic visit report” also indicates to participants that they will receive by mail a copy of the interpretation of their echocardiogram and selected blood tests, with feedback on their meaning.
- (2) Study data processed by the HCHS/SOL central laboratory and the HCHS/SOL reading centers are transmitted to the Coordinating Center where they are interrogated daily to generate a (daily) Alert Notification Report. From it, notifications to study participants are prepared at the Coordinating Center according to the criteria summarized in this document, and immediately made available the corresponding field center in a secure section of the HCHS/SOL website. Field center personnel download alert notifications and reports of study results on a daily schedule. If an alert report is received, field center personnel print a customized Participant Alert Letter (see Appendix) and a Physician Alert Letter (if permission was obtained to release these data to a physician).
- (3) Once all results from the Central Laboratory and the central reading centers are received at the Coordinating Center, the Summary of Results is prepared and made available to the field centers on their secure portion of the study website. These reports are to the study participants and their physician (if permission was obtained to release these data) by the field centers, under customized cover letters. The date a Summary of Results sent is recorded in the Report and Referral Tracking Form.

#### **20.4 Study Results Reporting Schedule**

HCHS/SOL implements an expedited notification schedule for study results of potential medical significance that may require prompt attention by the participant and his/her physician.

Field centers download the notifications of alert values (and also study results not processed on an expedited schedule) daily, by accessing the web based study data management system. Field sites that fail to access the Alert Reports page and have pending notifications are automatically contacted by the Coordinating Center through email messages addressed to the project manager until the pending notification has been acted on.

**Immediate Action/Notification.** The study identifies certain conditions as carrying high risk or constituting medical emergencies that require **immediate notification** of both the participant and his/her primary physician (if the consent authorized contacting the physician). Results that require immediate action by field center personnel include two consecutive blood pressure measurements exceeding a systolic of 200 mm Hg or a diastolic of 120 mm Hg, an average heart rate per the OMRON sitting blood pressure device that is 40 bpm or lower, or 100 bpm or greater, or an adverse event or medical emergency that occurs during the participant’s visit at the study field

center. The response by the staff is to bring this information to the attention to the Field Center study clinician on site without delay. The study nurse or the physician on call will evaluate the situation and arrange for a transfer of the participant directly from the field center to their physician or a hospital emergency room, as indicated.

Each time results are uploaded to the central database by the central laboratory the data are queried according to the threshold levels identified in Table 7. As an example, if a triglyceride value is  $\geq 1000$  m/dL an Alert Notification is generated for the respective field center, identifying it as an Immediate Action and posted on the corresponding center's secure website portion. Field centers review their alert notifications (and regular result reports) daily on their secure pages of the study website maintained by the HCHS/SOL coordinating center.

Once aware of an immediate notification field center staff initiates a phone call to the participant and his/her physician's office, in addition to sending the corresponding letters documenting this result. The telephone conversation should confirm the identity of the party and communicate the information in the relevant Alert Letter. Referral of an immediate alert value – during the Exit Interview or subsequently on receipt of an Immediate Alert Notification from the Echocardiography Reading Center or the coordinating center – requires that field center staff follow up with the participant or a designated contact person within days to find out whether the recommended referral was understood and implemented. If the participant has instructed the study personnel to report study results to him/her and not to a health professional, it is important for staff to verify that the study participant is aware of the nature of the condition being reported as an alert and its potential health implications.

**Alert reports** are urgent referrals made for abnormalities that require medical attention but not on an emergency basis. An alert report to the participant's physician is sent as soon as possible but no later than four days of receipt of the information by the field center.

A **routine summary report** of all study results is communicated in a report of results from the HCHS/SOL once all study results are available to the field center personnel, or on a partial set of results if requested by the field center for compelling reasons. Values that exceed the reference thresholds are identified as **referrals** since they meet established guidelines for medical diagnosis / care but do not require expedited notification. The text that accompanies such values in the summary report to the study participant (see Appendix) indicates that it represents a single determination of values that require confirmation, emphasizing that the report of study results does not substitute for a physician's examination.

Summary reports of results are sent as soon as the results for a study participant are complete, or after two months following the visit should a particular result / interpretation be delayed. In the latter case, the incomplete result is sent and a complete report of results follows as soon as the missing items become available.

