Manual 2
Field Center Procedures

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Study website - http://www.cscc.unc.edu/hchs/

Tracking of Revisions to HCHS/SOL Protocol Manuals

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APPENDICIES TO MANUAL 2 (Distinct documents - refer to listing below)

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- Administrative forms, checklists and logs
- Scripted instructions for field center procedures
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1. FOREWORD

This manual, entitled **Field Center Procedures** is one of a series of protocols and manuals of operation for the Hispanic Community Health Study (HCHS) / Study of Latinos (SOL). Because a large number of procedures need to be described in detail for this study, detailed manuals of operation have been organized into a set of protocol manuals. 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 field center examination, references to the procedures not covered here, and appendices of forms and question by question instructions for their administration. 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 lists the main components of the field center 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 familiar with this manual of procedures. To meet our scientific goals and to make this study a success, all HCHS/SOL field center technicians must be fully 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 ancestry, 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 us to be able to meet our obligations to the study participants, to the scientific community and to our 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.

2. 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 maintain 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.

Table 1. Outline of HCHS/SOL Baseline Field Center Examination Visit, with Reference to the Corresponding Manuals of Procedure and Study Form Codes

Exam Procedure, fasting status specification (F)	Manual of Procedure (MOP)	Form codes (Engl, Span)
Pre-visit screening (eligibility, safety)	2	ELE, PSE, PSS
Reception, itinerary checklist form (F)	2	CHK
Informed consent (F)	2	ICC
Change clothes / urine specimen (F)	2	--
Anthropometry (F)	2	ANT
ECG (F)	5, 2	--
Ankle brachial SBP (persons aged 45-74 yrs)	2	ABP
Seated BP (F)	2	SBP
Phlebotomy (F)	7, 2	BIO
Glucose load (F)	7, 2	BIO
Blood processing / lab	12	BIO, PHT
24-hr dietary recall, supplements	11	--
Other interviews:	2	--
Alcohol	2	ALE, ALS
Dietary behavior	2,11	DBE, DBS
Economic background	2	ECE, ECS
Health care use	2	HCE, HCS
Hearing Exam Qx	8, 2	HEE, HES
Hearing Hx	2	HHE, HHS
Medical Hx	2	MHE, MHS
Medication & Supplement use	2	MUE, MUS
Neurocognitive (persons aged 45-74 yrs)	9	NEE, NES
Occupation	2	OCE, OCS
Oral Health	10	OHE, OHS
Personal identifiers	2,13	IDE, IDS
Personal information	2,13	PIE, PIS
Physical activity	2	PAE, PAS
Respiratory Hx	4, 2	RSE, RSS
San Diego Claudication Qx	2	
SF-12 Health Status	2	SFE, SFS
Sleep Hx	6, 2	SLE, SLS
Social Network	2	SNE, SNS
Sociocultural	2	SCE, SCS
Tobacco use	2	TBE, TBS
Weight Hx	2	WHE, WHS
Wellbeing	2	WBE,WBS
Audiometry	8	AUD, OTO, TYM
Oral examination	10	OHE, OHS
Lung function	4	--
2-hr. phlebotomy	7, 2	BIO
Snack	2	--
Exit interview	2	--
Sleep & activity monitoring instructions and tracking	2, 6	CHK

3. SAMPLING AND RECRUITMENT

The sampling and recruitment plan for the study is designed to support two analysis objectives. First, the study sample supports estimates of prevalence of baseline risk factors, both overall and by country of origin and other demographic subgroups. Second, the sample supports evaluation of the relationships between the various risk factors and disease outcomes measured during follow-up. To accomplish both objectives, a representative sample of participants in the target areas at each field center is selected. Methods of sample selection, recruitment, and retention are designed to maximize participation rates, minimize non-response, and minimize attrition during the follow-up period.

Sample selection is accomplished through a two-stage area probability sample implemented for each site. At the first stage, a stratified sample of Census block groups is selected. Stratification factors common across the four field centers are (1) low versus high SES (as measured by the proportion of persons with at least a high school education) and (2) low vs. high concentration of Hispanic/Latino households, resulting in four strata per field center. Selection of block groups is carried out proportionately with respect to the SES strata and disproportionately with respect to the Hispanic/Latino concentration strata; that is, block groups in the high concentration stratum are selected at a higher rate than those in the lower concentration stratum. This over-sampling is carried out to maximize efficiencies in the field by increasing the probability that a selected household is a Hispanic/Latino household. In addition to these four strata, block groups in the Coop City area are isolated into a 5^{th} stratum in the Bronx, and block groups representing high concentration areas for Central and South Americans are isolated into a 5^{th} stratum in Miami. Both of these 'special' strata are defined to ensure selection of adequate numbers of households in the respective areas.

At the second stage, households in the sampled block groups are selected from a dual frame constructed from non-over-lapping lists of postal addresses and Hispanic/Latino surnames. Addresses are selected from the surname list at a higher rate than from the postal list to further maximize efficiency of field operations by increasing the probability that a selected household is a Hispanic/Latino household. Selected households are screened for eligibility, where eligibility is defined as at least one Hispanic/Latino household member aged 18-74 years. Eligible households in which all Hispanic/Latinos in the target age range are at least 45 years of age are selected with certainty (probability of selection = 1), while all other households are selected with probability ($0 \leq p < 1$) based on the expected household composition for the area. Once a household is selected, all members of the household are invited to participate. This household selection algorithm is designed to provide the target age distribution for the HCHS/SOL study, namely, 62.5% of participants aged 45-74 years and 38.5% aged 18-44 years, and to minimize the amount of information required for screened households that may not be selected for participation. Selection of households corresponds to an over-sampling of Hispanic/Latinos in the older age range, which is necessary given the age distribution of Hispanic/Latinos currently living in the US.

Considerable effort is expended to ensure adequate participation rates among sample members, once selected and identified as eligible. The recruitment protocol consists of advance mailings describing the study and its objectives, followed by telephone contacts. If possible, household screening and selection of household members is conducted via the telephone. For those not responding to the mailing or telephone contacts, in-person screening visits are conducted.
Recruitment is planned for a three-year period. The sample of households in each target area is randomly allocated to each of the three years of recruitment. Within each recruitment year, we anticipate fielding the sample in waves, with each wave corresponding to a random sub-sample of the original sample of households allocated to that year. Continued monitoring of field activities enables decisions concerning release of waves to be made in a timely manner.

3.1. Recruitment and Examination Goals by Center

Study participants are recruited from four field centers located in Bronx, New York; Chicago, Illinois; Miami, Florida; and San Diego, California. The study sites and the population of interest are described in further detail in Manual 1. Each field center recruits up to 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.

While sampling follows a common protocol adapted to each study area, recruitment modalities and schedules are optimized to each field center and the characteristics of its study community. Recruitment accrual is processed centrally by the coordinating center for ongoing feedback to each field center and periodic reports to the steering committee.

4. 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. Household Screening Rosters (HSR form), Screening Call logs and Tracking sheets (SCT form) are used in managing these household level recruitment activities. The eligibility of each individual is determined using the Eligibility Checklist (ELE form) which is also used to record the date of the 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 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.

Before calling a participant, field center personnel must have 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 screening, 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.

4.1. 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 HCHS/SOL Data Entry System (DES) on the staff person's laptop/desktop. Following an explanation of the HCHS/SOL study and the procedures involved, the interviewer requests an opportunity to verify the individual's eligibility for all procedures. The conditions reviewed during this interview (and listed on the form) include pregnancy, breast feeding, the participant's use of a pacemaker, defibrillator or other implanted electronic device, and screening questions for conditions that would preclude the periodontal measurements during the dental examination. 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 and a positive response to the periodontal probing questions are 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, difficulties in getting on or off an examination table or dental chair, 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.

4.2. 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 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. Participants using inhalers should be asked not to use their inhaler in the morning of their examination at the HCHS field center unless they experience discomfort. This is because 4-6 hours should elapse since the last use of a bronchodilator and the pulmonary function test.

Individuals who are diabetics 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 last 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. Some of these medications may need to be taken with food, and at set times. Field centers make it possible for the participant to take these medications accordingly; 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 10 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 where the clinic is; identify a clinic 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 just made, a bag for their medications, and with instructions. 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 and phone number; appointment time and transportation preference; and any special instructions. The "final status" screening status is recorded on an exam scheduling worksheet.

4.3. 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, and phone number of contact persons;
   d) Medication Instruction Sheet: Instructions to bring all prescription and over-the-counter medications, including vitamins and mineral supplements, taken within one month prior to the examination. This includes pills, liquid medications, skin patches, inhalers, and injections. A bag for the participant to bring all medications and supplements to the field center is enclosed.

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).

4.4. Split Baseline Examinations

Baseline examinations may be scheduled as split exams if the study participant is unable to commit to a full examination, or split to accommodate circumstances not anticipated at the time the examination was scheduled. The full sequence of split examinations must be completed no more than 10 days apart.

Under exceptional circumstances field center managers may authorize scheduling split examination beyond 10 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 10 days apart must not exceed 5% of a field center's baseline examinations during one year.

On occasion individual baseline interviews or examination components may be missing, inadvertently or to accommodate various circumstances in the field. Completion of the missing component may be scheduled at the time the participant is at the field center or subsequently, once flagged 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.

On October 13, 2010 the Steering Committee approved a waiver to the above "90 day rule" for the remainder of the baseline examination in order to: (1) minimize baseline exams that are not “full exams;” (2) keep “core only exams” below the threshold set by the Steering committee; (3) thus minimize the number of study participants ineligible for active follow-up. Accordingly, as of November 1, 2010 split or incomplete exams may completed beyond 90 days of the initial visit

If blood is drawn or seated blood pressure collected outside the 90 day window of the participant’s initial visit, selected information on medication use will be collected (or updated). Section C of the Medication Use Form (MUE/MUS) must be collected at this time (items 33-38). For this, "02" is typed in for the form sequencing number on the "ID screen" selection page, to identify this data collection as the second sequence of this participant’s baseline visit (thus contact 01 for this participant, visit 01, sequence 2).

5. 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, fasting status is determined and the medication bag is logged and labeled.

Prior to the participant's visit information on morbidity and special needs recorded on the screening form (PSE, PSS) are transferred to Participant Itinerary 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 Data Entry System (DES) monitor and confirms the identifying information on the form with the study participant. Staff confirms that special needs are noted on the Participant Itinerary Form. Unless already indicated on the form, the participant is asked whether she/he is diabetic and that Glucose Load is listed as N for 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.

After the medication bag is labeled, its contents are inspected with the participant to determine if it contains any medications that require refrigeration. Medications requiring refrigeration are labeled with the participant's ID number and placed in the refrigerator. The location of the medication is noted on the Participant Itinerary Form.

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 6 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 10 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.

6. INFORMED CONSENT

Informed consent (see HCHS/SOL informed consent template in Appendix 3) is the first data collection form administered during the course of the Exam. Its core content complies with guidelines from the National Heart, Lung, and Blood Institute and the HCHS/SOL Steering Committee. Its content and format are tailored to meet the specific requirements of each field center's Institutional Review Board.

The primary objective of re-administering 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 information 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.

6.1. 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 this process find out whether the participant prefers to communicate in Spanish or English and record language preference 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. Record this information on the Itinerary Form and explain to 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 ad avid 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 the form read to them prior to their arrival. Questions of clarification should be solicited also under these circumstances and the consent portion of the form must be filled out and signed in the presence of the staff person who serves as witness.

At field centers' discretion, a videotape / DVD is provided to the participant at the home or played at the reception station to explain the purpose of the genomic material collected, its use and disposition, and the participant's ability to exercise control over these options. Questions are encouraged and time is allowed for the person to read and sign the informed consent document.

If he/she 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. 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.

6.2. Training and Certification

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

6.3. Data Collection

The Informed Consent is a paper form. In some centers the form may be split into two forms (main consent and consent for specimen storage). When the participant receives a COPY of the informed consent, the field center has the option of providing a copy of the entire form, or 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.

6.4. 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 informed consent. 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 potential 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 specific procedures for vulnerable individuals there is need for guidelines common to the HCHS/SOL field centers to provide an environment that assists 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 brings this to the attention of the supervisor.

6.5. Consent Tracking Form

The consent form signed by the participant during the visit is used to complete the informed consent tracking form, which is NOT administered to participants. The purpose of the tracking form is to document the level of consent and to track any changes (revisions) following the clinic visit to a participant's consent on (a) access to medical records, (b) the use of DNA and (c) the use of other study data, (d) reporting the results to participant and others designated for that purpose. Changes to the consent are not actively solicited, but any change in consent status is documented as soon as a participant requests that a change be made to his or her consent status.

The Informed Consent Tracking form is an internal 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 ICTA, Appendix). This form tracks each participant's type of consent (full or partial), restrictions on use or storage of DNA, type of restrictions on the participant's data for different types of research questions, the ability to share de-identified data with investigators not affiliated with HCHS/SOL, or restrictions on the release of results to participant's physician and permission to access medical records. This form is completed by study personnel, and not administered to participants.

At the option 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. The participants are encouraged not to ask the staff for the results of their procedures at individual stations to avoid distracting the technicians. The reporting of results is described in detail in Section 28 of this manual.

7. 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 16 (Follow-up). To establish the ability for HCHS/SOL to maintain contact with its participants, during the baseline visit study participants are asked for their address as well as for individuals who can serve as contacts and their respective addresses. This information is updated annually as required.

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 is 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.

7.1. 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 / 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.

7.2 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 wants to modify the former scope of their consent to participant in the different elements proper documentation of that change is required. An Informed Consent Update form (ICU) serves to administratively capture those changes to any element of consent and preserve it in the study database. The ICU when keyed for a participant will automatically pre-fill with the responses from the 10 elements of consents from the participants existing informed consent tracking form.

The field center representative who is making the change will need to enter the date this change becomes effective and tab (jump) to the consent element(s) being changed from "yes" (allow) to "no" (dis-allow). Contact the coordinating center if the elements of consent were recorded using the ICT, version A since recording changes on the ICU are not automatic. Staff should modify the responses as needed and save the record. If any aspect of consent is modified again by the participant at a later date, such as adding or removing a restriction, then update the ICU completion date, staff ID fields, and save the changes in the DMS. Every time a change is made to the original scope of informed consent, field center staff must document the change by printing the tracking form and saving it in the participant file.

8. PARTICPANT FLOW AND ITINERARY

The sequence of examination procedures (participant flow) includes a series of 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 in the DES (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 with exchangeable blocks of procedures and interviews that optimize participant and staff time, as illustrated in Table 2. 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.

Table 2. Examples of HCHS/SOL Baseline Interview and Procedure Blocks to Enhance Time

Exam Procedure, fasting status specification (F)	Estimated time (min.)
Fasting block	80
Reception, informed consent, change clothes, urine specimen	30
Anthropometry (F)	08
ECG (F)	15
Ankle brachial SBP (persons aged 45-74 yrs)	17
Seated BP (F)	11
Phlebotomy (F), Glucose load	16
2-hour glucose load, snack	12
Procedures, flexible sequence	81
Audiometry + HHE questionnaire	22
Lung function	15
Oral examination + verification of screening status	20
Change clothes	07
Blocks of interviews, flexible sequence: A	45
24-hr dietary recall, supplements	
Blocks of interviews, flexible sequence: B	28
Alcohol	02
Dietary behavior	03
Economic background	02
Health care use	04
Hearing Hx	04
Medical Hx	07
Medication & Supplement use	06
Blocks of interviews, flexible sequence: C	44
Neurocognitive (persons aged 45-74 yrs)	16
Occupation	07
Oral Health	05
Personal identifiers	07
Personal information	09
Blocks of interviews, flexible sequence: D	43
Physical activity	05
Respiratory Hx	09
SF-12 Health Status	05
Sleep Hx	06
Social Network	02
Sociocultural	07
Tobacco use	03
Weight Hx	02
Well Being	04
Visit Termination	20
Exit interview	10
Sleep & activity monitoring instructions and tracking	10

The termination of the examination visit also represents a fixed sequence to assure that a DES-based data inventory is run to prevent inadvertent omissions in data collection, that the clinically relevant study results available at this point be reviewed with the participant, and that the instructions for the sleep studies and the physical activity monitoring be discussed with the study participant prior to departure. Modification of a fixed sequence is a matter of study protocol and requires Steering Committee approval.

The start and end time of individual procedures and of blocks of interviews are recorded on the Participant Itinerary Form, as well as the completion of status of individual tasks. While the DES tracks both the completion status and clock times for procedures and interviews, recording the information on the Participant Itinerary Form provides a convenient visual record as different study personnel interact with the study participant in the course of the field center visit. The sequence and timing of data acquisition documented on the Participant Itinerary Form serves additional 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.

Because of the length of the field center examination visit, participant comfort and safety are of concern. 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.

9. RECORDING MEDICATIONS AND SUPPLEMENTS

The Medication Use Questionnaire (MUE) records all prescription and over-the-counter medications, including cold and allergy medications, vitamins, herbals or supplements used by participants in the four weeks preceding their interviews. The MUE and the Question-by-Question instructions for its use are found in the Appendix under this section heading. The survey ascertains usage of up to 25 medications. Ascertainment includes scanning of twelve-digit Universal Product Code (UPC) bar code symbols when available. Medical Therapeutic Classification (coding) is automated where possible. Otherwise, manual coding is centralized (performed only in the Coordinating Center).

The goal of the MUE is to ascertain usage of all prescription and over-the-counter medications, vitamins, herbals, and supplements. This information assists in measuring patterns of medication use in the study communities, temporal changes in medical care practice, diagnostic classification of cardiovascular diseases, interpretation of laboratory results, and predictors of study end points.

9.1. Administration of the MUE

The MUE is divided into three major sections: (A) Reception, (B) Medication Record, and (C) Medication Use Interview, administered as described below. To reduce the length of the visit it is important that staff complete section B, Medication Record, while the participant is occupied with interviews or procedures, and prior to completing section C (Medication Use Interview). A further reason for staff to complete section C early during the visit is to make available the information on coded medications in the Data Entry System, where it can be interrogated by the spirometry software for medications that exclude a participant from using a bronchodilator.

9.1.1. Reception

Trained and certified study personnel places identification labels on the participant's medication bag and MUE. Once the medication bag is logged and labeled, the interviewer checks with the participant to determine if it contains any medications that require refrigeration. Medications that require refrigeration are labeled with the participant's ID and placed in the refrigerator. The interviewer then determines and records whether the participant has brought in all medications taken within the last four weeks. If the participant has not brought in any (all) medications, the interviewer inquires to differentiate between non-compliance with pre-visit instructions or non-use of medications in the prior four weeks. In case of inadvertent omissions, the interviewer makes arrangements for obtaining the information, preferably by having the participant return at a later date to the Field Center with the medications for scanning or transcription. The interviewer records deliberate omissions of medications on the MUE and on the Participant Itinerary Form / Check-off List so that the interviewer can attempt to convert participants to bring in omitted medications. Staff can administer subsequent parts of the MUE during Reception (if the work area affords the opportunity for maintaining confidentiality) or later, in areas of the field center usually designated for conducting interviews.