## 20.5 Thresholds for Referral and Reference Ranges for Study Results

### Seated Blood Pressure and Heart Rate

Three measurements of seated blood pressure are recorded with a OMRON HEM-907XL IntelliSense® digital blood pressure monitor, after a five-minute rest period. The averaged value of the three measurements is reported to the study participant during the exit interview. The blood pressure measurements and the actions to be taken are reviewed according the 2014 [Report From the Panel Members Appointed to the Eighth Joint National Committee \(JNC 8\)](#) *JAMA*. 2014;311(5):507-520.PMID These guidelines are used by the HCHS/SOL personnel in communications with the study participant and in making follow-up recommendations as summarized below.

Table 6A. Classification of Blood Pressure in Adults Aged 18 Years or Older, and Recommended Action per JNC 8\*

Age Group	Blood Pressure Goal -- Ppt. does not have Diabetes or CKD	Blood Pressure Goal -- Ppt. has Diabetes and/or CKD
Age <60 years	SBP <140 and DBP <90 mm Hg	SBP <140 and DBP <90 mm Hg
Age ≥60 years	SBP <150 and DBP <90 mm Hg	SBP <140 and DBP <90 mm Hg

SBP= systolic blood pressure. DBP= diastolic blood pressure.

\* Source: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8) *JAMA*. 2014;311(5):507-520.PMID

\*\* Diagnosis of hypertension must be based on two or more readings taken at each of two or more visits following an initial screening.

JNC 8 states that blood pressure classifications and referral recommendations are based on the average of two or more readings on two or more occasions. HCHS/SOL uses the average of 3 blood pressure readings in order to reduce the impact of reactivity (first readings are usually higher) on the estimate of the value of the underlying blood pressure. In deciding whether a participant meets criteria for an alert level, the average of the 2<sup>nd</sup> and 3<sup>rd</sup> readings are used. The data forms include fields for these averaged values and for any actions taken.

Safety alert notifications based on blood pressure values are described below. Unless an immediate referral (Diastolic BP ≥120 mmHg or Systolic BP ≥200 mmHg) has been initiated at the time the participant's blood pressure was measured, a referral may take place during the Exit Interview.

Table 6B. Classification of Blood Pressure in Adults Aged 18 Years or Older per JNC 8, and Recommended Action by the HCHS/SOL

Known Diabetes or CKD?	Age Category	Measured Blood Pressure Level and Blood Pressure-lowering Treatment (All values in mmHg)		Action Recommended
No	Age <60 yrs.	Not on treatment for HTN	SBP <140 and DBP <90	Your blood pressure is in the normal range for your age. Have your blood pressure measured by a health professional at least every two years
			SBP ≥140 or DBP ≥90	Your blood pressure is above normal for your age. Have your blood pressure measured by a physician within two months
		On treatment for HTN	SBP <140 and DBP <90	Your blood pressure is in the normal range for your age. If you are being treated for high blood pressure, please follow your physician's instructions
			SBP ≥140 or DBP ≥90	Your blood pressure is high. Please have your blood pressure checked by a physician within two months.
No	Age ≥60 yrs.	Not on treatment for HTN	SBP <140 and DBP <90	Your blood pressure is normal for your age. Have your blood pressure measured by a physician at least every year
			SBP 140-150 and DBP <90	Your blood pressure is somewhat elevated. Please have your blood pressure measured by a physician within six months
			SBP ≥150 or DBP ≥90	Your blood pressure is high. Please have your blood pressure measured by a physician within a month.
		On treatment for HTN	SBP <140 and DBP <90	Your blood pressure is in the normal range for your age. If you are being treated for high blood pressure, please follow your physician's instructions
			SBP 140-150 and DBP <90	Your blood pressure is somewhat high. Please report this blood pressure result to your physician at your next appointment.
			SBP ≥150 or DBP ≥90	Your blood pressure is high. Please have your blood pressure checked by a physician within a month
Yes	Not Applicable	Whether or not treated for HTN	SBP <140 and DBP <90	Your blood pressure is in the normal range. If you are being treated for high blood pressure, please follow your physician's instructions
			SBP ≥140 or DBP ≥90	Your blood pressure is high. Please have your blood pressure checked by a physician within two months.