9.2. Medication Record

The interviewer first verifies that the name on the medication bag matches the participant's name. Then the interviewer removes all medication containers from the medication bag and places them on the work area. When there are more than 25 medications for scanning / transcription, staff uses the following algorithm to guide prioritization: [1] prescription medications; then [2] aspirin, aspirin-containing medications and anti-inflammatory drugs (see Appendix, Question-by-Question instructions, List #1 and List #2); followed by [3] over-the-counter medications; and finally [4] vitamins, herbals, and supplements.

The interviewer scans / transcribes the UPC (part a of Items 5-29) into the Data Entry System. The Data Entry System will try to match a Medical Therapeutic Classification (MTC) to the UPC. If MTC-UPC matching is successful, the Data Entry System will skip the rest of the fields (parts b-d) for this medication item and move to the next medication. If an UPC is not available or the Data Entry System does not successfully match the UPC, the interviewer transcribes the medication National Drug Code (NDC) (part a). If an NDC is not available or the Data Entry System does not successfully match the NDC, the interviewer transcribes the medication name (part b), strength (part c) and units (part d).

If this is done in the presence of the study participant the interviewer shows each medication to the participant as it is scanned / transcribed, while keeping the other medications in view. The interviewer verifies scanned / transcribed information against container labels, making corrections when necessary to ensure accuracy. If a bar code label is not on the medication container or a bar code cannot be successfully scanned and a medication name exceeds the number of positions for the medication name (b) in the Data Entry System, the interviewer right-truncates the name without abbreviating the name in any other fashion. After successfully scanning / transcribing each medication, the interviewer returns corresponding containers to the medication bag to minimize confusion and to assure that all medications are returned to the participant.

Loose pills and medications in containers that are unmarked are examined only in the presence of the participant. With his/her permission and help, the interviewer examines loose pills and unclearly labeled containers, or those which hold more than one medication (e.g. medisets). The interviewer uses pill imprints, the Facts and Comparisons Drug Identifier on the desktop computer, and the Ident-A-Drug Reference on the web to identify these medications.

9.3. Medication Use Interview

The interviewer ascertains via a series of questions whether any of the participant-reported medications were used to treat pulmonary or cardiovascular diseases and/or their symptoms, whether any aspirin or aspirin-containing medications were used in the last four weeks, and whether any other non-steroidal anti-inflammatory drugs are being used on a regular basis.

9.4. Training

Interviewers are centrally trained and when certified, assume responsibility for providing local staff training in medication scanning / transcription.

9.5. Certification

Interviewers are certified to administer the MUE by attending the central training, completing the scanning / transcription exercise designed by the central trainer, and passing with a score of $\geq 80\%$. New staff, unable to attend central training, are eligible for remote certification when:

- The candidate is trained by the lead certified interviewer at the corresponding Field Center.
- The candidate has completed five taped interviews demonstrating adequate technique based on review and approval by the lead interviewer.
- The Study Coordinator has submitted a request for certification to the Coordinating Center on behalf of the candidate.
- The Coordinating Center has sent to the Study Coordinator a mock medication bag with detailed instructions for the candidate's certification.

- The candidate independently completes an MUE and enters it into the Data Entry System.
- The Study Coordinator returns the medication bag with all of its contents, the instructions, and printouts of the MUE screens to the Coordinating Center for evaluation.
- The candidate passes with a score of ≥ 80%.

9.6. Quality Assurance

With participant's approval, most staff-administered interviews are taped for quality control. The Coordinating Center Monitors also observe technique and adherence to protocol. The Quality Control Committee monitors data quality semi-annually.

9.7. Data Collection

The MUE is designed to be interviewer-administered and collected by direct data entry unless a workstation is not available. A paper version of the form is available for back-up and delayed data entry. Medication UPC/NDCs (part a of Items 5-29), medication names (part b), strengths (part c), and units (part d) are listed alphabetically in hard copy and Data Entry System versions. Details of data collection are provided in the Question-by-Question instructions for the MUE (see Appendix).

10. 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. record the time of voiding on the label, and
3. bring the specimen cup back to the staff member, OR
4. place the sample container in a refrigerator designated for urine samples, and report to a staff member that the specimen has been collected, depending on locally approved OSHA regulations.

Scripted instructions (in English and Spanish) are provided in Appendix 5.

Bathrooms are 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.

11. 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.

11.1. 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)

11.2. 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.

11.2.1. Anthropometry Form (ANTA)

The ANT form records anthopometry 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.

11.3. 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.

11.3.1. 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.

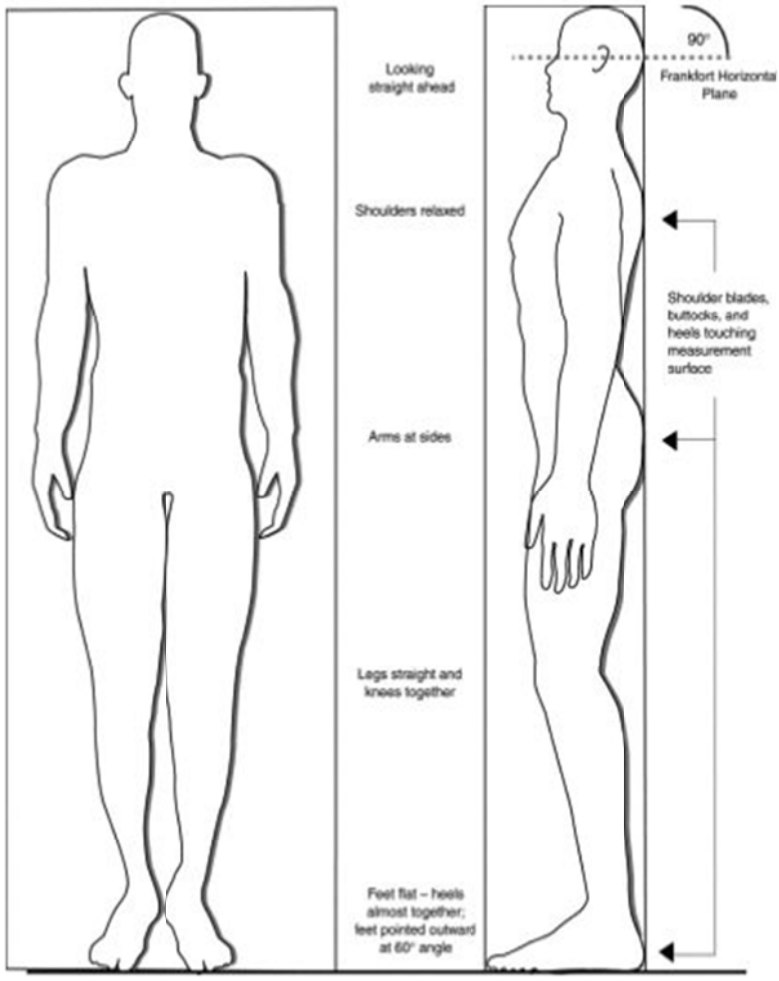
Have the participant stand on the floor (see Figure 1) with the heels of both feet together and the toes pointed slightly outward at approximately a 60˚ angle. Make sure the body weight is evenly distributed and both feet are flat on the floor. Check the position of the heels, the buttocks, shoulder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



11.3.2. 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).

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.

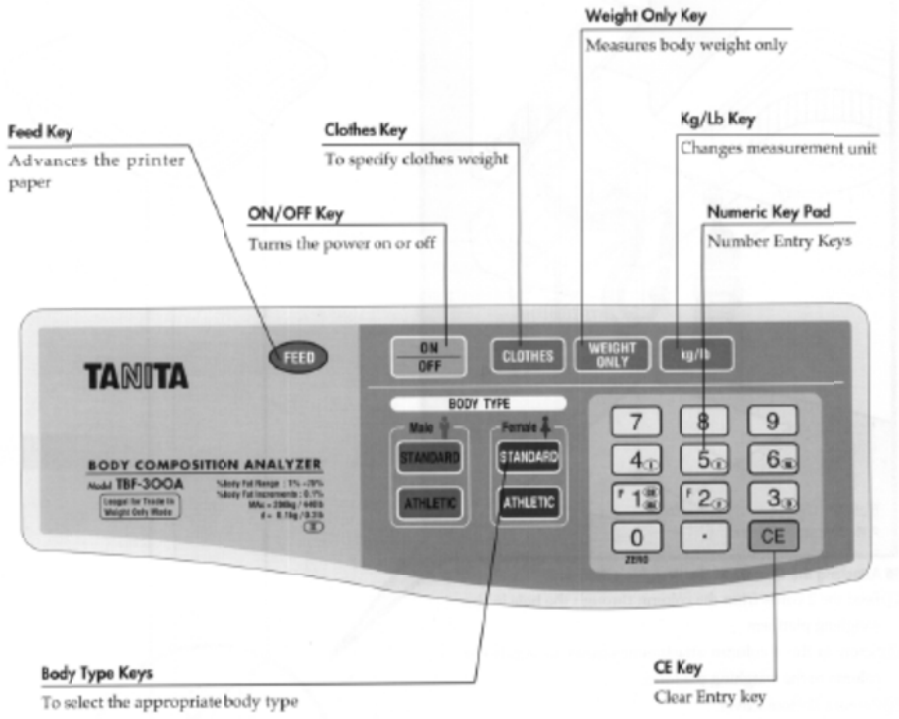


Figure 2. Control Panel of Tanita Body Composition Analyzer, TBF-300A

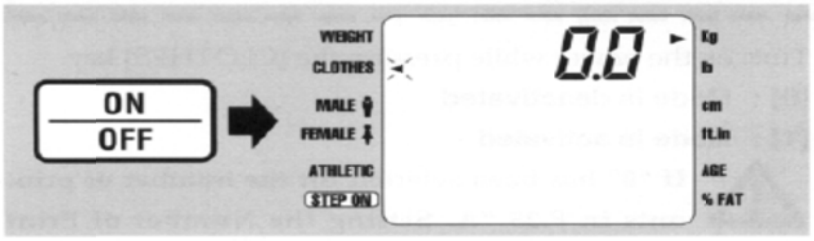
a. Initial set up

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



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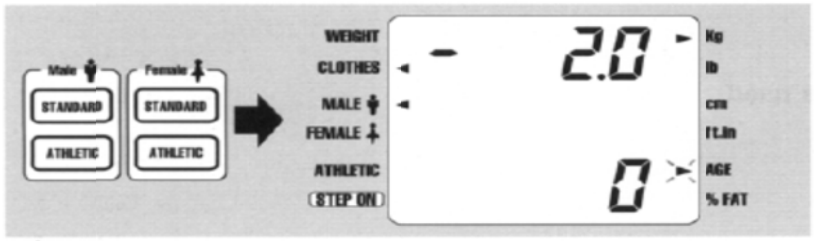

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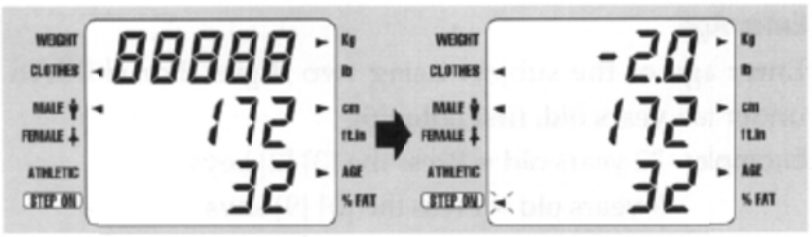

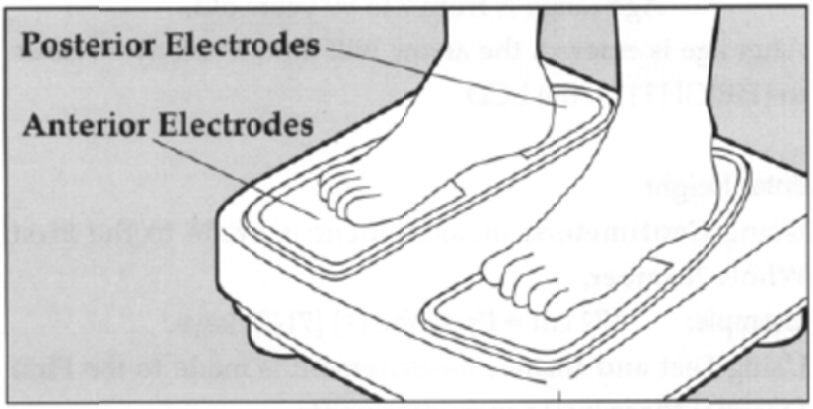

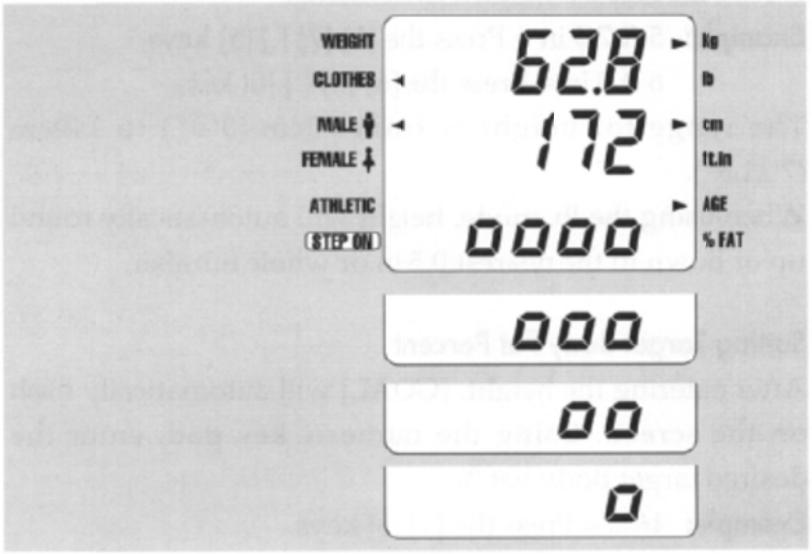

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If the screen returns to ---- for weight, the participant weighs more than 440 lb. Record 999.9 for weight and 99.9 for % body fat on the data form.

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, DEFIBBRILLATOR OR OTHER INTERNAL ELECTRONIC DEVICE SHOULD BE MEASURED IN 'WEIGHT ONLY' MODE.

Do not weigh participants who have a cast that cannot easily be removed, or that the participant is comfortable 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.

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.

11.3.3. Waist Circumference

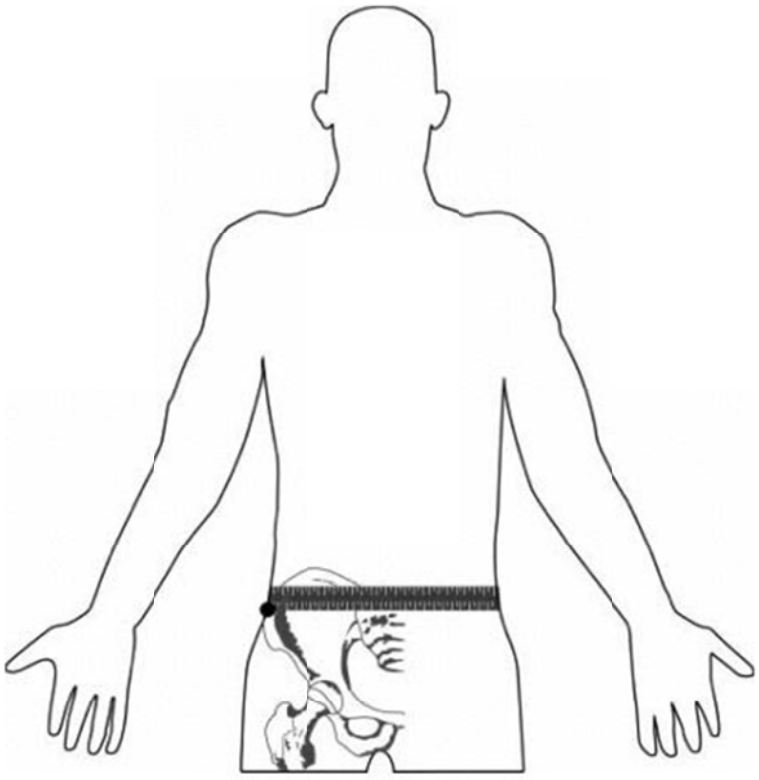
To define the level at which the waist of abdominal circumference is measured, you must first locate and mark a bony landmark, the lateral border of the ilium. Have the participant stand and hold their t-shirt above the waist. Lower the pants and underclothing of the participant slightly, and standing 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.

11.3.4. 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



11.4. Quality Assurance/Quality Control

11.4.1. 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.

11.4.2. 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 Anthopometry 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.

12. SITTING BLOOD PRESSURE

12.1. 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.

Equipment	Supplies
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	

Figure 4 OMRON sphygmomanometer and 4 cuffs

OMRON HEM907XL – with four cuffs

12.1.1. 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.

12.2. 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.

12.2.1. 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.

12.2.2. 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).

12.2.3. 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 along side 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.

12.2.4. Choosing the Correct Cuff Size

Identify the measured arm circumference under column 1 in Table 3 below. Use 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.) Record the cuff size on the SBP form in Item A.3.

Table 3.

Arm Circumference (cm)	OMRON CUFF SIZE
17.0 to 21.9	index 17- 22cm (CS19)
22.0 to 32.5	index 22-32cm (CR19)
32.5 to 42.5	index 32-42cm (CL19)
42.6 to 50.0+	index 42-50cm (CX19)

12.2.5. Positioning the HCHS/SOL Participant and Placing the Cuff

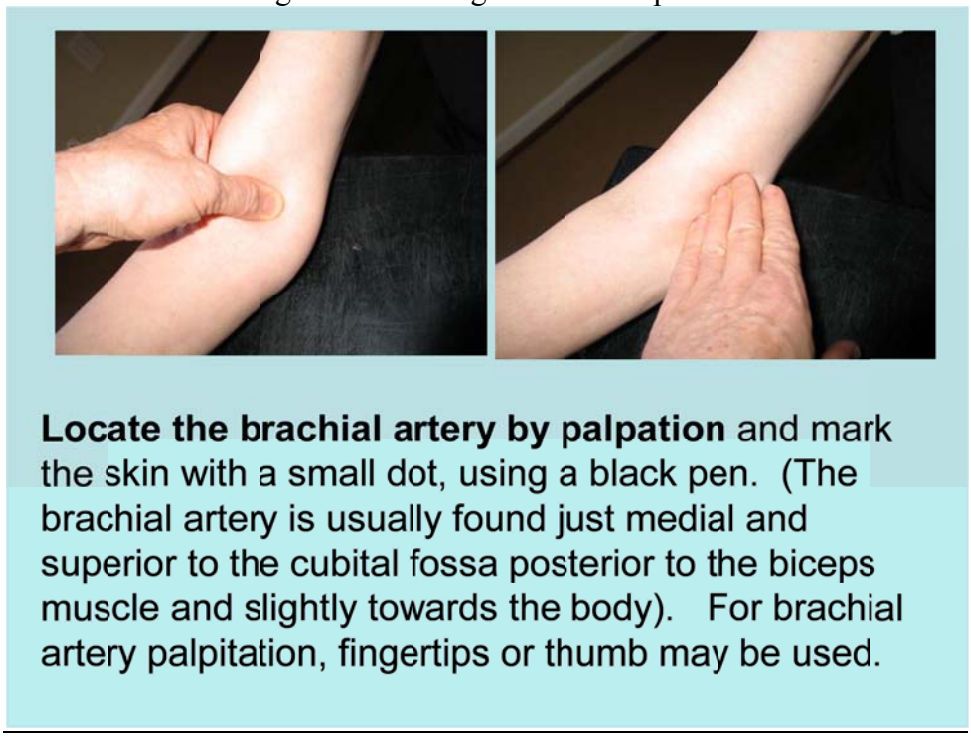
Ask the participant to sit and rest quietly in the chair after adjusting it, if necessary, to allow participant's feet to rest flat on the floor when legs are in the uncrossed position. The technician then explains the next steps using the following script: "Before taking your first blood pressure reading, 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.