\* When recommendation for follow-up of DBP and SBP are different, the shorter recommended time for recheck and referral should take precedence. This classification applies only to participants not taking antihypertensive drugs.

### **20.5.1.1 Heart Rate**

At the time the average heart rate is recorded on the SBP form, HCHS/SOL personnel takes action on heart rate values that are 40 bpm or lower, or 100 bpm or greater, by bring this result to the attention of the study clinician on site before participant leaves the field center. The study nurse, or the physician on call will evaluate this situation and refer the study participant for evaluation by their provider of care or to an Emergency Department, as deemed appropriate. If after evaluation by the study nurse or physician the participant is encouraged to proceed with the HCHS/SOL examination the echocardiography technician should be alerted to the observed average heart rate value.

### **20.5.1.2 Reporting of Echocardiographic Findings to Field Centers**

Echocardiography is performed in the HCHS/SOL to assess cardiac structure and function by qualified sonographers trained in the HCHS/SOL protocol study. Studies are acquired digitally and transferred electronically to the HCHS/SOL Echocardiography Reading Center, where all quantitative measures of cardiac structure and function are performed. Please see protocol manuals 17a – Echocardiography Field Centers, and 17b – Echocardiography Reading Center.

Reporting of findings to participants or site investigators occurs at multiple points:

1. Sonographers performing echocardiographic studies occasionally identify abnormalities that they consider important. These findings include, but are not limited to, tamponade, aortic dissection, thrombosed or frankly dysfunctional prosthetic valve, pseudoaneurysm, intracardiac abscess or obvious vegetation, and intracardiac thrombus. The site investigator is notified directly by the sonographer for review and action, and the Echocardiography Reading Center also is informed via a “critical alert” checkbox and a free text field in the electronic Echocardiography Transmittal Form (ETF) to facilitate an expedited analysis of the study. Site investigators are responsible for handling alert findings (either as alerts requiring emergency/immediate referral, urgent referral, or routine referral as they deem appropriate), including relaying findings to study participant and, where consent has been provided, to the participant’s provider of medical care.
2. Over-reading cardiologists at the Echocardiography Reading Center may identify critical abnormalities that would require emergent notification and arrangements for care. Such findings are reported within 24 hours of review by the Reading Center to the Coordinating Center and are communicated to the field centers as an Immediate Alert Notification.

Abnormalities that trigger a critical result include, but are not limited to a) tamponade, b) aortic dissection, c) thrombosed or frankly dysfunctional prosthetic valve, d) pseudoaneurysm, e) intracardiac abscess or obvious vegetation, f) intracardiac thrombus. Each field center has a plan for handling these types of alerts, including relaying findings to study participant and, where consent has been provided, to the participant’s treating provider.

3. Over-reading cardiologists at the Echocardiography Reading Center may identify specific non-critical abnormalities that would be important for a patient and physician to be aware of, but that don’t necessarily require emergent attention. These findings are incorporated into the routine data transfers from the Echocardiography Reading Center to the Coordinating Center.

Such findings include: a) moderate or greater mitral regurgitation, b) moderate or greater mitral stenosis, c) moderate or greater obstructive lesions of left ventricular outflow, including aortic stenosis and dynamic left ventricular outflow tract obstruction, d) moderate or greater aortic regurgitation, e) moderate to severe pulmonary hypertension, f) severe right ventricular enlargement.

- Limited quantitative data is included in the routine reporting letter generated by the data coordinating center for all HCHS/SOL participants. This includes three commonly used measures of cardiac structure and function: a) left ventricular ejection fraction, b) left ventricular diastolic diameter, c) left ventricular wall thickness. These data are presented in a table with reference values.

### Blood Chemistries

All laboratory assays are performed at the HCHS/SOL Central Laboratory at the University of Minnesota, which also maintains the HCHS/SOL biospecimen repository (see Manual 7). The reference and alert values used by the Central Laboratory, summarized in Table 7, correspond to current recommendations by the National Cholesterol Education Program and national professional associations. The Bronx Field Center has received assurances that glycosylated hemoglobin (hemoglobin A1c) for the HCHS/SOL examinees need not be reported to the NYC Health Department.