12.2.6. Locating the Pulse Points

Figure 5: Locating the brachial pulse



12.2.7. 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

12.3. 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.

12.3.1. 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

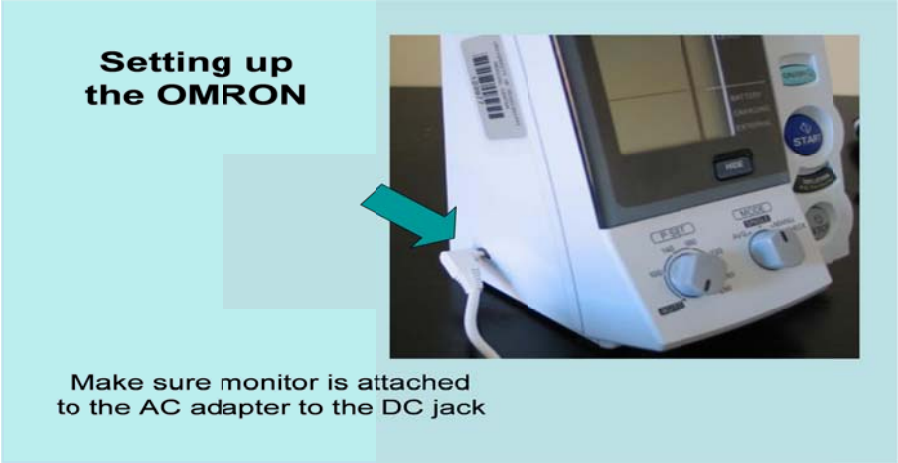
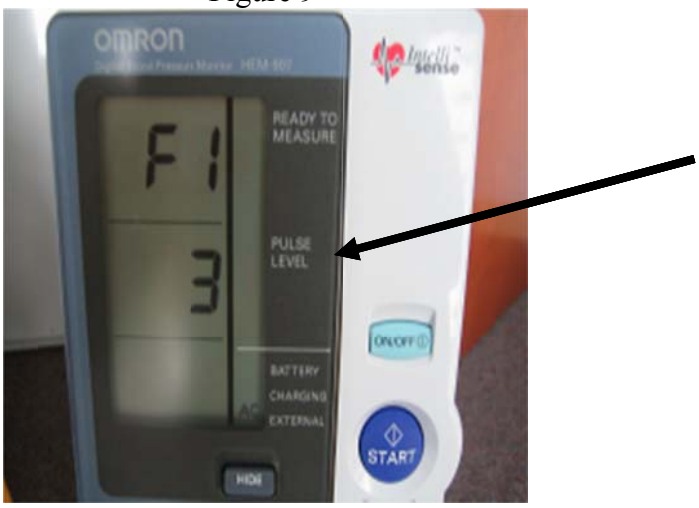


Figure 8

When the power is OFF, push the ON/OFF (power) button for more then three seconds while holding the START button simultaneously: F1 is displayed in the first window and three inflation (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 9



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 10

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).

Figure 11

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

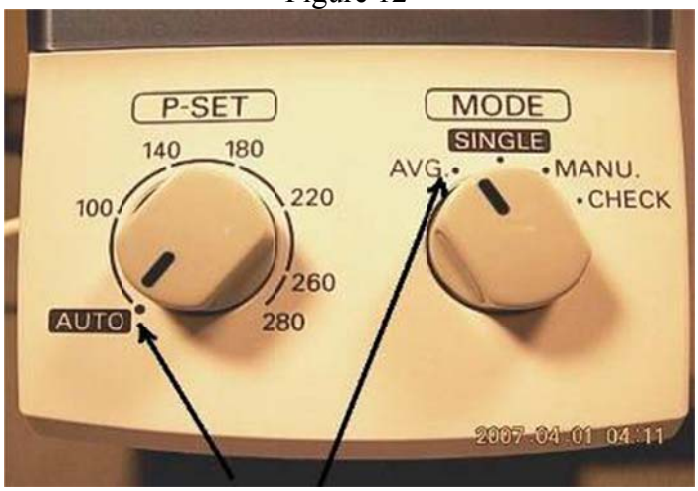
Table 4 summarizes the needed setting for the exam

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

12.3.2. 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).

Figure 12



AUTO AVG

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

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 1st , 2nd , and 3rd measurements with 30 seconds between each listing (Figure 14).

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

12.4. 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 1st set on the SBP form in Items C.8-C.10. Repeat this process by pushing the DEFLATION button to display and record the 2nd and 3rd sets of measures on the SBP form in Items D.11-D.13 and Items E.14-E.16, respectively.

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

12.5. 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 Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7).

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 25 of this manual of operations describes the procedures used to report study results.

12.6. 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.

12.7. Inspection and Validation of the OMRON Sphygmomanometer

12.7.1. 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.

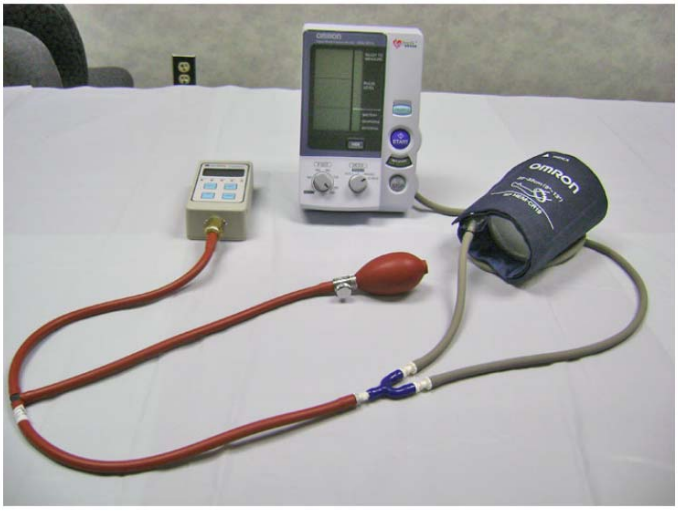
12.7.2. Quarterly Validation of the OMRON Sphygmomanometer

Each OMRON unit is checked every 3months 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 **adapte**r 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.

12.8. 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.

13. 12-LEAD ECG

A 12-lead electrocardiogram (ECG) is acquired during the HCHS/SOL baseline examination following a standardized protocol (Manual 5). The timing of the ECG during the field center exam is important to the quality of our data because an increase in blood sugar has been shown to affect the wave forms on the ECG, and because the use of a bronchodilator importantly affects the heart rate and may induce minor arrhythmias. As a result, for participant who will not be getting a glucose load, (i.e. will be getting only one fasting blood draw) the ECG may be taken either while the participant is fasting prior to the blood draw, or after the blood draw but at least two hours after a snack or after lunch. For participants who will be getting a glucose tolerance test (i.e. will be getting a blood draw, a glucose load, and then another blood draw two hours later), the ECG should be done either before the first blood draw, in the fasting state, it is preferred to take ECG early in the exam sequence while the participant is fasting, prior to the oral glucose load and prior to the snack. If that is not practical the ECG should be taken or at least two hours after the glucose load (and prior to the snack). Alternatively, it can be done after the second blood draw but then it must be done two hours after the lunch meal or snack. Thus some participants may get the ECG in the morning and others in the afternoon, depending on whether or not they are having have a glucose tolerance test and depending on the timing of the lunch or snack. If a bronchodilator has been administered to a participant as part of lung function testing the maximum time should be allowed before an ECG is taken, preferably two hours or longer.

13.1. Local ECG Reading

ECG findings as coded by the Central ECG Reading Center (EPICARE) are provided to the study participants and their personal physicians 5 to 6 weeks after the field center examination, along with other results of clinical value. A local clinical reading of the ECG at the time the of the field center examination is part of HCHS/SOL protocol for safety purposes, if triggered by ECG abnormalities defined as “alerts” because of their potential severity.

Minor, clinically insignificant ECG findings are commonly found in samples drawn from the general population; most of these do not need immediate attention. "Alert" ECGs on the other hand should be reviewed by the clinically trained HCHS/SOL personnel at the field center and evaluated for possible referral. Although specific directions for HCHS/SOL personnel to follow are provided for each alert condition, a physician can override these instructions according to individual circumstances. In reviewing the ECG tracings HCHS/SOL staff does not make diagnoses or convey information that may alarm the participant. A list of ECG abnormalities defined as alerts follows.

13.1.1. "Alert" ECGs (Major/acute abnormalities)

Alert Abnormalities	Figures in MOP	Action
- Atrial fibrillation. - Atrial flutter.	5.7 5.8	These are not an emergency in a person without symptoms but ECGs should be reviewed by a physician. If confirmed, the participant and his/her physician are notified. The clinic physician determines the level of urgency for this notification.
- WPW - Idioventricular rhythm - Ventricular tachycardia	5.11 5.9	These are not an emergency in a person without symptoms but the ECG should be reviewed. If confirmed by a physician the participant and his/her physician must be notified. The clinic physician determines the level of urgency for this notification.
- Complete heart block - Left bundle branch block - Acute pericarditis - Acute or marked injury, infarct, or ischemia	5.12 5.13 5.10	Each of these is a potential emergency. If confirmed by the HCHS/SOL physician s/he determines whether urgent transportation for further care is required. The participant and his/her physician are notified immediately.
Pacemaker	5.14	Not an alert ECG (this finding will be included in the results letter). Verify that the Itinerary Form indicates that the participant has a pacemaker and that participant is not exposed risk while at the center
Heart Rate	NA	Refer for review by the study physician if heart rate is 40 bpm or lower, or 100 bpm or greater, before participant leaves the field center

13.1.2 Minor Abnormalities

Alerts that do not require review of the ECG by a physician include1st degree AV block, Axis deviation, Early repolarization, Intra-ventricular conduction defect, Low voltage, Occasional PAC, Occasional PVC, Sinus bradycardia and Sinus arrhythmia. There are many other abnormalities than can be seen on an ECG that similarly do not require a review by physician, but the ones mentioned here are the most common.

13.2 Training and Quality Assurance

HCHS/SOL personnel responsible for the acquisition of the ECG data are centrally trained and certified by EPICARE. Throughout the baseline examination period, quality control feed-back is provided to technicians by EPICARE, and data quality is periodically reviewed by the HCHS/SOL Quality Control Committee as described in Manual 12.

14. BIOSPECIMEN COLLECTION AND PROCESSING

Blood specimen samples are collected at the HCHS/SOL baseline 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. The HCHS/SOL Central Laboratory performs the tests on the blood and urine; DNA is prepared from the packed cells of EDTA blood; 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 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 28.

15. ORAL GLUCOSE LOAD

15.1. 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.
2. If participant is on kidney dialysis.
3. If participant has had partial removal of the stomach or small intestine.
4. If the participant has consumed food less than 10 hours prior to the time of the blood draw.

If none of the above conditions apply the technician proceeds with the fasting blood draw and 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 #4). A SureStepPro Glucose Meter is used for this purpose, with instructions for this procedure provided in Manual 7.

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 will be administered.

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 ≥ 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.

1. If the FPG ≥ 400 mg/dL **STOP** the examination and refer to the emergency room (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.

15. 2. 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 ≥ 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 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 15.1 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).

15.3. Administration of the Oral Glucose Load

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.

15.4. 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.

15.5. 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. If the ECG is to be taken at this time before the fast is broken, the snack is offered after the ECG has been recorded. 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.

15.6. Documentation of Side Effects

If a participant complains of any problems during the test, this should be reported to the Study Coordinator or the Study Nurse and documented on the field center's Incident Log. 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 (diarrhea is not a side effect of the OGTT). If vomiting has occurred, a 2-hour blood draw is not be done, and the reason for the incomplete test recorded in Item 23 of the BIO form.

15.7. Emergencies

Field centers keep on hand orange juice or equivalent, sugar-containing beverages at all times. Participants with known or undiagnosed diabetes may develop low blood sugar or an "insulin reaction". If recognized promptly by clinic staff, it should be mild and easily treated with orange juice or a similar sugar containing beverage. 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. 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 under Participant Safety (Section 27).

16. ANKLE BRACHIAL INDEX

The presence of peripheral arterial disease (PAD) will be assessed with the ankle brachial index (ABI) in all persons aged 45-74. A low ABI is a reproducible and valid measure of lower extremity arterial disease and has been shown to predict all-cause and cardiovascular mortality. A normal ABI is 1.00 to 1.40, with progressively lower values below 1.00 corresponding to more severe arterial disease. Many persons in the group with an ABI >1.40 will also have PAD. These higher ABIs are uncommon and reflect medial arterial calcification and partial or complete incompressibility of blood vessels, and primarily occur in persons with diabetes.

The ABI examination should always precede the blood draw since it requires the use of an ultrasound probe over the brachial artery in the antecubital fossa of the arm. Since this is also the area where the venipuncture occurs, there exists the possibility of participant to participant blood contamination by the ultrasound probe. If for any reason the ABI examination follows the blood draw, it is mandatory that the venipuncture site be bandaged and that the ultrasound probe be cleaned with alcohol prior to and after use for ABI determination.

16.1. Equipment and Supplies

- Two Nicolet Doppler probes, Elite 100R, EN 50R with rechargeable batteries.
- Two full tubes of ultrasound transmission gel.
- Two aneroid sphygmomanometers, DS66 trigger type, #5098-30.
- Eight Welch Allyn adult arm blood pressure (BP) cuffs, 2 piece, 1 tube bladder, #5082-43 (4
- of these 8 will be for the ankle).
- Four large adult arm BP cuffs, 2 piece, 1 tube bladder, #5082-44.
- Four thigh size BP cuffs, 2 piece, 1 tube bladder, #5082-77.
- Tissue or wash cloth to remove ultrasound contact gel.
- Non-toxic dry erase marker
- ABI form
- T-Spray (Pharmaceutical Innovations, Inc.) and/or Clorox Disinfecting Wipes (both contain the same disinfectants)
- Tegaderm (3M)
- Polylined towels (sterile drapes - multiple internet sources)

16.2. Definitions

1. PAD, peripheral vascular disease, peripheral atherosclerosis, lower extremity arterial disease, and peripheral arterial obstructive disease are synonyms. PAD does not refer to venous disease, small-artery obstructive disease, vasospastic disease, cold sensitivity, or capillary disease. For this protocol, PAD does not refer to carotid artery disease, or to other peripheral non-coronary atherosclerotic disease.
2. The ABI is a ratio of the ankle to arm systolic blood pressure (SBP), and is computed separately for each leg. Specifics of the ABI computation for HCHS/SOL are given below.
3. An ABI of 0.90 or less is generally considered PAD, although PAD could also be present if the ABI is 0.91 to 0.99, or > 1.40.

16.3. Methods

Preparation. Explain the procedure to the participant and allow him/her to ask questions, using the scripted text found in Appendix 5. Conduct the examination in a quiet, warm, and comfortable room. If the room is cool, a blanket may be used to cover the participant (including arms, hands, and feet), except while the actual measurements are being made. Have the participant lie supine on a comfortable horizontal examination table. The head and heels must be at the same level, and

therefore the table must be long enough so that for each participant, the entire head and both feet must be on the table, not overhanging. Because having the feet even slightly lower than the rest of the body will produce an invalid ABI measurement an oversized examination table is available at the field center for tall study participants. Arms below the shoulder and legs below the knee should be bare.

Inspect all four BP cuffs before placement and use only cuffs that are clean and dry. Do not place blood pressure cuffs over any lesion that could be a potential source of contamination. Do a visual exam and use a protective, non-penetrable covering over any such lesions. See below for specific instructions.

Have the participant rest quietly for at least 5 minutes before beginning the measurement procedure. The participant may be sitting or supine while resting.

While the participant is resting, place an appropriate BP cuff around both arms, based on arm circumference at midpoint. The general rule is that the cuff width must be at least 40% of the arm circumference. The 3 cuff sizes should be employed as follows:

- Adult (12 cm width) for arm circumference of < 32 cm
- Large adult (16 cm width) for arm circumference of 32-42 cm
- Thigh (20 cm width) for arm circumference of ≥ 43 cm

The widths of the bladder for "Adult", "Large Adult" and "Thigh" cuffs are 12, 16 and 20 cm, respectively. Please note that on the Welch Allen cuffs, there are numbers next to the names of the cuffs (e.g. "Adult 11" and "Large Adult 12"). These numbers do **not** correspond to the width of the cuff and should **not** be used to determine which cuff is placed on the arm.

Place an adult (12 cm) cuff size on each ankle. Place the cuff so that the tube is facing the torso, not the toes, and the lower portion rests 3 cm proximal to the greatest protuberance of the medial malleolus (ankle bone).

Once all four cuffs are in place and the 5 minutes of resting are complete, you may begin the measurements as described below.

Record the date of the examination on the ABP Form and the staff code number. Before you begin the procedure, instruct the participant to remain relaxed and to refrain from helping you (e.g. lifting the arm to facilitate placement of the cuff). Once you begin the procedure, explain the steps to the participant as you proceed.

Arterial Blood Pressure Measurement *This step is optional, but will likely be necessary in some participants*: By palpation, locate the brachial artery on both arms (antecubital fossa), and the dorsalis pedis (dorsum of the foot and often in direct line with the 2nd toe) and posterior tibial (medial ankle just behind the medial malleolus) arteries on both legs. Mark the location of each artery with a marker. Sometimes an ankle pulse will not be palpable but can be found with the Doppler.

SCRIPT: "With water-soluble ink, I am going to mark the location of your arteries for the blood pressure measurements."