Table 7. HCHS/SOL Visit 2 Laboratory Assays, Reporting Reference and Alert Ranges

<u>Test Name</u>	<u>Reference Range</u>	<u>Units</u>	<u>Reported to Participant</u>	<u>Alert Value</u>
<b>*Hemogram (CBC):</b>				
White Blood Count (WBC)	4.0-11.0	x 10 <sup>9</sup> /L		<2 and >25
Red Blood Count (RBC) – male	4.4-5.9	x 10 <sup>12</sup> /L		
Red Blood Count (RBC) – female	3.8-5.2	x 10 <sup>12</sup> /L		
Hemoglobin - male	13.3-17.7	g/dL		<8 and >20
Hemoglobin - female	11.7-15.7	g/dL	Yes	<8 and >20
Hematocrit – male	40.0-53.0	%		
Hematocrit – female	35.0-47.0	%		
Mean Corpuscular Volume (MCV)	78-100	fL		
Mean Corpuscular Hemoglobin (MCH)	26.5-33.0	pg		
Mean Corpuscular Hemoglobin Concentration (MCHC)	31.5-36	g/dL		
Red Cell Distribution Width (RDW)	10.0-15.0	%	No	
<b>*Platelet Count</b>	<b>150-450</b>	<b>x 10<sup>9</sup>/L</b>	<b>Yes</b>	<b>&lt;50 and &gt;1000</b>
<b>WBC Differential:</b>				
Neutrophils	40-75	%		
Lymphocytes	20-48	%		
Monocytes	0-12	%		
Eosinophils	0-6	%		
Basophils	0-2	%	No	
Absolute Neutrophils	1.6-8.3	x 10 <sup>9</sup> /L		
Absolute Lymphocytes	0.8-5.3	x 10 <sup>9</sup> /L		
Absolute Monocytes	0-1.3	x 10 <sup>9</sup> /L		
Absolute Eosinophils	0-0.7	x 10 <sup>9</sup> /L		
Absolute Basophils	0-0.2	x 10 <sup>9</sup> /L		
<b>*Total cholesterol</b>	<b>&lt;200</b>	<b>mg/dL</b>	<b>Yes</b>	
<b>*Triglycerides</b>	<b>&lt;150</b>	<b>mg/dL</b>	<b>Yes</b>	<b>&gt;1000</b>
<b>*HDL-cholesterol</b>	<b>&gt;40</b>	<b>mg/dL</b>	<b>Yes</b>	

Table 7. HCHS/SOL Visit 2 Laboratory Assays, Reporting Reference and Alert Ranges

<u>Test Name</u>	<u>Reference Range</u>	<u>Units</u>	<u>Reported to Participant</u>	<u>Alert Value</u>
*LDL-cholesterol, calculated	<129	mg/dL		
*Glucose, fasting	60-99	mg/dL	Yes	<50 and >400
Glucose, post OGTT	50-139	mg/dL	Yes	
*Glycosylated Hemoglobin	4.3-6.0	%	Yes	
Insulin, fasting	12-150	pmol/L	No	
Alanine aminotransferase (ALT), male	0-40	U/L	Yes	
Alanine aminotransferase (ALT), female	0-31	U/L	Yes	
Aspartate aminotransferase (AST), male	0-37	U/L	Yes	
Aspartate aminotransferase (AST), female	0-31	U/L	Yes	
Gamma-glutamyltransferase (GGT), male	11-51	U/L	Yes	
Gamma-glutamyltransferase (GGT), female	7-33	U/L	Yes	
Cystatin C	0.51-1.05	mg/L	No	
*Creatinine, male	0.5-1.2	mg/dL	Alerts only	>2.0
*Creatinine, female	0.4-1.1	mg/dL	Alerts only	>2.0
*eGFR	>60	mL/min/1.73m <sup>2</sup>	Yes	
*Albumin/creatinine ratio	<30	mg/g creatinine	Yes	

#Reference ranges for these tests are given in the form of a comment accompanying all result reports: National Cholesterol Education Program guidelines suggest that : 1) LDL-cholesterol values less than 100 mg/dL are optimal, 100-129 mg/dL are near or above optimal, 130-159 mg/dL are borderline high, 160-189 mg/dL are high. 190 mg/dL and above are very high; and 2) HDL-cholesterol values below 40 mg/dL are undesirable. (JAMA 2001; 285:2486-2497).

\* Reported if requested by the study participant

## 20.6 Conveying the Report of Results to the Study Participant

Given the relatively large number of results reported, the lack of familiarity of the public with such results, and possible language barriers since the results are provided in English, HCHS/SOL the Study provides a user-friendly overview of the report of study results to facilitate their comprehension and reduce the chance for study participants to miss potentially important results.

To implement this approach field centers prepare a personalized cover letter in the participant’s preferred language, to accompany the report of results and identify key study results (if any are clinically significant). In turn, to assist field center personnel in reviewing a participant’s results and prepare the cover letter, an algorithm has been developed that prints the results that exceed laboratory or clinical guideline thresholds (see below). From this – and an awareness of the participants’ age, possible comorbidity and other elements – the field center clinician can ascertain whether a result that exceeds threshold is trivial or potentially important. This list for the field center personnel is printed as an extra page marked “not for distribution,” each time a report is downloaded at the field center. Examples of such overviews are attached.

**List of the Messages Displayed for Field Center Clinical Personnel,  
Based on Result Values that Exceed Reporting Thresholds  
*Not for Distribution to Participants***

- The heart rate is low
- The heart rate is high
- The blood pressure is very high.
- The blood pressure is high.
- The blood pressure is high (With Medication).
- The Glycosylated Hb is high
- The White Blood Cell count is high.
- The White Blood Cell count is low.
- The Hepatitis B/C test is/are positive

(Different for Men and Women)

- The Red Blood Cell count is high.
- The Red Blood Cell count is low.
- The Hemoglobin count is high.
- The Hemoglobin count is low.
- The Hematocrit is high.
- The Hematocrit is low.
- The triglyceride is very high.
- The triglyceride is high.
- The MCV is high.<BR>
- The MCV is low.<BR>
- The MCH is high.<BR>
- The MCH is low.
- The MCHC is high.
- The MCHC is low.
- The RCDW is high
- The RCDW is low.
- The Platelet count is high.
- The Platelet count is low.
- The fasting blood glucose is very high.
- The fasting blood glucose is high.
- The 2-hour blood glucose test was somewhat high.
- The 2-hour blood glucose test was high.
- The Total blood cholesterol is high.
- The HDL cholesterol is low.
- The LDL cholesterol is very high.
- The LDL cholesterol is high.
- Estimated kidney function less than 60 ml/min/1.73 m
- Estimated kidney function less than 30 ml/min/1.73 m
- The serum creatinine value is high.
- There is a mild elevation of protein in the urine.
- The protein in the urine is elevated.

## **20.7 Quality Assurance**

Actions taken in response to an alert value are documented on the Report and Referral Tracking form. The occurrence of an alert condition and its processing from the originating laboratory or reading center to the notification of a study participant and/or the physician is journaled by the data management system maintained by the Coordinating Center. The timeliness of this process and its successful completion according to study protocol are included in the quality analyses performed by the Coordinating Center and are periodically reviewed by the Quality Control Committee

## **21. Appendix I List of Study Forms**

The Study has all forms posted on the Investigator's website at the Forms page found from the Documents tab [ <https://www2.csc.unc.edu/hchs/forms> ]. Forms are divided logically by purpose: Administrative, Data Collection, and Annual Follow-Up.

## **22. Appendix II Evening Examination Visits and Examination of Relocated SOL Participants**

On January 11, 2017 the HCHS/SOL Steering Committee approved the following procedures to conduct Visit cohort examinations as evening visits, and for cohort members that relocated in proximity to another HCHS/SOL field center.

### **I. Abbreviated Visit 2 exams conducted as evening visits**

Background. The steering committee approved conducting Visit 2 examinations as evening visits, as an option field centers may consider for hard-to-recruit participants.

#### **a. Study Protocol**

Per standard study protocol: split the exam visit to allow for fasting blood draw and a snack in the AM, with the remainder of the data collected in the afternoon/evening. This option is best suited to preserve data quality and standardization.

As an exception to protocol: if it is not possible for the participant to have blood drawn in the AM, schedule abbreviated exam in the PM. Make the participant aware of the limitations to their study results introduced by non-fasting values. When reporting the study results to the participant and the provider of medical care the field center personnel has to identify the reported study results as non-fasting.