Using the procedure below, measure SBPs in the following order on the ABP screens:

1. Right brachial artery (ABP Q1a)
2. Right dorsalis pedis artery (ABP Q1b)
3. Right posterior tibial artery (ABP Q1c)
4. Left posterior tibial artery (ABP Q1d)
5. Left dorsalis pedis artery (ABP Q1e)
6. Left brachial artery (ABP Q 1f)

Place an appropriate amount of ultrasound conducting gel over the end of the Doppler.

On occasion, there may be skin lesions on the arms, legs or at the insonation site that are of concern for performing the measurement of the systolic blood pressure. In these instances, we recommend the following procedures be followed in an effort to reduce the potential for contact with blood borne pathogens.

1. For major open lesions, omit the BP measurement in the affected extremity. For minor lesions that are a potential source of contamination (lacerations, abrasions, rash, etc) at the site for placement of the blood pressure cuff, either arm or leg, wrap the affected area with a polylined towel (i.e. sterile drape). Then wrap the blood pressure cuff around this towel and conduct the pressure measurement as described.
2. For lesions with contamination potential at an insonation site, do not perform the Doppler measurement at the affected site.
3. For the specific circumstance when the lesion is a venous puncture due to a blood draw performed before the ABI measurement, apply a Tegaderm dressing over the puncture site and perform the measurement as described. In this situation, the Doppler probe should be cleaned with T-Spray or a Clorox Disinfecting Wipe both before and after insonation.

After palpating the location of the pulse, turn on the Doppler and place the probe over the artery. With this large probe, careful angulation is not necessary. Place the probe in line with the artery and move it from side to side until the strongest pulse is heard. Don't press too hard on the artery with the probe. Rest your hand comfortably so that the probe is secured in place once a strong pulse is heard. Then proceed to explain the procedure to the participant using the scripted text provided in Appendix 5 and ask if the participant has any questions before the measurements begin. If applicable, suggest to the participant to rest comfortably and to be quiet. *In a small percentage of participants, you may not be able to find the posterior tibial or dorsalis pedis pulse. If you are having trouble, be patient and continue to search for at least three minutes. If you are still unable to locate a pulse, enter a systolic pressure of "000" for that artery.*

Inflate the cuff until the pulse is no longer audible. **Inflate to 20 mm Hg above the level at which the pulse sound disappeared**. (If the pulse cannot be obliterated, you may raise pressure to a maximum of 300 mm Hg. If not obliterated at that point, record "300"). Deflate the cuff slowly allowing the pressure to drop at a rate of **2 mm Hg per second**. Record the pressure at which the first sustained (more than one beat) pulse reappears. This is the SBP at this location. Deflate the cuff completely. *Record the measurement on the ABI Form immediately*. Then repeat the process to obtain a pressure measurement at each of the remaining sites.
If the signal remains faint as more pressure is released or if the probe moves off the artery, deflate the cuff completely, and then repeat the measurement.

After completing the ABI measurements, thoroughly clean the Doppler probe with T-Spray or a Clorox Disinfecting Wipe. Please note that the Doppler must be completely clean and dry between participants.

Important note: record “000” for arteries where the pressure is not detectable, and record "300" also for arteries that are not compressible as the highest pressure attempted (typically "300"). For arteries that could not be assessed due to lesions that could not be covered or because of amputation, record "===". In item 2 of the ABP form/screen record “completed per protocol / no observations” if all 6 pressures were obtained as specified above, without incidents or discomfort. If one or more arteries could not be occluded, if the pressure at an arterial site is listed as “===” or if the participant experienced discomfort (even when a pressure was recorded), specify these conditions in item 3 of the ABP form.

Calculation of the ABI A computer program will calculate the ABI from your measurements. For your information, the procedure is given below.

The ABI denominator - There is only one ABI denominator per participant for both the left and right ABIs. This denominator is the higher arm SBP as the denominator.

The right ABI numerator is defined as the higher of 1) the right posterior tibial SBP or 2) the right dorsalis pedis SBP.

The left ABI numerator is defined as the higher of 1) the left posterior tibial SBP or 2) the left dorsalis pedis SBP.

The right ABI is the right ABI numerator divided by the ABI denominator.

The left ABI is the left ABI numerator divided by the ABI denominator.

17. 24-HOUR DIETARY AND SUPPLEMENT INTERVIEW

A 24-hour dietary and supplement interview is conducted on two occasions. The first is an in-person interview conducted at the baseline clinic visit, and the second interview will be conducted by telephone within one month of the first interview. The data collection includes both the dietary and supplement recalls. The dietary interviewer conducts the interviews using direct data entry into NDSR software, and refers to the amount estimation tools and Food Amount Booklet to aid in quantifying amounts of foods and beverages.

Each field center installs the NDSR software on two or more computers and has at least two bilingual interviewers for the dietary and supplement recalls. Each dietary interviewer also has a headset for use in conducting the telephone dietary and supplement recall. NCC provides each field center with two sets of amount-estimation tools (standardized cups, bowls, etc.) and a supply of the Food Amount Booklets which are used during the in-person and telephone interview, respectively.

The NDSR program automatically guides the dietary and supplement interview through standardized passes for collecting the dietary data: PASS 1, Using the NDSR Quick List; PASS 2, Reviewing the Quick List; PASS 3, Collecting complete meal, food, and amount detail; and PASS 4, Reviewing the recall. The Dietary Supplement Assessment Module follows the 24-hour recall and consists of three tiers: Tier 1, Screening for the use of dietary supplements; Tier 2, Entering the dietary supplements; and Tier 3, Reviewing the supplement details. The dietary interviewer asks the participant regarding all supplements taken during the past 24 hours and during the past 30 days. Interviews may be conducted in Spanish and/or English at the discretion of the participant. It is important to conduct the interviews in a space that is quiet and free from distractions.

Due to the need to fast prior to the exam visit, the 24-hour interval covered by the in-person dietary interview begins with the first food or beverage the participant had from 10:00 PM the day previous to the recall until 10:00 PM the night prior to the interview. During the in-person interview, the participant will be oriented to the process of the 24-hour recall and will learn how the food models and the Food Amounts Booklet are used to help estimate the quantities of foods consumed.

At the end of each in-person recall, the Telephone Recall Availability form is completed for each participant listing several potential days and times to receive the telephone recall. The participant identifies several best days and times, since the exact timing of the telephone recall is unannounced. After the in-person interview, the dietary interviewer provides a copy of the Food Amounts Booklet to each participant to keep for use in the subsequent telephone recall.

The telephone interview is collected at least five days, but no more than 30 days, following the initial examination interview. The 24-hour interval covered by the second recall is the 24 hours preceding 12:00 AM (midnight) of the previous night. The exact day of the week for the telephone recall is chosen by field center staff from available participant times, with an aim that the distribution of days across participants includes all days of the week possible, given clinic schedules. The 24-hour dietary recall should not be collected without the Food Amounts Booklet. If at the time of the call, the participant no longer has the Food Amounts Booklet, a replacement should be mailed to him/her and the telephone recall should be attempted a few days later.

The HCHS/SOL Dietary and Supplement Recall Checklist (one per dietary and supplement recall collected) is completed with each dietary recall and serves to document each step of field-site quality control. A Telephone Contact Log is kept for each participant to record all attempts to contact him/her for the telephone recall.

The dietary interviewer should review and edit dietary and supplement recalls as soon as possible after administration. At the end of each dietary and supplement recall, the dietary interviewer prints NDSR reports that are used for local quality assurance and that also serve as a secondary backup of the dietary and supplement recall.

The lead interviewer at each field center is responsible for ensuring the overall quality of the dietary data collection. The dietary interviewers review the diet and supplement interviews, document unusual foods and amounts, and flag unreliable recalls. Field-site quality control includes two steps: review and editing of each dietary recall by dietary interviewers within one or two days of collection; and review and editing of dietary recalls by the lead interviewer within one week, with feedback provided to the respective dietary interviewer.

On a weekly basis, after quality assurance activities have been completed, the lead interviewer combines the recalls collected into a single NDSR project, creates a new NDSR backup file, and submits it to NCC.

See Manual 11 for details on the procedures summarized above for the dietary and supplement interview.

18. PHYSICAL ACTIVITY MONITORING

Study participants will wear a portable motion sensor (i.e., accelerometer) to measure the frequency, duration, and intensity of physical activity over 7 days. The accelerometer provides an objective measure of physical activity that will supplement the interviews for self-reported regular physical activity. Clinic staff will give participants the instructions for wearing the device near the end of the clinic examination and provide participants with a padded stamped envelope to mail the unit back to the clinic after 7 days.

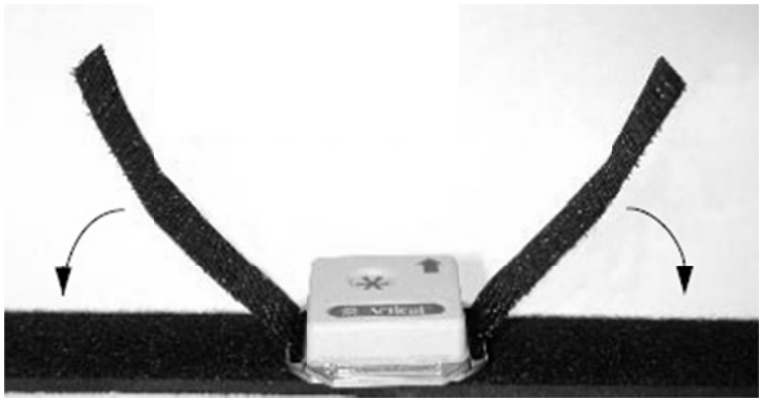
18.1. Technical Information about the Actical Accelerometer

The Actical™ (MiniMiter Respironics®, Bend, OR) accelerometer (model 198-0200-03) is a small, lightweight motion sensor that is attached to a belt and worn on the body. The Actical device measures the occurrence and intensity of motion in all directions by generating an electrical signal proportional to the force of the displacement. A microprocessor inside the accelerometer digitizes the signals, sums and stores them as "activity counts" over a user-defined time interval that can be as short as 1 second. Data can be collected and stored for approximately 6 weeks before being downloaded for data analysis. In addition to the activity counts per unit of time, the average time spent in light, moderate, and vigorous activity can be estimated.

18.2. Protocol

Clinic staff will give participants accelerometers following all of the physical examinations at the clinic examination. Study staff will select the appropriate size waist strap for the participant and thread the Actical unit onto the waist strap as pictured below. With the belt loop on the right, the orientation of the arrow on the monitor should be facing up.

Figure 18a. Actical



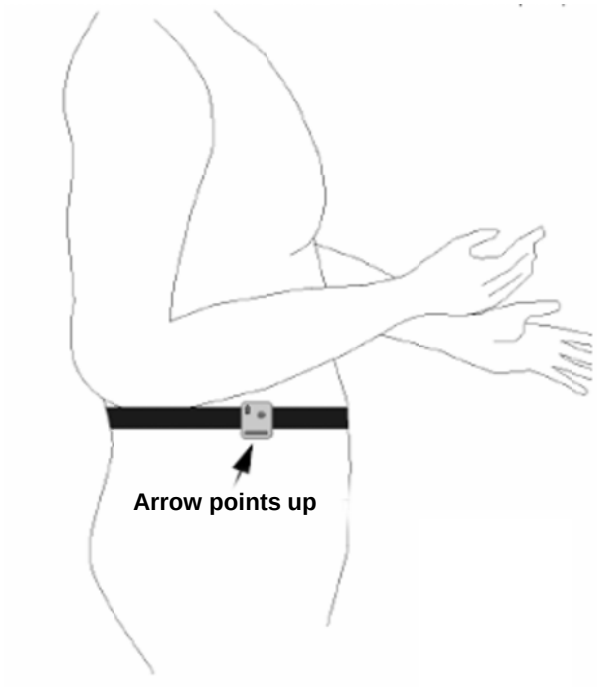
Study staff will briefly describe the purpose of physical activity monitoring and ask participants to undertake their normal activities for the week while wearing the monitor. Staff will emphasize that participants should not engage in activities that they ordinarily would not specifically because they are wearing activity monitors.

Staff will demonstrate how the device is worn, and specify that it is worn over the right hip on the waist strap. The belt should be mounted on the body so that the device rests on the iliac crest (the uppermost and widest of the three bones constituting either of the lateral halves of the pelvis) of the hip with the arrow pointed up (toward the head). The unit should be snug against the body (but not tight) so that it does not bounce around (Figure 16). The unit can be worn underneath or on top of

clothing, whichever is most comfortable to participants. During the clinic examination, participants will practice putting the monitor on properly with study staff present to provide feedback.

Based on best practice research recommendations, we will measure 7 days of recording so that we can capture intra-individual variability in total, moderate and vigorous activity and increase the likelihood of capturing at least four days of activity—the length at which reliability is expected to be 0.80. Participants are asked to wear the accelerometer continuously over 7-days and to remove it only for swimming, showering, and sleeping.

Figure 18b. Proper placement of the Actical



Participants are told that on the third day of recording a staff member will telephone them to answer any questions or concerns about the device and to make sure that the instructions are clear. The telephone call also provides staff with the opportunity to remind participants to wear the monitor continuously.

Before leaving the clinical examination, staff will give participants a dated reminder card indicating when they should stop wearing the device and mail it back to the clinic in the pre-addressed and stamped mail envelope provided to them by clinic staff. As specified in the consent form, we will mail participants their honorarium once we receive the accelerometer back at the clinic. Staff will call participants again two weeks after completion of the recording period if their accelerometer has not been returned to the examination clinic.

18.2.1 Equipment and Supplies

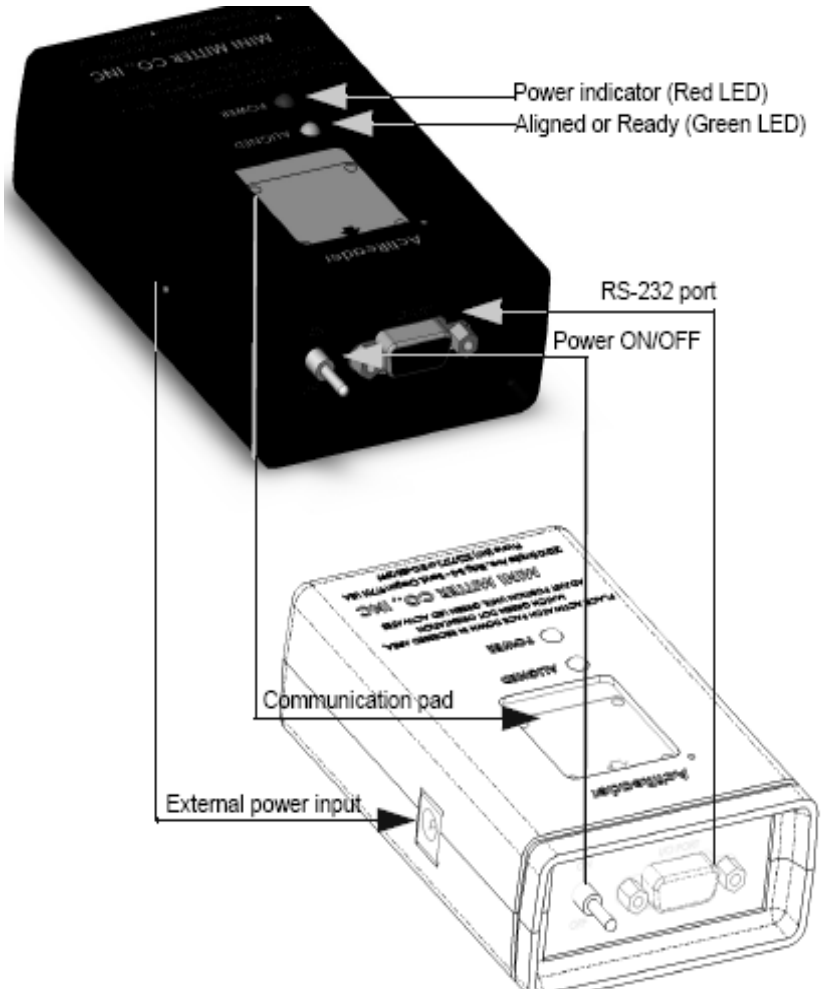
Each field center will receive 400 Actical accelerometers. In addition to the accelerometers, the coordinating center will provide the following items to each field center:

- 400 waist bands of varying sizes
- 1 ActiReader unit
- cables for connecting the ActiReader to the computer
- Actical software
- User's Manual
- Flathead screwdriver for opening accelerometer and changing battery
- "O"-rings (to be changed when replacing batteries)

Each field center is responsible for purchasing the following:

- Approximately 4000 padded 4" x 6" envelopes to give participants for returning accelerometers
- Postage for the mailing envelopes
- Mailing labels for return envelopes
- CR2025 lithium Coin cell ion batteries

The reader interface unit(s) will be connected to the study computer(s). The computers do not need to be dedicated to collecting the accelerometry data; however, they should be available whenever units are returned so that data can be downloaded and stored when the units are received.
Actical units are calibrated at the factory and the calibration offset factors are entered into the memory at that time. On a yearly basis and after consultation with the Coordinating Center, units are returned to the factory for operational evaluation and re-calibration. A log is to be kept of the serial numbers of accelerometers that are out for calibration.



18.3. Initial Hardware and Software Set-Up

Actical software needed for initializing and reading Actical data will already be installed on each laptop computer. However, each field center will be given a copy of the Actical software and a User's Manual. If necessary, the software can be re-installed following detailed instructions in the User's Manual. To test the ActiReader device

1. Connect the serial port to the serial-to-USB converter. Then connect the USB to the one end of the serial communication cable to a COM Port on the PC and the other end to the ActiReader (see figure, above)
2. Test the ActiReader set up by opening the Actical software, selecting: Reader > Test Reader. Follow the prompts through the test procedure. If the test fails, follow the prompts to correct the problem.
3. If the problem cannot be corrected, contact the HCHS Coordinating Center.

This procedure is repeated for each computer/reader used in the study.

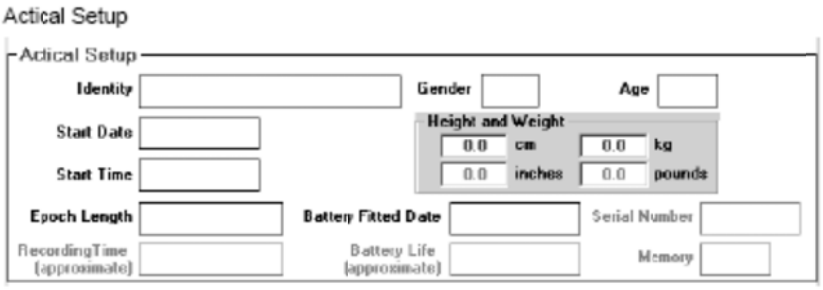
18.4 Preparing for the Participant Examination

Before a participant arrives at the clinic, the clinic staff should carry out the following steps:

1. Select an accelerometer and record the monitor serial number, participant ID (ID) into the accelerometry tracking system.
2. Initialization should not take place more than two days before the participant arrives.
3. Initialize the accelerometer using the following steps:

Each Actical device must be uploaded with setup information (initialization) prior to collecting data. This is done within the Actical software and then loaded onto the Actical device using the ActiReader.