The exception to study protocol is captured in the database by recording the time of venipuncture and specimen processing, time food was last consumed, etc., as provided on the BIO study form. At the time of statistical evaluation of the HCHS/SOL data, analysts will be responsible for decisions concerning the minimum desirable length of fasting for individual analytes, and for the pertinent exclusions from statistical analyses.

#### **b. Staffing and participant safety**

Functions to be covered by certified staff in the evening: anthropometry, biospecimen collection & processing, sitting blood pressure, interviews, clinically trained staff on site while a participant is on the premises.

#### **c. Data quality and Logistics**

For afternoon blood draws the last FedEx package pick-up guaranteed for next day delivery is typically 4:00 pm. Shipments that are not ready by 4 pm require drop-off by the closing time at the local shipping office. Local options for such arrangements differ by center. The quality of the CBC data will likely be compromised. As reviewed on the 12/16 call: CBC samples dropped off in the late afternoon are effectively 2 days old when processed at the Central Lab.

### **II. Field center exams of HCHS/SOL cohort members that relocate**

Background. A small number of HCHS/SOL cohort participants has moved out of their original geographic study area, and in several instances have relocated in relative proximity to other HCHS/SOL field centers. This enables visit 2 examinations conducted at a host field center,

according to the following study management and procedures approved by the HCHS/SOL Steering Committee.

- i. HCHS/SOL participants may be examined following the standardized study protocol at any of the HCHS/SOL field centers
- ii. Cohort members that move from their original HCHS/SOL study site to an area in proximity to another HCHS/SOL field center are transferred to a host center based on the participant's stated willingness to participate in HCHS/SOL examinations at the host center, and that center's agreement. The procedures by which this transfer is implemented are presented in the memorandum from Marston Youngblood and Maria de los Angeles Abreu dated January 26, 2016 (see below). The record of HCHS/SOL participants transferred to another field center and their ID assignments is kept on administrative forms at the Coordinating Center staff.
- iii. Relocated study participants that are not transferred to another HCHS/SOL field center continue to be followed up – and their reported health events investigated – by the HCHS/SOL field center of origin.
- iv. The host center is responsible for scheduling, staffing, supplies, reimbursements and participant incentive.
- v. The host center communicates alerts and reports the study results.
- vi. Completed examinations by relocated HCHS/SOL cohort members are tracked by the Coordinating Center so that the host field center and the field center of origin can be credited toward the 80% re-examination of the cohort.
- vii. For purposes of statistical analyses & publication of the HCHS/SOL data, cohort members retain their study site of origin.
- viii. HCHS/SOL participants that relocate are eligible for ancillary studies. They may be recruited by the host field center for ancillary studies.

FROM: Marston Youngblood and Maria de los Angeles Abreu,  
HCHS/SOL Coordinating Center

TO: HCHS/SOL Clinic and Project Managers

DATE: January 26, 2016

RE: Procedures for Transfer of HCHS/SOL Participant to Another Field Center

On occasion a HCHS/SOL cohort participant may notify their contact at the field center that they are moving permanently to another city, but wish to remain engaged in the study by attending examinations and participating in annual follow-up interviews. The participant will need to actively agree that their contact information should be shared with the staff at the new location. If the participant is relocating to within one of the four metropolitan area covered by the HCHS/SOL their continued participation is highly encouraged. However, in order for us to manage the secure transfer of the cohort member information to the new center, the following procedures will need to be followed.

**Participant Transfer protocol:**

- The process should start with basic communication between sites related to the participant, i.e. when they find out that the transfer will definitely happen. The original baseline exam site and new transfer site should inform each other of the expected date that the participant will arrive in their new host city.
- Baseline site will provide the participant ID to be transferred and the new site city location to the CSCC.
- CSCC will provide new Site the HCHS/SOL transfer ID for that participant.
- Data from the old ID number (baseline visit ID) will be transferred to the new ID number (HCHS transfer ID) into CDART for future data entry for Visit 2, new AFU interviews, and ancillary studies.
- It is important to understand the participant will be fully engaged at the new site when the transfer becomes effective. This means future calls for AFU and investigation of hospitalizations that occur in the new locale will both be done from the new transfer site.
- Investigations of old/ongoing hospitalizations that occurred at the original center need to be completed at that location using the original ID.

If field centers have specific questions that are unique to their participant's circumstances they should contact the coordinating center for guidance.