1. Open the Actical main window and select Reader > Write and follow the prompts that alert you that setting up a device will erase previously stored data.
2. Click "yes" in response to the question "Do you want to continue?"
3. Place the device on the ActiReader. It is properly in place on the communication pad, the green LED will light up. Rotate 90 degrees until green light illuminates. The "communication" bar at the bottom of the screen will demonstrate a connection.
4. The following setup screen will appear:



5. Under "Identity" enter the participant ID number. Enter the participant's gender by using the mouse to point to the box, then toggle between F and M. All other entry boxes can be accessed using the "Tab" key. Enter age as appropriate and enter the start date as the day of the scheduled visit and start time as 05:00 (5 AM) on the day of the visit. Epoch length should be set to 01:00 (1 minute).
6. When all information has been entered, click "Send". The information will be sent to the Actical activity monitor device.
7. The initialization progress will be shown by the red bars at the bottom of the window.

18.5. Instructions to the Participant

Instructions for use and return of the accelerometer are given to the participants before he/she leaves the HCHS/SOL field center, as described in Section 24 of this manual, Exit Interview. Arrangements for the return of the accelerometer are established at the time, according the procedures in place at each field center.

18.6. Downloading the Data

As soon as the accelerometer is returned, download the data. This should be done on the same computer on which the accelerometer was initialized.

1. Place the device into the ActiReader and open the Actical software

2. Click on Reader > Read and follow the prompts. The data download will be shown by the red progress bars at the bottom of the window. A prompt will tell you when the download is complete.
3. Click on Energy Expenditure, and select the default "Hip" setting.
4. Click on File > Export > Epoch-by-Epoch List.
5. Select the default file name, but remove the "_list" part.
6. Process the participant reimbursement according to field center procedures.
7. Once per day, follow the procedure outlined in section X.X of the Data Management Manual to transfer all downloaded Actical files to the CC.

18.7. Equipment Maintenance

The User's Manual provides the most complete information about accelerometer equipment maintenance. Each field center should have one hard copy of the manual.

18.8. Cleaning

The Actical devices should be disinfected after each participant use by wiping the surface with a non-alcohol based germicide such as Lysol disinfectant wipes. Cleaning should only be carried out when the battery cover is in place and fully sealed

Waist bands should be rinsed in a cleansing solution such as Tide after each use.

18.9. Battery Replacement

The Actical unit runs on a CR2025, 3-volt, 220-m-Amp-hour Lithium Manganese cell battery. The battery is required for data collection, reading, and writing. Although stored data are not lost after the battery has run down, it is important to change the batteries at regular intervals. A battery indicator light on the reading device will display a green light when the battery is charged. A log of battery changes (Appendix 4) should is kept for each Actical unit. Detailed instructions with graphics can be found in the product manual. The steps are as follows:

1. Remove the band from the watch and use the flathead screwdriver supplied with the devices to loosen and remove the 4 screws on the slots in the battery cover of the device.
2. Turn the cover clockwise to display the battery (if the screws are loosened). Lift the cover off if the screws are removed.
3. Remove the battery and discard/recycle.
4. Clean the O-ring channel with alcohol.
5. Place a new O-ring into the channel on the back cover by pre-stretching the O-ring by gently flexing it in several directions. Be sure that it is properly sealed in the channel and is not twisted or deformed.
6. Place a new battery into the Actical case, positive (+) side up.
7. Rotate the back cover counterclockwise until the slots in the back are firmly sealed around the screws and the back is square with the case (or replace the cover and screw it firmly back on).
8. Tighten all 4 screws in an "X" pattern until snug.
9. Test the Actical battery by placing it on the ActiReader. A green LED light indicates successful battery replacement and installation.
10. Record the Battery Fitted Date in the Actical set up.

All other service related questions should be managed through support at Mini Miter Respironics: http://ribn.respironics.com/

19. 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 baseline examination. This section of Manual 2 presents a general description of interviewing in the intake examination of the HCHS/SOL. Specialized interviews such as the 24-hours dietary recall and dietary supplements are detailed in a separate manual.

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. Questionnaires that are not administered using the HCHS/SOL DES include the 24-hour dietary recall, the oral health questionnaire and the screens using during spirometry and audiometry to collect participant responses. 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.

19.1. 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 that rereading it in exactly the same manner.

19.2. 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.

19.3. 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.

19.4. 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.

19.5. 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?"

The cautions in using probes are similar to those for the 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.

19.6. 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.

19.7. Quality Assurance of Interviews

The quality of data collected during interviews is maintained through a series of 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 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.

Successful completion consists of demonstrated ability in the following five areas:

(1) Knowledge of the substantive matter in the interview;

(2) Use of an even pace and conversational tone;

(3) Demonstration of a professional and nonjudgmental demeanor;

(4) Use of appropriate probing techniques;

(5) Ability to accurately record the participant's response.

Interviewers unable to attend central training are trained at each HCHS/SOL field center by the interviewer supervisor, using the HCHS/SOL training materials, standards and certification procedures.

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 a bi-annual schedule. One tape with three interviews and their corresponding paper forms for each interviewer are assembled and participant identifiers on the study form are removed/masked. The taped interviews only specify the interviewer code and field center name. One field center's supervisor reviews another center's taped interviews with the help of the certification check list (see Manual 12 – Quality Control).

According to round robin comments returned to the field center supervisor and to the coordinating center, field center supervisors determine whether interviewers require additional training. If the retraining is extensive, a new tape with three interviews is prepared and submitted for review by the original round robin partner.

At the conclusion of the round robin, each field center's supervisor sends the following materials to the coordinating center:

(1) one check list for each interviewer; and

(2) three interviews recorded on tape(s) and three paper forms per interviewer.

20. SLEEP STUDIES

The equipment chosen for sleep apnea monitoring is the *Apnea Risk Evaluation System (ARES*) Unicorder. This device uses a novel pulse oximeter with highly accurate recording characteristics compared to gold standard co-oximetry (measuring oxygen saturation and heart rate), and sensors which measure: airflow (by nasal a cannula and pressure transducer; i.e., considered the "gold standard" for airflow assessment during polysomongraphy), snoring sounds (by microphone), and head movement and body position (by accelerometry). All sensors are housed within a small unit stabilized on the forehead with a self applied band. The unit is powered by a rechargeable battery that can support 14 hrs of recording. The data collected enable computation of the apnea hypopnea index (AHI), an index associated with important health outcomes for this study, including, hypertension, impaired glucose tolerance, cardiovascular disease and sleepiness and functional impairment.

Each site receives 18 or 19 sleep monitors with which to collect approximately 40 sleep studies per week. Each site also receives the necessary software with which to upload participant information, download studies, and transmit studies to the Case Sleep Reading Center (CSRC) for review and scoring. Field sites will be responsible for instructing the participant in use of the sleep monitor, collection and transmittal of sleep data to the CSRC, maintaining the sleep monitors, and follow-up with appropriate site staff for Urgent Sleep Alerts. The CSRC will be responsible for receipt, processing and storage of study data, providing feedback to the field site, and for transferring the data to the HCHS Coordinating Center.

20.1. Preparing Unicorder for Use

The field sites will be responsible for preparing the Unicorders for each use, properly fitting the monitor as well as instructing the participant in proper use. Prior to participant arrival for the clinic visit, the technician should prepare the Unicorder for data collection and gather a complete packet of supplies, instruction sheets, and data forms to be given to the participant at the clinic visit. The field site will explain to each participant the purpose of the sleep study and how assessment of the quality of sleep can help provide information about sleep apnea and its link to health, and will explain the importance of collecting representative data of a normal night of sleep. The field site will explain to the participant how the Unicorder should be placed on the head and how the device alerts the participant to indicate when it needs adjustments during the recording. Sites should provide the participant with specific instructions and mailing supplies for packing the Unicorder after use and on how it will be retrieved.

Each site will be responsible to maintain sufficient supplies in stock for use with the Unicorder sleep monitor. Unicorder disposable supplies (Salter cannula, enclosure strap, enclosure foam, sensor foam) are intended for single participant contact only and must be discarded after use. Preparation of the Unicorder prior to the clinic visit requires the participant identification information be uploaded and that participant ID labels be placed on the storage case and head strap.

20.2. Equipment Maintenance

To prevent others from coming into contact with the Unicorder, gloves must be worn when it is unpackaged and the Unicorder must be cleaned and disinfected before downloading the study.

After cleaning and disinfecting the Unicorder, the study should be downloaded promptly and battery plugged in for recharging using the Ziplinc Wall Battery Charger. Up to 3 hours are allowed for the recharge, although this may be shorter depending on the length power usage from the last use.

Proper working order of the sleep monitor will be confirmed at the time of each download. If a problem is detected, further maintenance checks and unit calibration will be performed; CSRC and/or the manufacturer will be contacted regarding monitor problems the site is unable to resolve and/or monitors that fail calibration checks.

The sleep monitors will undergo routine maintenance every 50 nights of use as well as maintenance checks every six (6) months. A log record book of all maintenance checks as well as problems with individual units and problem resolution will be maintained at each local field site. Field sites will track the use, location and status of each monitor, assuring timely retrieval after study completion.

20.3. Download and Transmittal of Study Data

Upon return of the monitor, recorded data will be downloaded, reviewed for quality standards and transmitted to the CSRC. After cleaning and disinfecting, the Unicorder and its paperwork are carried to the downloading computer and connected for downloading. It is verified that the participant information downloaded matches the label and paperwork. During download the software performs a preliminary quality review of the study. Quality problems identified at this stage will be noted and will indicate whether or not the Unicorder should be flagged for troubleshooting before reuse. After download the next screen will ask for data entry of the information on the Sleep Study Log form. An additional field will be available to include notes to the CSRC regarding any quality issues noted at download that need to be communicated. Data are uploaded to the CSRC via a secure FTP over SSL connection. Confirmation that all data have been received will be available for viewing at the CSRC website. If no quality issues are identified at download the Unicorder can be prepared for re-use and the battery recharged.

20.4. CSRC Processing

The site will receive the following information from the CSRC: 1) Signal Quality (including Pass/Fail status); 2) Urgent Alert Identification; 3) Participant Feedback.

Data from any studies flagged as failed quality grades or noted to have marked drops in oxygen levels will receive priority scoring, with reports generated within 48 work hours of receipt at the CSRC. The CSRC Manager will contact the site by phone or email with information on possible equipment malfunction, participant acquisition problems (possibly requiring repeat studies), or urgent alerts (requiring timely feedback to the participant and/or the participants' physician). Reports for these studies will be emailed to the site. All other studies will be triaged for complete scoring within 2 weeks.

20.5. Urgent Alerts

Field centers receive email notification of any study that meets the following alert criteria: 1) AHI >50; 2) Oxygen saturation <90% for > 10% of Total Sleep Time; or 3) Heart rate > 150 bpm for ≥ 2 minutes or < 30 bpm for ≥ 2 minutes. Studies so identified will require timely feedback to the participant who should be advised to consult with their physician. A copy of the sleep record should be made available to such participants at the time they are notified of a possible sleep concern.

In the event that a sleep recording submitted to the CSRC meets the above criteria for Urgent Sleep Alert the field site, after notification from CSRC, will be responsible for assuring that the appropriate follow-up has been accomplished, which in most cases will require that the participant be contacted and urged to follow-up with their physician. A disposition log for Urgent Sleep Alerts will be maintained at each local field site.

21. LUNG FUNCTION TESTING

In addition to questionnaires on respiratory function and symptoms, spirometry is done in the HCHS/SOL as an objective means to detect asthma and COPD. The main spirometry measurements are the forced vital capacity or FVC (the greatest volume of air exhaled from a maximal inspiration to a complete exhalation); the forced expiration volume in one second or FEV_1 (the volume of air exhaled in the first second of the FVC maneuver); and the ratio between these two values: FEV_1/FVC. The SensorMedics model 1022 dry-rolling seal volume spirometer is used in the HCHS/SOL, fitted by OMI with a digital volume encoder, temperature sensor, and RS232 serial computer interface. The OMI spirometry software (version 3.3) is installed on a notebook computer with Windows XP that is part of the work station. No other tests are conducted in the room during spirometry testing. The study procedures, the equipment, the technician training and the measurement technique are described in HCHS/SOL Manual 4. The instruments and the protocol used in the HCHS/SOL conform to the guidelines of the American Thoracic Society (ATS) and the European Thoracic Society (ERS), and their combined ATS + ERS spirometry guideline published in 2005.

Spirometry requires the participant to produce an adequate effort. Thus, results are very sensitive to the ability of the technician to instruct and motivate the study participant and the participant's ability and willingness to completely inhale and forcefully exhale throughout the entire expiratory maneuver. The technician instructs and demonstrates the test procedures to the participant and provides feed-back based on observation of the flow-volume curves, volume-time curves, test values, and the quality assessments provided by the OMI software.

Study participants with airway obstruction are offered post-bronchodilator spirometry to determine if the airway obstruction is reversible (indicating that asthma is more likely than COPD). For this purpose, airway obstruction is defined as a low FEV1/FVC below 5th percentile and an FEV1 below 90% predicted.

22. AUDIOMETRY

A brief otoscopic evaluation of each ear is performed, noting the presence of cerumen (ear wax), inflammation, blood or foreign bodies in the ear canal and structural defects of the ear and canal. Inter-examiner reliability and validation against tympanometrically assessed conditions have been demonstrated to be high in the EHLS. A screening tympanogram is obtained according to ASHA recommendations using a machine calibrated to ANSI standards. These testing protocols are similar to those used in the National Health and Nutrition Examination and Survey (NHANES).

Field sites use slightly modified NHANES procedures to improve the quality of the audiometric data Audiometric testing in HCHS/SOL uses manual methods to determine air conduction thresholds from 500-8000 Hz. Testing is conducted in a sound-treated booth using TDH-50 earphones and a clinical audiometer in a manner consistent with the guidelines of the American Speech-Language-Hearing Association. If needed, insert earphones are used to prevent collapse of ear canals that might lead to invalid audiometric results. Masking is employed as needed to ensure accurate thresholds and bone conduction thresholds determined at 500, 2000 and 4000 Hz to assess the presence of conductive hearing losses.

23. ORAL HEALTH EXAMINATION

A dental examination is conducted to estimate the prevalence of oral diseases and to study the factors associated with oral disease. Prior to the examination HCHS/SOL personnel identifies the need for prophylactic antibiotics prior to periodontal probing; this is confirmed at the time the dental examination is begun. Measures collected during the examination are of coronal and root caries, restoration materials, periodontal disease, and functional occlusal contacts. At the conclusion of this examination, the study participant receives feedback on examination findings.

The dental examinations in HCHS/SOL are conducted by a dental hygienist or dentist. All are trained in the HCHS/SOL examination protocol and certified prior to commencement of the study as part of which examiners have achieved acceptable proficiency as determined by good agreement with the Reference Examiner and other examiners.

To assist the Examiner, a Dental Recorder is present during the examination to enter the examination calls into the HCHS/SOL Dental Data Entry System (DDES), an interactive program resident on a study laptop for entry of all clinical data as well as responses to questions assessing the need for prophylactic antibiotics.

24. 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, run the Participant Inventory Report found on the "Reports" page of the study Data Management System (DMS). Supply the HCHS/SOL participant ID and the application will list the set of completed forms and procedures, noting which ones are missing. Refer to Manual 13 for more details about running reports and use of the DMS in general. As part of this 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 and the instructions for the sleep studies and physical activity monitoring are assembled and placed in the participant's folder at this time.

25. 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 re-establish rapport with the study participant and to seek commitment for a long-term association with the HCHS/SOL. The participant is reminded of the one-month follow-up call and at the field center's discretion the call can be scheduled at that time.

The "end of visit" study results are reviewed with the study participant and results identified for confirmation or referral for 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 28 of this manual. Before proceeding to the instructions for the sleep study and physical activity monitoring, the participant is asked whether he/she has any remaining questions about the study, the results to be received, or any concerns.

26. INSTRUCTIONS FOR USING THE ACCELEROMETER

Instructions for use and return of the accelerometer are given to the participant during the exit interview and include the following points:

1. What the accelerometer is and what it records;
2. Importance of wearing it every day, all day;
3. Proper placement of the accelerometer;
4. Importance of returning the accelerometer promptly;
5. Expect telephone call after the clinic visit to make sure he/she is wearing the accelerometer and understands the instructions;
6. Expect telephone call to check up on the return of the accelerometer if not received back at the agreed time.

Field center personnel follow scripted instructions (below) and give study participants a copy of the written instructions, in English or Spanish.

26.1. Example of Initial Script for Distributing the Accelerometer in Clinic

"This is the activity monitor that we are asking you to wear for the next 7 days. It's small, light weight and there is no way to know that it's running. I have activated it to start today, and it will run continuously now, on a small battery, until you send it back to us and we download the data. We have put the monitor on an elastic waistband with an adjustable buckle. Put the band around your waist, with this notch here pointing up at you on your right side, underneath your clothing. This will help the monitor remain in place better than if it were on the outside of our clothing.

We need you to wear the monitor from the time you wake up in the morning to the time you actually go to bed. You do not need to wear the monitor while showering, bathing or swimming, but don't worry about getting it wet. It will still work and record your movements. Also, you don't need to wear it while you're sleeping. If you fall asleep with the monitor on it won't hurt you or the data. If in the morning you go directly from bed to the shower, put it on after your shower. But if you're going to be up for 15 minutes or more before getting into the shower, go ahead and put it on, then take it off prior to your shower and then put it back on when you've finished showering.

Please do wear the monitor until you actually go to sleep at night, even if you're just sitting reading or watching TV. If you just get up to answer the phone or go to the bathroom, the monitor will collect these movements as you walk through the house. Does this all make sense?"

After waiting for participants to ask questions, continue:

"Finally, I'm giving you a stamped, pre-addressed envelope that you should use to return your activity monitor at the end of the 7 days of recording. Please remember to send this back to us. If we don't receive them within a week of the end of your recording period, we will call you. Also, please remember that we can't reimburse you for your study participation until the monitor is returned to the study center.

If any questions arise during this next week, there are names and phone numbers of study staff whom you can call for help inside the envelope we will give you. We'll also be calling you in the next day or so to see if you have any questions or problems. Do you have any questions?"

16.2 Actual Check-Up Call

Participants should be contacted on the 2nd or 3rd day after leaving the clinic. This call is to ensure that participants are wearing the monitor correctly and to answer any questions that the participant has. The call is meant to be brief. "Hello, I am (full name), from the Study of Latino Health at (Fill in University). Can I speak to _____?

If the desired person is on the phone	*When the desired person gets to the phone*	*If that person is not available*
"Hello Mr./Ms._____ **Continue**	"Hello Mr./Ms._____. I am (first name) from the Studies of Latino Health at (University). **Continue**	"Is there a better day and time to reach Mr./Ms. _____? Note days and times Thank you. I will try to call back then. **Terminate Call**

"Hello Mr./Ms._____. I am calling to make sure that the directions for wearing the activity monitor made sense and to ask whether you have any questions about wearing the activity monitor."
Optional script:

- "It is important that you wear it on your waist, not in a pocket or in a bag, with the monitor right above your right hip bone.
- Wear it snugly around your waist, either underneath or over your clothing.
- Wear it for 7 whole days, preferably on consecutive days"

If you reach an answering machine:

"Hello, I am (full name) calling from the Studies of Latino Health at the (University). I am calling because I want to make sure that the directions for wearing the activity monitor make sense. I will try to call back tomorrow or the day afterwards, but you can also call me if you have any questions about wearing the monitor."

26.3. Instructions for the Use of the Sleep Monitor

26.3.1 Additional Study Explanation

"Sleep Apnea is a condition characterized by repeated breathing pauses occurring in sleep, occurring between 5 to as many as 100 times per hour. Most people with sleep apnea snore and some make gasping or snorting noises during sleep. Because sleep is interrupted by these breathing pauses, many people with sleep apnea may feel as though their sleep did not refresh them, and they may feel sleepy or tired during the day. Also, oxygen levels may drop when a breathing pause occurs, and drops in oxygen levels may cause stresses on the body's normal functions. Because of this, sleep apnea may increase a person's risk for high blood pressure, heart disease and diabetes. A major goal of HCHS/SOL is to understand risk factors for high blood pressure, heart disease, diabetes and other health problems. Therefore, as part of this study, we would like you to wear a small device to sleep while at home that will measure your breathing, snoring and oxygen levels during sleep, which are indicators of your risk for sleep apnea."

26.3.2 Demonstrating the Unicorder

"The device is called the ARES Unicorder. It is worn on your head while you are sleeping. The recorder is fairly light weight, so it will feel like you are wearing a cap or hat to bed.

This is what the unit looks like. **(*Show participant the unit.)*** The main part of the recorder rests on your forehead, and the strap goes around your head. There are plastic tips that are gently placed into your nose measure breathing. The recorder also measures snoring sounds, head movements, and oxygen levels (this is done by the use of modern technology where a light from the device is shown

onto the forehead skin and can this light reflected back to the device can estimate oxygen in your body.) There are no needles, glue, or anything that needs to be worn in other places on your body."

26.3.3 Measuring/Fitting the Unicorder

"I will measure your head first to determine the strap size that fits you the best. It is important that the strap fit around your head firmly, but not be uncomfortable. We want things to be comfortable enough so you can wear this AND get your typical night's sleep.

(If participant hair is long) It is usually recommended that you wear your hair up during recording to prevent the Unicorder from slipping down during the night. Will you be wearing your hair up for the study? ***(If so)*** Can you hold your hair up for me, so I can get an accurate measurement?"

(Measure the circumference of the participant's head. Enter the measurement on the Sleep Log Form and look up the proper setting in Strap Setting Chart.)

"Your initial strap setting should be X. ***(Show participant how the holes on the Unicorder strap should line up and MARK this with a marker.)*** If this setting at any point in the study feels uncomfortably tight, you can loosen it one notch. Or, if it should feel too loose so that it is slipping on your forehead, you can tighten it one notch."

26.3.4 Putting on the Unicorder

"The Unicorder should be placed on your head about 15 minutes before bedtime. Before putting the Unicorder on, it is important to wash and dry your forehead where the sensor will be resting and wipe it thoroughly with an alcohol wipe we will give you."

(If an extra unit is available, tech should demonstrate on self as well as walking the participant through the following steps.)

"To position the Unicorder, hold the plastic tube tips against the on/off label at the bottom of the unit. With the strap set at the correct setting, slide the strap around your head and remove any hair from under the forehead box. Center the Unicorder sensor over your nose and slightly above your eyebrows on the flattest part of your forehead, so the entire forehead box touches your skin.

Place the two plastic tips in your nose and pull the tubing at the back of your head until it is snug. Grasp the slip tube label at the back of your head and slide it downward until the cannula is snug and in place. To test the cannula for correct tightness, try and pull the tips away from your nose. If they barely move, it should mean the fit is good. If they come out of the nose, readjust the slip tube to make it tighter. Remember, it is important that the plastic tubing tightens at the back of your head to keep the cannula from slipping during the night."

26.3.5 Starting the Sleep Study

"Once the Unicorder is properly positioned and you are ready for bed, turn off the TV or radio. (Noise in the room will interfere with the recorders microphone that measures snoring sounds.) .

With the switch at the bottom of the unit, turn on the Unicorder. ***(Show participant on the demo unit.)*** You will hear one chirp. This lets you know the unit is on. Once the unit is on, it is important that you not turn it off during the night. If you need to get out of bed during the night for any reason, leave the unit on. Do not turn the unit off for any reason during the night.

Next, lie flat on your back as still as possible until the Unicorder chirps twice. This usually takes between 30 seconds and two minutes. When you hear the two chirps, it means that the Unicorder is ready to begin collecting information. It will not record if this step is not completed. After you hear the two chirps, you can lie in any position that is comfortable."

26.3.6 Special Alerts

"If you should hear a two chirp alert at any time during the night after the Unicorder has begun recording, it means the Unicorder needs to be adjusted on your forehead. Move it slightly, so the sensor is in full contact with the flattest part of your forehead. If necessary, tighten the strap one position smaller.

If you should hear a three chirp alert during the night, it means the cannula is too loose. Readjust the cannula in your nose, and tighten the slip tube at the back of your head.

If you should hear a four chirp alert, it means that there may be a problem with the unit. Call Technical Support at 1-866-677-2737.

If any alert sounds more than two times during the night, call Technical Support.

To temporarily stop an alert, turn your head back and forth like you are shaking your head "No". Do not turn off the unit or take it off during the night."

26.3.7 In the Morning

"When you wake up in the morning, turn the Unicorder off. Remove the Unicorder and put it in the plastic bag, being careful not to damage the forehead box. Put the unit back in the supply box, along with all the other supplies that you were given. Note the time you went to sleep and woke up in the Sleep Log and put that in the supply box with the recorder, as well."

Common questions and answers are found in Appendix D of Manual 6.

27. 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 various conditions are ascertained as part of HCHS/SOL protocol that make a person ineligible for an exam procedure. These include: A. Use of a pacemaker or defibrillator for bioimpedence estimation and bronchodilator use; B. Use of other implanted electronic devices or artificial joints for periodontal measurements; C. Reported physician diagnosis of diabetes for oral glucose tolerance testing; D. Reported heart attack, stroke, or eye surgery or abdominal surgery in the last 6 months for pulmonary function testing. The presence of these conditions is ascertained at various stages ranging from recruitment, scheduling, and the examination process, by different staff. 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 PSAEA 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.

27.1 Measures to Protect the Participant

Examination procedures which convey potential, small risk to participants include the venipuncture, the administration of an oral glucose tolerance test, periodontal probing, spirometry and the administration of albuterol. 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. Methods by which participant risk is minimized (more fully described elsewhere in the HCHS/SOL Manuals) include the following. 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 (*PSE/PSS ver. B,* 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 PSE/PSS questions 2 – 10, and the study participant is informed of the exams and procedures she/he should not do.

The following procedures should not be done without verification that pertinent safety question(s) have been asked and a negative answer is recorded on the PSE/PSS form:

-Bioimpedence measurement
-Oral glucose load/administration of glucola
-Spirometry, use of the bronchodilator
-Periodontal measurements.

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 periodontal examination was conducted despite an exclusion condition, the Study Coordinator, Study Physician, or Field Center PI will notify the participant and (with their permission) their physician about what happened. If a periodontal examination was conducted despite an exclusion condition, the Study Coordinator, Study Physician, or Field Center PI notify the participant and (with their permission) their physician about what happened. It is the responsibility of the field center PI to have the need for antibiotic coverage addressed on the day of the HCHS/SOL examination.

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, anginal pain, ECGs with acute pattern abnormalities 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.

27.2 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 at all times during which participants are interviewed and examined either a physician, a physician assistant or a registered nurse. Each field center has, in addition to trained personnel and emergency equipment, posted in conspicuous places (e.g., the reception area): phone number 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 are available in the DES. Emergency situations are coordinated by the staff person designated, a priori, or by a physician if present. Each center has a designated physician on duty. 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 duty 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 are alert to early signs. In any situation in which syncope is likely, e.g., after the venipuncture, staff verify 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 can include anxiety, tremor, palpitations, faintness, hunger cold, clammy skin, rapid heart rate, sweating, numbness around the lips or on the tongue, tiredness, weakness (generalized), motor incoordination, slurred speech, irritability, appearing to be “absent” or not behaving “normal”. Hypoglycemic symptoms can occur with a glucose level within normal range (in those who are chronically hyperglycemic). These individuals need oral glucose replacement as well. If untreated, a further decrease in blood glucose may lead to confusion followed by loss of consciousness. 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.* Treated diabetics are excluded from the oral glucose test.

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 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 ≥ 100 mg/dL, and the participant is symptom-free. If ≥ 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 ≤ 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.

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.

27.3 Procedures to Document Adverse Events and Emergencies

Adverse Event Definition and Reporting in HCHS/SOL

An adverse event (AE) is an adverse change in health or "side-effect" that occurs in a person who participates in HCHS/SOL, which may or may not be caused by participation in the study. Serious adverse events (SAEs) and adverse events that are not anticipated in the study protocol or referred to in the informed consent must be reported to the local Institutional Review Board (IRB) and to the study sponsor (NHLBI).

AEs must be addressed promptly according to institutional safety guidelines and the HCHS/SOL study protocol, to 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 safety protocol.

AE Classification in HCHS/SOL

Serious (vs. minor or not serious)

An adverse event is serious 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
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.

Expected (vs. unexpected)
An adverse event is unexpected if the risk information is not mentioned in the consent form, if the 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.

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.

Reporting of Adverse Events and Information Flow
Once the participant safety and comfort concerns have been addressed all AEs are recorded in the HCHS/SOL DMS, and the Institutional Review Board (IRB) is notified according to each IRB's guidelines. All adverse events (whether serious or not serious) are recorded in the HCHS/SOL DMS. The Serious Adverse Event form or the Minor (not serious) Adverse Event form is used for this purpose. Completion of an Adverse Event form in the DMS results in a report of the SAE to the NHLBI by the Coordinating Center, within 72 hours. No direct notification of an adverse event to NHLBI is required of the field center unless additional information is needed. Adverse events not considered serious are summarized periodically by the Coordinating Center for the NHLBI, the OSMB, and/or the Steering Committee, as required. Summary tables of adverse events are included in the management reports prepared by the Coordinating Center. The reporting schedule of AEs in the HCHS/SOL is presented in Table 27.3 (below)

Table 27.3 Adverse Events - Actions by the HCHS/SOL Study Agencies and Timing						
Type of AE	HCHS/SOL Field Center			Coordinating Center	HCHS/SOL Ops and Measmts. Cmte.	Steering Committee
Serious (SAE)	Address any ppt. safety issues; inform medical director and PI	Record SAE in the HCHS/SOL DMS	Report AE to IRB	Notify NHLBI Review event & report to SC, FC Managers, Lab, as appropriate	Review study procedures with experts; propose revisions if required	Review report of AE and study procedures; modify protocol if required
Time / Schedule	Immediate	48 hrs.	72 hrs.	72 hrs.	2 weeks	4 weeks
Unexpected (AE, not serious) whether Related, Possibly Related, or Unrelated	Address any ppt. safety / comfort issues	Record AE in the HCHS/SOL DMS	Report AE to IRB	Notify NHLBI, SC, FC Managers & Centers if warranted	Review study procedures with experts; propose revisions if required	Review report of AE and study procedures; modify protocol if required
Time / Schedule	Immediate	72 hrs.	72 hrs.	Quarterly	4 weeks	As needed
Expected (AE, not deemed serious)	Address any ppt. safety / comfort issues	Record AE in the HCHS/SOL DMS	No	Update HCHS/SOL management report	N.A.	N.A.
Time / Schedule	Immediate	72 hrs.	N.A.	Quarterly	N.A.	N.A.

27.4 Conditions Ascertained at the Time of Scheduling Field Center Visit

1. Pregnancy (re-schedule)

2. Medications that need to be taken on schedule

27.5 Exclusions from Study Procedures

Exclusion from Any Study Component

SBP >= 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 Spirometry

a. **Assessed earlier in exam**

1. SBP >= 200 or DBP >120 mmHg. Stop exam visit, arrange for urgent care.
2. Pregnancy
3. Automatic implanted cardiac defibrillator (AICD)

b. **Questions asked at the time of spirometry**

1. Has had heart attack, a stroke, or eye surgery in the last 3 months.
2. Has had any significant problems doing spirometry in the past

Exclusions from the Bronchodilator Test
(Only applicable to participants selected for bronchodilator)

1. Technician shows albuterol metered dose inhaler and asks whether participant has had any significant problems taking a puffer.
2. Lactation
3. Report of use of a Class 1 anti-arrhythmic drug, monoamine oxidase inhibitor, or tricylic antidepressant.
   a. These preparations are flagged by the medication coding system. If following spirometry the participant is selected for a bronchodilator test a report is run on the DES to determine whether a medication taken by the participant meets this exclusion criterion.

   b. If the medications are not transcribed at this point or not all medications are coded, the technician retrieves the medications brought by the participant and in his/her presence reviews the medications/ containers/ prescriptions to identify any of the following in Table 27.4 (below):

Table 27.4

Anti-Arrhythmics That Exclude Participants from Bronchodilator Testing	**MAO Inhibitors that Exclude Participants from Bronchodilator Testing**	**Tricyclic Antidepressants that Exclude Participants from Bronchodilator Testing**
Amiodarone (Cordarone) Bretylium (Bretylol) Bretylol (Bretylium) Cardioquin (Quinidine, Quinalan, Quinidex, Quinaglute) Cordarone (Amiodarone) Disopyramide (Norpace) Dofetilide Enkaid (Encainide) Ethmozine (Moricizine) Flecanide (Tambocor) Ibutilide Lidocaine (Xylocaine, Xylocard) Mexiletine (Mexitil) Mexitil (Mexilitine) Moricizine (Ethmozine) Norpace (Disopyramide) Procainamide (Pronestyl, Procan SR) Procan SP (Procainamide, Pronestyl) Pronestyl (Procan SP, Procainamide) Propafenone (Rhythmol) Rhythmol (Propafenone) Tambocore (Flecainide) Tocainide (Tonocard) Tonocard (Tocainide) Quinaglute (Cardioquin, Quinidine, Quinora, Quinalan, Quinidex) Quinidine (Quinora, Quinalan, Cardioquin, Quinidex, Quinaglute) Quinalan (Quinora, Cardioquin, Quinidex, Quinaglute, Quinidine) Quinora (Quinidine, Quinalan, Cardioquin, Quinidex, Quinaglute) Xylocaine (Lidocaine, Xylocard) Xylocard (Lidocaine, Xylocaine)	Isocarboxazid (Marplan) Phenelzine Sulfate (Nardil) Tranylcypromine Sulfate (Parnate) Phenelzine Sulfate Tranylcypromine Sulfate	Amitriptyline (Elavil, Vanatrip) Amoxapine (Asendin) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Sinequan, Zonalon) Imipramine (Tofranil) Maprotiline (Ludiomil) Nortriptyline (Aventyl, Pamelor) Protriptyline (Vivactil, Triptil) Trimipramine (Surmontil)

Exclusions from Periodontal Probing (not from the rest of the dental exam)

Table 27.5

Safety Exclusions for the Periodontal Examination: Screening Questions Based on guidelines of the American Heart association and the American Dental Association (Wilson W et al. Circulation, April 19, 2007).	
Optimally: at the time of scheduling a field center appointment	Immediately prior to Oral Health Exam Administer if not present in the DES
Do you have artificial valves in your heart?	I would like to confirm that you do not have artificial valves in your heart.
Have you been treated by a physician for infective endocarditis?	You have never been treated by a physician for infective endocarditis.
Do you have a serious heart condition from birth?	You do not have a serious heart condition from birth.
Have you had a heart transplant?	You have not had a heart transplant operation.
Do you have artificial joints or prostheses?	You do not have any artificial joints or prostheses.

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 ≥ 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 ≥ 400 mg/dL **STOP** the examination and refer to the emergency room (regardless of the presence of symptoms).

27.6 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 mat 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 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.

27.7 Mental Health Emergency Procedures

In the course of the HCHS 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, 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.

a. Suicidal Ideation

In instances in which the participant can be assessed to be in moderate or extreme danger of attempting suicide, the medical personnel identified as responder for emergencies should be notified to obtain guidance prior to the participant's departure from the building.

Any spontaneous comments or circumstances indicative of suicidal ideation made by the participant (i.e., "life not worth living," "be better off dead," etc.) at any point during the study should be explored with the participant. If suicidal ideation (thoughts of suicide or wanting to take one's life) is present, it is the responsibility of the staff to determine the imminence/ dangerousness of risk.

Assessments of imminence/dangerousness can be completed in a number of ways, depending on the degree to which the participant appears to be forthcoming about her or his suicidality. First, the participant should be asked directly, "Are you feeling suicidal right now?" This should be followed by another direct question: "Have you felt suicidal in the past?" and then, "When was the last time you felt suicidal?"

The following items may also be used as a general framework in which to formulate questions about suicide for the participant you believe to be potentially at risk.

1. What is her current motivation for suicide? Current level of depression?
2. Does he/she have any prior suicide attempts?
3. What has stopped her from committing suicide up to this point?
4. What is his current affect? (is it blunt or flat?) Current mood?
5. Does she have a plan? Is it well-formulated? Is it lethal? Does it allow for rescue?
6. What environmental support does he have? What's his support network like? What are his perceptions of support from others?
7. What has he done? What arrangements have been made? Has he already begun to follow some type of plan?

If the suicidal threat is judged to be **immediate** (the participant cannot categorically state that he/she will not hurt him/herself), the staff must maintain contact with the participant, contact Dr. _____ for consultation, and ensure that the subject is taken to a psychiatric emergency setting. A crisis mental health unit or equivalent emergency facility located in proximity to the field center is referenced in this manual (_____). If this information is conveyed by phone or

the participant is unwilling to accept a voluntary evaluation and requires commitment (Baker Act), the police department may be contacted for transport (call 911 or (Security / Police).

A suicidal threat is judged to be **significant** but not immediate, if it is of concern and questionable risk. In this situation, the staff person must maintain contact with the participant and contact Dr. _____ to discuss an assessment and disposition. Recommendations for further action will be made by this individual. In most cases, the participant will be provided with a comprehensive list of community referrals (see appended). The following script may be used:

> Mr./Ms. _____, I'm concerned to hear that you have been feeling this way. A lot of individuals who have had similar symptoms have found several things helpful – first to talk to their doctor about possible medication to help with your symptoms, and secondly to talk to a mental health service provider to treat these symptoms.
>
> Have you thought about seeking help for this? You should talk to your doctor or contact any of these mental health service providers in your community (hand them community referral list).

Once the participant leaves, write a clear report of what has occurred immediately, co-signed by Dr. _____. The report should document:

1) What the participant initially said to warrant further assessment,
2) How the participant was assessed,
3) The conclusions that were drawn,
4) Who was consulted, and
5) What was done to protect the participant's well-being.

b. 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.

c. 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 maybe 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 _____.

Very rarely will a participant openly state an intent to harm and elaborate on the plan without direct questioning. Instead, s/he might say, "I get so mad I could kill." Rather than assume that the participant was speaking figuratively, it is important to investigate further without making the participant defensive. For instance, the interviewer might say, "When you feel like killing, who do you want to kill?" Even in the face of denial, interviewers may proceed with this line of questioning by asking, "Have you ever imagined what you might do if you were going to kill someone (or the person's name if known)?" Another question is, "You say that you'd never do it. What keeps you from killing [person's name]?" Then, using the person's response, "How far are you now from losing control and killing [person's name]?"

If the person has a weapon (such as a gun) s/he is planning to use specifically, it may be appropriate to request that the participant arrange for safe keeping of the weapon. Calm, explicit questioning is usually the best way to approach such an assessment, but the interviewer should be continuously gauging the extent to which they might be antagonizing the person and putting him or herself in danger. Be cautious enough to recognize when enough information has been gathered, or when a consultation break is required. It may be necessary to request that a supervisor join the session in order to add comfort and security. Consultation or follow-up with the study Principal Investigator is always required when a lethality assessment has been necessary with a potentially homicidal participant.

When interacting with a homicidal person it is necessary to identify the victim. It may be appropriate to inform the participant that a warning may be required. The interviewer may inform the participant that s/he will act to prevent harm to the intended victim, but it is not necessary to specifically describe the different courses of action available. Finally, if the interviewer considers the homicidal lethality to be high, the interviewer should always follow the emergency procedure. As stated above, the emergency procedure entails contacting the designated clinical psychologist – and upon recommendation contacting the police and attempt to have the client placed in a 72-hour hold. A detailed documentation of the incident and actions taken by the interviewer should be completed.

27.8 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.

28. 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 procedures are not identical to those performed in a regular clinical examination, and that they will only receive study results that are of known value to medical practitioners.

Information on examination and laboratory test results are shared with HCHS/SOL participants during an interview at the end of their field center examination visit, and subsequently as test results are returned by the HCHS/SOL central laboratory and reading centers responsible for the central and standardized processing of the data. The reporting schedule incorporated into this process is a function of alert ranges that define emergent, urgent or routine notification. This process is described in the following sections.

28.1. 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. The secondary purposes of the exit interview are to verify that all components of the field center clinic visit have been completed, to solicit comments and feed-back from the participant, to return the participant’s medications, and answer any remaining questions. An additional purpose of the exit interview is to instruct the study participant on the use of the physical activity monitor and the somnography equipment.

28.2. 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 to 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.

28.3. 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 central reading centers. 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 to the collaborative database. This report includes any results previously reported to the study participant on an expedited schedule (such as “alert values”).

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, a staff member gives the participant a "clinic visit report" and reviews their weight, height, current blood pressure ankle-brachial index, results of the respiratory function test results, a copy of their electrocardiogram, and of a report of their hearing test. This “clinic visit report” also indicates to participants that they will receive by mail a copy of the interpretation of selected blood tests and 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 HCHS/SOL 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 through the Reports section of the study Data Management System (DMS). These reports are provided with customized cover letters by the field centers and sent to the study participants and their physician (if permission was obtained to release these data). The date of the Summary of Results sent is also recorded in the Report and Referral Tracking Form.

28.4. 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 contacted by the data management system at the Coordinating Center through email messages addressed to the project manager and the principal investigator until the pending notification has been acted on.

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 210 mm Hg or a diastolic of 120 mm Hg, or an accident or medical emergency that occurs during the participant's visit at the study field center. The response by the staff is to arrange for a transfer of the participant directly from the field center to their physician or a hospital emergency room.

Each time results are uploaded to the central database by the central laboratory the data are scanned according to the threshold levels identified in Table 8. As an example, if a triglyceride value is >= 1000 m/dL an Alert Notification is generated for the respective field center, identifying it as an Immediate Action. Field centers review their alert notifications (and regular result reports) daily from their secure Reports pages of the DMS maintained by the HCHS/SOL coordinating center. If a field center does not access a participant report flagged as an alert, email notifications are generated after 72 hours to notify the field center personnel, the field center manager, and the coordinating center manager.

For 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. Depending on field center procedures, the letter to the physician's office can be faxed prior to the phone call so that the caller can refer to the fax sent about an alert value obtained on the participant as part of a research study. Referral of an immediate alert value – during the Exit Interview of subsequently on receipt of an Immediate Alert Notification from a central laboratory or reading 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 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 heath 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 within the week of the field center receiving the information.

A **routine summary report** of all other study results is communicated in a report of results from the HCHS/SOL once all study results are available to the field center personnel. 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 messages that accompany such values in the summary report to the study participant (see Appendix) indicate

that this represents a single determination of values that routinely require confirmation, and emphasize 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 within two months and a complete result follows as soon as the missing items become available.

28.5. Thresholds for Referral and Reference Ranges for Study Results

a. Seated Blood Pressure

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 2003 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII). 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 5. Classification of Blood Pressure in Adults Aged 18 Years or Older, and Recommended Action per JNC VII*

Category	SBP mmHg		DBP mmHg
Normal	< 120	and	< 80
Pre-hypertension	120 – 139	or	80 – 89
Hypertension, Stage 1**	140 – 159	or	90 – 99
Hypertension, Stage 2**	> = 160	or	> 100

SBP= systolic blood pressure. DBP= diastolic blood pressure.
* Source: The JNC 7 Report. JAMA 2003;289:2560-2572
** Diagnosis of hypertension must be based on two or more readings taken at each of two or more visits following an initial screening.

JNC VII 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 the 2nd and 3rd 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 2nd and 3rd 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 $\geq$120 mmHg or Systolic BP $\geq$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 6. Classification of Blood Pressure in Adults Aged 18 Years or Older per JNC VII, and Recommended Action by the HCHS/SOL

Category		Action Recommended During Exit Interview
Not on treatment for HTN	Normal SBP <120 and DBP <80	Have your blood pressure measured by a health professional at least every two years
	Pre-hypertension SBP 120-139 or DBP 80-89	Have your blood pressure measured by a health professional every year
	Hypertension, Stage 1 SBP 140-159 or DBP 90-99*	Your blood pressure is high (specify and show results on report). Please have your blood pressure checked by a physician within two months.
	Hypertension, Stage 2 SBP >=160 or DBP >=100*	See below
On treatment for HTN	Hypertension (2) SBP <160 and DBP <100*	If you are being treated for high blood pressure, your physician may have given you a schedule for your next check-up. Please follow that schedule.
Whether or not treated for HTN	Hypertension, Stage 2 SBP 160-179 or DBP 100-109*	Your blood pressure is high (specify and show results on report). Please have your blood pressure checked by a physician within a month.
Whether or not treated for HTN	Hypertension, Stage 2 SBP 180-199 or DBP 110-119*	Your blood pressure is very high (specify and show results on report). Please have your blood pressure checked by a physician within one week.
Whether or not treated for HTN	Hypertension, Stage 2 SBP >= 200 or DBP >120*	Your blood pressure is very high (specify and show results on report). We strongly recommend that you see a physician at once. [Assist the participant in making an appointment for the same day, or at en emergency care facility]

* 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.

b. Ankle-Brachial Ratio

The presence of peripheral arterial disease (PAD) will be assessed with the ankle brachial index (ABI) using the Nicolet Doppler Elite 100R, EN 50R. A normal ABI range is 1.00 to 1.40, with progressively lower values below 1.00 corresponding to more severe arterial disease. Most persons in the group with an ABI >1.40 will also have a form of PAD. These higher ABIs reflect medial arterial calcification and partial or complete incompressibility of blood vessels, and primarily occur in persons with diabetes.

The ABI denominator for both the left and right ABI is the average of the four brachial SBPs. If the difference between the average brachial SBPs in the two arms is 10 mm Hg or more, and one arm has a higher SBP for both measurements, the higher arm average SBP is used as the denominator. The right ABI numerator is defined as the higher of 1) the average right posterior tibial SBP or 2) the average right dorsalis pedis SBP. The left ABI numerator is defined as the higher of 1) the average left posterior tibial SBP or 2) the average left dorsalis pedis SBP. The right ABI is the right ABI numerator divided by the ABI denominator. The left ABI is the left ABI numerator divided by the ABI denominator. The report to the participant and the medical practitioner indicates that an ABI value <0.90 is strongly suggestive of a blockage of the arteries in the leg. An ABI value between 0.90and 1.00 is considered borderline, and a value above 1.40 also may be abnormal. It is further mentioned that an ABI outside the 1.00 to 1.40 range should be discussed with your health care provider as it may require additional testing.

c. **Twelve-Lead Electrocardiogram**

A twelve-lead electrocardiogram will be acquired on all HCHS/SOL study participants according to the standardized study protocol, using the GEMSIT MAC 1200 portable electrocardiograph. The records will be transmitted via phone lines to the ECG reading center (EPICARE) for coding and a local ECG screening of the paper tracing for major abnormalities that require urgent referral will be conducted by a medical practitioner at the field center. Following processing of the ECG record at EPICARE a report of the abnormalities listed below or their absence) will be transmitted to the HCHS/SOL Coordinating Center to be incorporated into the report to study participants that field center personnel download from the secure server maintained by the Coordinating Center. A paper tracing of the 12-lead ECG enclosed with the report to the study participant.

Table 7. HCHS Major and Minor ECG Abnormalities Reported and their Descriptors

Associated Report Variables	Codes	Flag Description
mc_1 (l,v,f)	1.1.x, 1.2.x	Major Q Wave abnormalities [old Myocardial Infarction (MI)]
mc_4, mc_5 (l,f,v)	4.1.x, 4.2, 5.1, 5.2	Major Isolated_ST_T_abnormalities
mc_1, mc_4, mc5 (l,f,v)	1.3.x and (4.1.x, 4.2, 5.1, 5.2)	MINOR Q,QS waves with ST,T abnormalities (possible old MI)
mc_c3; mc_4, mc_5 (l,f,v)	3.1 and (4.1.x, 4.2, 5.1, 5.2)	Left Ventricular Hypertrophy
		Major AV Conduction Abnormalities
mcr_61	6.1.1	Complete (third degree) A-V block
mcr_62	6.2.1	Mobiz Type II
	6.2.2	Partial (second degree) A-V block
	6.2.3	Wenckebach's phenomenon
mcr_64	6.4.1	Wolff-Parkinson-White pattern
mcr_86	8.6.1	A-V dissociation with ventricular pacemaker (without capture)
	8.6.2	A-V dissociation with ventricular pacemaker (with capture)
qti, jti		Major QT Prolongation, QTi >= 116%, codes not suppressed
mcr_83	8.3.1	Atrial Fibrillation or Flutter
mcr_68	6.8.1	Pacemaker
		Other Major Arrhythmias
mcr_82	8.2.1	Ventricular fibrillation or ventricular asystole
	8.2.2	Persistent ventricular rhythm with no codable segment, regardless of rate
	8.2.3	Intermittent ventricular tachycardia
	8.2.4	Ventricular parasystole
		Ventricular Conduction Defect
mc_c7	7.1	Complete/Intermittent LBBB
	7.2	Complete/Intermittent RBBB
	7.4	Nonspecific Intraventricular Block
	7.8	Complete/Intermittent RBBB w/ Left Anterior Hemiblock

Table 7. HCHS Major and Minor ECG Abnormalities Reported and their Descriptors

Associated Report Variables	Codes	Flag Description
mc_1 (l,f,v)	1.3.x	MINOR ISOLATED Q,QS waves
mc_4, mc_5 (l,f,v)	4.3, 4.4, 5.3, 5.4	MINOR ISOLATED ST,T Abnormalities
mc_c3	3.1, 3.2, 3.3, 3.4	HIGH R waves
mc_l92	9.2.1	ST Segment Elevation, Anterolateral Site
mc_f92	9.2.1	ST Segment Elevation, Posterior Site
mc_v92	9.2.1	ST Segment Elevation, Anterior Site
mc_c7	7.3	Incomplete RBBB
mc_c7	7.6, 7.7	Incomplete LBBB
qti, jti		Minor QT Prolongation, QTi >=112%; codes not suppressed
mcr_65	6.5.1	SHORT_PR
mc_c2	2.1	Left axis deviation
mc_c2	2.2	Right axis deviation
mcr_81	8.1.2, 8.1.3	Frequent Ventricular Premature Beats
		Other Minor Arrhythmias
mcr_63	6.3.1	P-R Interval > .22 sec
mcr_81	8.1.1	Frequent atrial or junctional premature beats
	8.1.4	Wandering Atrial Pacemaker
	8.1.5	Frequent atrial or junctional premature beats and Wandering Atrial Pacemaker
mcr_84	8.4.1	Supraventricular rhythm
mcr_87	8.7.1	Sinus Tachycardia
mcr_88	8.8.1	Sinus Bradycardia
mc_c91	9.1.1	Low QRS amplitude
mc_c93	9.3.1	P-wave amplitude high

d. Respiratory Function Testing

Spirometry will be conducted using the SensorMedics model 1022 dry-rolling seal volume spirometer, fitted by OMI with a digital volume encoder, temperature sensor, and RS232 serial computer interface. The main spirometry measurements are the forced vital capacity (FVC), the forced expiration volume in one second (FEV_1), and the ratio between these two values (FEV_1/FVC). Testing, interpretation of the results and reporting will follow the spirometry guidelines of the American Thoracic Society (ATS) and the European Thoracic Society (ERS) (combined ATS + ERS spirometry guideline published in 2005).

The spirometry interpretation scheme in use for the MESA Lung Study will be used for the HCHS/SOL, with the addition of an interpretation of the post-bronchodilator results. Per the HCHS/SOL manual of operations, the criteria for a post-bronchodilator spirometry is FEV1/FVC below fifth percentile for age and FEV1 <90% predicted.

If pre-bronchodilator spirometry shows mild obstruction or mild restriction, but post-bronchodilator spirometry is normal, restriction and COPD have been ruled out. Study participants with pre-bronchodilator obstruction and a 'significant' bronchodilator-response per ATS criteria, will be considered to have symptoms suggestive of asthma. If this is not previously known (diagnosed asthma) the HCHS/SOL participants will be advised to seek med cal attention within 4-6 weeks. The presence of pre-bronchodilator obstruction but no significant bronchodilator-response will be interpreted as not excluding the possibility of a clinical response to inhaled medications. Smoking cessation will be strongly advised to individuals with post-bronchodilator airway obstruction who are current smokers.

Care is taken to not "over-interpret" tests, e.g., borderline results are not interpreted as mild lung disease. In the case of suboptimal quality test sessions the report makes allowance for the associated uncertainty.

Reporting. A software-generated report is printed immediately after a satisfactory spirometry test is completed and a copy is given to the participant to discuss with the provider of care if desired. An electronic copy of the report is sent to the coordinating center to be integrated with other medically relevant test results for the consolidated report of study results four to six weeks later. A sample report is shown below.

Lung Function Measurements

Hispanic Community Health Study Spirometry Results

Study ID: xxxxxxx	Acrostic: yyyyyyy
Age: < Your Age >	Height: 173 cm
Session: 50	Gender: F

During your HCHS/SOL examination you did several tests of your **lung function**.
The results of your best efforts are:

	Pre Bronchodilator		Post-BD Results
Measures	**Results**	**% Predicted**	**% Change**
FVC	2762 mL	82.3 %	+6.0 %
FEV1	1673 mL	60.8 %	+12.1 %
FEV1/FVC	60.6%	82.5%	----

INTERPRETATION:

Moderate airways obstruction indicated by the moderate reduction in FEV1.

Abbreviations: Post-BD = after albuterol
Spirometer: Sensormedics 922 / 1022, ID (Serial#): 4567888 OMI Version: 5.05
Normals Used: Hankinson(C)-1999 RA Factor: 1.00
Calibration date: 07/18/2007 Temp: 37.0 C. BP: 760 torr BTPS Factor: 1.000
Pre-Test
Effort = Maximal, Position = Standing, FVC Quality = B, FEV1 Quality = A
Post-Bronchodilator-Test
Effort = Maximal, Position = Sitting, FVC Quality = B, FEV1 Quality = A

Spirometry abnormalities assessed at the time of the HCHS/SOL examination have typically developed over many years; thus, no alerts or urgent referrals apply. However, when lung function is below 50% predicted, the participant will be told that they probably have a severe abnormality. If this is not previously known (diagnosed lung disease), the HCHS/SOL participants will be advised to seek medical attention within 4-6 weeks.

e. **Hearing Tests**

Hearing test results will be included in the consolidated report of study results to be received by the study participant within six weeks of the field center examination visit. Feedback at the time of the exam will include a programmed flag if the ECV is >=3.0, in which case the participant will be told that he/she may have a perforated eardrum. The participant will be instructed to avoid getting water in this ear, as that may lead to an infection and should contact his/her physician for medical evaluation of the perforation. A summary of the examination results is sent to the Coordinating Center but expedited notification will not be required. The results to be provided to the study participants and their interpretive statements are summarized below.

Equivalent canal volume right ear (cc): (value) Equivalent canal volume left ear (cc): (value)	Consult your doctor if this value is greater than 3.0 as you may have a perforation (hole) in your ear.
Peak Compensated Y in right ear (mmho): (value) Peak Compensated Y in left ear (mmho): (value)	Consult your doctor if this value is less than 0.2 as you may have effusion (fluid) in your middle ear.

Average hearing threshold in right ear (dB HL): (value) Consult your doctor if your average
Average hearing threshold in left ear (dB HL): (value) hearing threshold is 25 or greater or if you experience difficulty with communication.

Other findings: No other significant findings (or specified).

f. Sleep Studies

Physiologic sleep data will be acquired and sleep apnea monitoring will be done with the Apnea Risk Evaluation System (ARES, Unicorder, Advanced Brain Imaging, Carlsbad CA). An apnea event will be defined as complete cessation of Nasal Flow signal for at least 10 seconds in duration, and a hypopnea event will be defined as at least 50% reduction in Nasal Flow signal for at least 10 seconds.

Computer analysis at the Case Sleep Reading Center (CSRC) will identify desaturation levels and permit the calculation of traditional measures of the Apnea Hypopnea Index (AHI). For participant feedback the primary AHI (Apnea/Hypopnea Index) will be defined as the total number of all apneas (regardless of desaturation) and all hypopneas with $\geq$ 3% desaturation (AASM 2007 criteria). Urgent alerts from the Unicorder recording are defined as: 1) RDI/AHI >50; 2) Oxygen saturation <90% for > 10% of Total Sleep Time; 3) Baseline saturation <90%; 4) Heart rate > 150 bpm for $\geq$ 2 minutes or < 30 bpm for $\geq$ 2 minutes.

Studies identified as potential urgent referrals will be triaged for immediate full scoring (within 48 hours of assignment to the scorer). Once fully scored and determined to meet criteria for Urgent Referral, a physician investigator will be asked to review the study. If after scoring the study meets the alert criteria it will be logged in the Scoring Alert Log of the CSRC and the alert report sent to the HCHS/SOL field center through the Coordinating Center. In the absence of alert or urgent findings a report will be generated for each sleep study. Respiratory events, oximetery, heart rate, snoring level and sleep time will be reported. The report provided to the study participant is summarized below.

g. Sleep Apnea Study Results

"As part of the HCHS/SOL examination, you underwent an overnight sleep apnea screening study. In this study, your breathing, oxygen levels, head position, and snoring level were measured using a portable recorder. Please note that the study performed was for research purposes and not for diagnostic reasons. Therefore, you and your doctor should use this information to point out areas that may require further evaluation. Also, regardless of the results of the sleep study, if you regularly experience poor sleep or daytime sleepiness, you should discuss these findings with your doctor.

The results of research sleep studies include:

Total Recording Time: This is the total time that information was collected on your sleep and breathing patterns. Generally, recording times of at least 4 hours are needed to make sure the information that was collected is reliable.

Oxygen Saturation Levels (SpO_2): The monitor on your forehead contained an oximeter, which uses light rays to measure the amount of oxygen in your blood. Oxygen levels are one indicator

of general health, and low levels may indicate problems with the heart, lungs, or of breathing problems occurring at night. Normal oxygen levels are usually >92%.

Number of Breathing Pauses During Sleep (AHI): The Apnea/Hypopnea Index (AHI) is the average number of breathing pauses per hour of estimated sleep time. A pause is when breathing becomes shallow or breathing stops for 10 seconds or longer. A high number of breathing pauses may indicate a condition called ***"sleep apnea,"*** in which breathing pauses disrupt sleep, and may be associated with loud snoring, daytime sleepiness or tiredness, as well as increase risk for high blood pressure and heart disease. When breathing stops, oxygen levels may drop for a short time."

The results of your research sleep study showed:

	Your Results	Interpretation
Total Recording Time		If **less than 4 hours**, the information collected may need to be repeated on another night to make sure this information provided a good estimate of your usual breathing at night.
Baseline Oxygen (SpO_2)		Baseline Oxygen level **less than 90%** is considered low and indicate a need to check with your doctor.
Percentage of time with a low oxygen level (% sleep time with SpO2 < 90%)		Spending **more than 10%** of time at a low oxygen level is considered low and indicates a need to check with your doctor.
Lowest Oxygen During Sleep		Generally, oxygen levels should stay above 90% during sleep. If they fall **below 90%**, this may be because of sleep apnea or another breathing problem. **Values below 90% indicate a need to check with your doctor.**
Apnea / Hypopnea Index (AHI)		An AHI of less than 5 is considered normal. An AHI of 5-15 is considered mildly increased. An AHI of 16-30 is considered high. An AHI of 31 and higher is considered very high.
If your AHI is above 5 or if you experience poor quality sleep or daytime sleepiness (regardless of your AHI level), we suggest you speak with your doctor.		

h. Oral Health Examination

Individuals at high risk of infective endocarditis will be excluded from periodontal examination of the oral health assessment. These safety exclusions follow the guidelines recently updated the American Heart Association and the American Dental Association (Wilson W et al. Circulation, April 19, 2007). Because preventive antibiotics prior to a dental procedure are advised for such patients, the HCHS/SOL will exclude from a periodontal exam individuals with either (a) artificial heart valves, (b) a history of infective endocarditis, (c) a serious heart condition present

from birth (congenital heart condition), or (d) a heart transplant. Whereas only specific congenital heart conditions and cardiac transplant patients who develop heart valve problems meet the guidelines for antibiotic prophylaxis, the HCHS/SOL safety criteria are designed to be more sensitive in excluding individual at high risk of infective endocarditis. Screening questions are asked at the time the study participants schedules an appointment to the HCHS/SOL field center and again immediately prior to the oral health examination. The participant's responses to the screening questions are captured in the Data Entry System and are thus accessible to the HCHS/SOL personnel from any point of access.

Results from the Oral Health Examination. With the help of algorithms built into the computer-based data entry system the dental examiner prepares specific recommendations for follow-up care based on evaluation of the components of the standardized HCHS/SOL examination. Four levels of referrals are defined in the system, as follows: 1. Participant should see a dentist immediately; 2. Participant should see a dentist within the next 2 weeks; 3. Participant should see a dentist at his/her earliest convenience; 4. Participant should continue with his/her regular routine dental care.

The details that make up these levels are summarized below.

Level 1- Emergency dental condition: In the opinion of the examiner, a dental or oral condition exists which may require immediate services for the relief of symptoms and stabilization of the condition. Such conditions include but are not limited to: severe tooth pain, hemorrhage of the oral tissues, acute infectious processes of the oral cavity, traumatic injury to the teeth and surrounding tissues, unusual swelling of the face, gums or other oral tissue, or oral conditions that obstruct the airway.

Level 2- Urgent dental condition: In the opinion of the examiner, a dental or oral lesion or condition exists for which the Participant should seek medical/dental services within a few weeks for diagnosis, relief of symptoms and/or stabilization of the condition, counseling about the condition or other appropriate follow-up. Such conditions may include but are not limited to: tooth fracture, oral lesion or condition visible to the examiner or Participant, lost restoration, chronic pain, or other condition that is unlikely to resolve without professional intervention.

Level 3- Earliest convenience: In the opinion of the examiner, a need for oral hygiene services or non-emergency conditions exist which should be addressed prior to the next scheduled visit with a dentist. Such non-emergency conditions may include incipient/early caries lesions or mild gingivitis.

Level 4- Continue regular care: Applies when none of the above conditions exist.

It is the examiner's responsibility to assign an overall examination recommendation for care level based on his/her best professional judgment. In preparing feed-back to the study

participant the dental examiner will choose one or more of the conditions printed on the Referral Letter and Report of Findings shown below.

> Thank you for participating in the Oral Health examination. As you are aware, the examiner did not conduct a complete examination like one conducted in a dentist's office and cannot provide you with a diagnosis. However, in some circumstances, the examiner may see some obvious conditions that your dentist should check. Based on the collection of dental information for this study, it is suggested that:
>
> □ You should continue with your routine dental care as suggested by your dentist
> □ You should make an appointment to visit your dentist due to:
> □ possible cavities
> □ potential gum problems, such as pockets around one or more of your teeth or loss of bone support for one or more teeth.
>
> □ You should see your dentist immediately to:
> □ Have the dentist look at a suspicious lesion in your mouth.
> □ Evaluate a potentially acute condition.
>
> Comments _____
> _____
>
> Signature of Examiner

i. **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. The reference and alert values used by the Central Laboratory, summarized in Table 8, 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.

HCHS/SOL assays include hepatitis A serology, hepatitis B core antibody, hepatitis B surface antigen and hepatitis B surface antibody. Hepatitis C serology – and positive – also hepatitis C nucleic acid (RNA) test also are measured. Reporting of these results to the study participants follows a decisions algorithm based on the premise that the presence of surface antigen is indicative of infectivity, irrespective of other markers, and represents the test result that needs to be reported and requires medical attention. If surface antigen is not positive, infectivity is quite unlikely. However, if core antibody is the only positive test, confirmation is needed because it is a more robust test than the surface antigen, which might be at too low a titer to measure, although this is uncommon. The reporting decisions followed by HCHS/SOL are summarized in Table 9.

In notifying study participants whose hepatitis serology is positive and suggestive of infectivity HCHS/SOL field centers take extra precautions to ensure that this information is conveyed promptly, with protection of confidentiality and in a culturally appropriate manner, and with sufficient information for the study participant to understand the implications for him/herself, friends, family and work. After confirmation of study participant's identity, field centers conduct this result notification protocol according to the procedures in place at their institution.

The HAV testing is for total anti-HAV antibody and therefore does not distinguish between acute and chronic infections. Because the vast majority of those positive for total anti-HAV antibody will have had old infections or have been vaccinated for HAV, and HAV does not cause chronic infections, most jurisdictions do not require its reporting to local health public health agencies. Hepatitis B result interpretation is more complex and as a result, three tests are potentially performed. HCHS/SOL participants who test positive for HBV core antibody will have testing for HBV surface antigen or HBV surface antibody. Interpretation of various combinations of HBV test results are given in Table 9.

HCV can also cause chronic infections. When the hepatitis C antibody is positive the HCHS/SOL Central Laboratory will perform HCV nucleic acid (RNA) testing, often called HCV NAT testing. Even if the HCV NAT test is negative, there is some clinical value in reporting HCV antibody results because of HCV potential for causing chronic infection in which measurable viremia can be intermittent. Thus, antibody to HCV indicates exposure to HCV and the possibility that a person may transmit HCV. However, a negative HCV RNA result indicates that the person is much less likely to transmit an HCV infection, is less prone to serious liver disease, and may have actually eradicated the HCV from their body. In consultation with the corresponding state health departments and local medical practices, the HCHS/SOL proposes to report HCV antibody positive, HCV RNA negative study participants.

Hepatitis reporting will be implemented according to specifications of the state health departments with jurisdiction over each HCHS/SOL study community in San Diego, CA; Miami, FL; The Bronx, NY; and Chicago, IL. The common ground of the respective Laboratory Reporting Guidelines for Notifiable Diseases or Conditions requires reporting of positive results for HBV and HCV antibody.

Table 8. HCHS/SOL Central Laboratory Reporting Reference and Alert Ranges

Test Name	Reference Range	Units	Reported	Alert Value	Sample Type
Hemogram (CBC):					
White Blood Count (WBC)	4.0-11.0	x 10^9/L		<2 and >25	EDTA - whole blood
Red Blood Count (RBC), male	4.4-5.9	x 10^{12}/L			EDTA - whole blood
Red Blood Count (RBC), fem.	3.8-5.2	x 10^{12}/L			EDTA - whole blood
Hemoglobin - male	13.3-17.7	g/dL		<8	EDTA - whole blood
Hemoglobin - female	11.7-15.7	g/dL		<8	EDTA - whole blood
Hematocrit - male	40.0-53.0	%			EDTA - whole blood
Hematocrit - female	35.0-47.0	%	Yes		EDTA - whole blood
Mean Corpuscular Volume (MCV)	78-100	fL			EDTA - whole blood
Mean Corpuscular Hemoglobin (MCH)	26.5-33.0	pg			EDTA - whole blood
Mean Corpuscular Hemoglobin Concentration (MCHC)	32-36	g/dL			EDTA - whole blood
Red Cell Distribution Width (RDW)	10.0-15.0	%			EDTA - whole blood
Platelet Count	150-450	x 10^9/L	Yes	<50 and >1000	EDTA - whole blood
WBC Differential:					
Neutrophils	40-75	%			EDTA - whole blood
Lymphocytes	20-48	%			EDTA - whole blood
Monocytes	0-12	%			EDTA - whole blood
Eosinophils	0-6	%			EDTA - whole blood
Basophils	0-2	%			EDTA - whole blood
Absolute Neutrophils	.6-8.3	x 10^9/L			EDTA - whole blood
Absolute Lymphocytes	0.8-5.3	x 10^9/L	No		EDTA - whole blood
Absolute Monocytes	0-1.3	x 10^9/L			EDTA - whole blood
Absolute Eosinophils	0-0.7	x 10^9/L			EDTA - whole blood
Absolute Basophils	0-0.2	x 10^9/L			EDTA - whole blood
Total cholesterol	0-200	mg/dL	Yes		Serum
Triglycerides	0-150	mg/dL	Yes	>1000	Serum
HDL-cholesterol	#	mg/dL	Yes		Serum
LDL-cholesterol	#	mg/dL	Yes		Calculation
Glucose, fasting	60-115	mg/dL	Yes	<60 and >200	EDTA - plasma
Glucose, post OGTT	0-139	mg/dL	Yes		EDTA - plasma
Glycosylated Hemoglobin	4.3-6.0	%	Yes		EDTA - whole blood
Insulin, fasting	2-25	mU/L	No		EDTA - plasma
Insulin, post OGTT		mU/L	No		EDTA - plasma

Table 8. HCHS/SOL Central Laboratory Reporting Reference and Alert Ranges

Test Name	Reference Range	Units	Reported	Alert Value	Sample Type
Alanine aminotransferase (ALT), male	0-66	U/L	Hep + only		serum
Alanine aminotransferase (ALT), female	0-44	U/L	Hep + only		Serum
Aspartate aminotransferase (AST), male	0-52	U/L	Hep + only		Serum
Aspartate aminotransferase (AST), female	0-42	U/L	*		Serum
Creatinine, male 20-50y	0.8-1.5	mg/dL	Alerts only	>2.0	Serum
Creatinine, male 50-60y	0.8-1.7	mg/dL	Alerts only	>2.0	Serum
Creatinine, male >60y	0.8-2.0	mg/dL	Alerts only	>2.0	Serum
Creatinine, female 20-50y	0.6-1.3	mg/dL	Alerts only	>2.0	Serum
Creatinine, female 50-60y	0.6-1.4	mg/dL	Alerts only	>2.0	Serum
Creatinine, female >60y	0.6-1.6	mg/dL	Alerts only	>2.0	Serum
eGFR	<60, >60	mL/min/1.73m^2	Yes		Calculation
Albumin/creatinine ratio	0-20	mg/g creatinine	Yes		urine, neutral
Creatinine, urine	NA	NA	NA		urine, neutral
High sensitivity CRP			No		
Iron, male	45-160	ug/dL	No		Serum
Iron, female	30-160	ug/dL	No		Serum
Total Iron Binding Capacity (TIBC)	228-428	ug/dL	No		Calculation using iron and UIBC
Transferrin saturation	15-50	%	No		Serum

#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

Table 9. HCHS/SOL Hepatitis Reporting Conventions (Rev. June, 2010)

Hepatitis A - Test Result	Interpretation	Reported to State/City Health Department
Hepatitis A Negative	Your hepatitis A test is negative (Hepatitis A Total Antibody)	Not applicable
Hepatitis A Positive	Your hepatitis A test is positive (Hepatitis A Total Antibody). This test indicates that you may have had hepatitis A infection sometime in the past or were vaccinated. It does not indicate an acute infection.	No action

Hepatitis B - Test Results			Interpretation	Reported to State/City Health Department
Hepatitis B Core Antibody	Hepatitis B Surface Antigen	Hepatitis B Surface Antibody		
Negative	Note tested	Negative	Your Hepatitis B test is negative.	Not applicable
Positive	Positive	Negative	Your Hepatitis B test is positive. Hepatitis B is a serious disease caused by a virus that attacks the liver. Please consult with a physician as soon as possible to confirm these results.	Reported to Health Department
Positive	Negative	Positive	Your Hepatitis B test is positive. Your test results are consistent with a old natural infection which has been cleared.	No action
Positive	Negative	Negative	Your Hepatitis B test is positive. Your test results are consistent with a old natural infection which has been cleared.	No action
Negative	Not tested	Positive	Your Hepatitis B test is positive. Your test results are consistent with a vaccination for hepatitis B or an old natural infection which has been cleared	No action

Hepatitis C – Test Results				Interpretation	
Anti-HCV	s/co ratio	NAT	RIBA		
Negative	<1	Not done	Not done	Your test for hepatitis C (hepatitis C antibody) is negative.	Not applicable
Positive	1 to 4	<25	Negative	Your test for hepatitis C is negative (hepatitis C antibody is weakly positive at s/co ratio less than 4, but the anti-HCV RIBA is negative and no hepatitis C virus (RNA) was detected in your blood).	Not applicable
Positive	1 to 4	<25	Indeterminate	Your test for hepatitis C is indeterminate (hepatitis C antibody is weakly positive at s/co ratio less than 4, no hepatitis C virus (RNA) was detected in your blood, and anti-HCV RIBA is indeterminate). Please consult with a physician to confirm and discuss these results. We recommend that you have hepatitis C re-testing.	No action
Positive	1 to 4	<25	Positive	Your test for hepatitis C is positive (hepatitis C antibody is positive at s/co ratio less than 4, no hepatitis C virus (RNA) was detected in your blood, and anti-HCV RIBA is positive). Please consult with a physician to confirm and discuss these results.	Reported to Health Department
Positive	>4	<25	Not done	Your test for hepatitis C is positive (hepatitis C antibody) but no hepatitis C virus (RNA) was detected in your blood. This suggests you have had hepatitis C in the past, but no longer have an active hepatitis C infection. Please consult with a physician to confirm and discuss these results.	Reported to Health Department
Positive	>4	≥25	Not done	Your test for hepatitis C is positive (hepatitis C antibody is positive and hepatitis C virus (RNA) was also detected in your blood). Hepatitis C is a serious disease caused by a virus that attacks the liver. Please consult with a physician as soon as possible to confirm and discuss these results.	Reported to Health Department

Anti-HCV: antibody to hepatitis C virus; S/Co ratio: signal to cut-off ratio; NAT: nucleic acid testing; RIBA: recombinant immunoblot assay

The Hepatitis CRNA Quanititation assay is a real-time polymerase chain reaction (PCR) utilizing analyte specific reagents manufactured by Abbot Laboratories. Analyte Specific Reagents (ASRs) are used in many laboratory tests necessary for standard medical care and generally do not require FDA approval. This test was developed and its performance characteristics determined by Fairview University Medical Center Clinical Laboratories. It has not been cleared or approved by the US Food and Drug Administration. The International Unit (IU) is a designated unit value assigned to the International Standard for Nucleic Acid Amplification Technology Assays for HCV RNA which is accepted by the WHO Expert Committee on Biological Standardization.

28.6 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 field centers highlight salient study results to the participants. For this purpose 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 blood pressure is very high.
- The blood pressure is high.
- The blood pressure is high (With Medication).
- Average hearing threshold in right ear is high.
- The Right Ankle-brachial Index is low.
- The Right Ankle-brachial Index is high.
- The Left Ankle-brachial Index is low.
- The Left Ankle-brachial Index is high.
- During sleep AHI 3% greater than 50 was observed.
- During sleep baseline SaO2 less than 90% was observed.
- During sleep SaO2 less than 90% for at least 10% of recording was observed.
- During sleep a Heart Rate greater than 150 bpm was observed.
- During sleep a Heart Rate less than 30 bpm was observed.
- 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.
- The MCV is low.
- The MCH is high.
- 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.

28.7 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.