WOMEN'S INTERAGENCY HIV STUDY

SECTION 7: FOLLOW-UP VISITS

A. FOLLOW-UP VISIT SCHEDULING WINDOWS

1. DEFINITION

Beginning October 1, 1998, WIHS visit windows will be defined by a fixed period of calendar time as opposed to the system wherein visit windows were defined by the number of visits a participant has completed since her anniversary date. In this calendar-based visit system, two dates are chosen so that any visit initiated between those two dates is associated with the same visit number. (See table below for definitions of visit windows.) All follow-up visits will should be scheduled approximately every six months based on the participant's anniversary date. A participant's anniversary date is defined as the day on which her baseline visit was conducted. (If the baseline visit was split into multiple appointments, the first appointment is considered the anniversary date.)

The preferred visit window is 3.5 to 8.5 months from the previous visit; however, if the alternative is to not have a visit at all, a participant can be brought in outside this window. If a visit is not conducted on the anniversary of the baseline visit, the site will reset the visit date for future visits to the baseline anniversary date. To ensure that all visits are at least 3.5 months apart, this reset may take more than one visit.

Definition of WIHS Visit Windows

Start of Visit Window	*End of Visit Window*	*Visit Number*	
October 1, 1994	March 31, 1995	1	
April 1, 1995	September 30, 1995	2	
October 1, 1995	March 31, 1996	3	
April 1, 1996	September 30, 1996	4	
October 1, 1996	March 31, 1997	5	
April 1, 1997	September 30, 1997	6	WIHS I
October 1, 1997	March 31, 1998	7	
April 1, 1998	September 30, 1998	8	
October 1, 1998	March 31, 1999	9	
April 1, 1999	September 30, 1999	10	
October 1, 1999	March 31, 2000	11	
April 1, 2000	September 30, 2000	12	
October 1, 2000	March 31, 2001	13	
April 1, 2001	September 30, 2001	14	
October 1, 2001	March 31, 2002	15	
April 1, 2002	September 30, 2002	16	WIHS II
October 1, 2002	March 31, 2003	17	
April 1, 2003	September 30, 2003	18	
October 1, 2003	March 31, 2004	19	
April 1, 2004	September 30, 2004	20	
October 1, 2004	March 31, 2005	21	
April 1, 2005	September 30, 2005	22	
October 1, 2005	March 31, 2006	23	
April 1, 2006	September 30, 2006	24	
October 1, 2006	March 31, 2007	25	
April 1, 2007	September 30, 2007	26	WIHS III

Start of Visit Window	*End of Visit Window*	*Visit Number*	
October 1, 2007	March 31, 2008	27	
April 1, 2008	September 30, 2008	28	
October 1, 2008	March 31, 2009	29	
April 1, 2009	September 30, 2009	30	
October 1, 2009	March 31, 2010	31	
April 1, 2010	September 30, 2010	32	
October 1, 2010	March 31, 2011	33	
April 1, 2011	September 30, 2011	34	
October 1, 2011	March 31, 2012	35	
April 1, 2012	September 30, 2012	36	WIHS IV
October 1, 2012	March 31, 2013	37	
April 1, 2013	September 30, 2013	38	
October 1, 2013	March 31, 2014	39	
April 1, 2014	September 30, 2014	40	
October 1, 2014	March 31, 2015	41	
April 1, 2015	September 30, 2015	42	
October 1, 2015	March 31, 2016	43	
April 1, 2016	September 30, 2016	44	
October 1, 2016	March 31, 2017	45	
April 1, 2017	September 30, 2017	46	
October 1, 2017	March 31, 2018	47	
April 1, 2018	September 30, 2018	48	
October 1, 2018	March 31, 2019	49	WIHS V

2. BENEFITS

The calendar-based visit system allows for efficient implementation of new substudies that need to be conducted over a short period; data will be collected over a six-month period and available for editing by WDMAC. The calendar-based visit system also facilitates study conduct and makes participant management easier at the sites. Prior to implementation of the calendar-based visit system, sites needed to maintain protocols for multiple visit numbers. Under the calendar-based visit system, there will be virtually no overlap of visits windows, and clinic staff will automatically know which visit protocol to implement for any woman initiating a visit within a given six-month period. Form changes, protocol changes, Apollo changes, and data freezes naturally coordinate with the transition from one visit to the next. This facilitates the editing process, as fewer concurrent forms can possibly be entered.

3. CONSEQUENCES

A consequence of the implementation of the calendar-based visit system is that, by condensing a 14-month visit window into a six-month visit window, some women will appear to have “missing” visits due to the overlap between current visit windows. These visits will be referred to as “skipped” visits. Thus, all women who have initiated visit 8 by October 1, 1998, will have no skipped visits – their next visit six months later will be classified as visit 9. All women who have only initiated visit 7 by October 1, 1998, will skip visit 8, since their next visit will be classified as visit 9. Lastly, women who have only initiated visit 6 by October 1, 1998, will skip both visits 7 and 8.

Another consequence occurs with tests that are performed or data that are collected only at odd or only at even visits. For tests performed at odd-numbered visits, those women who skip visit 8 will have the test performed twice in six months. For tests performed at even-numbered visits, those women who skip visit 8 will go 18 months without having the test performed. Hence, the cost of assays or tests that occur at even or odd visits may be shifted forward or backward by six months.

4. SCHEDULING VISITS TO FACILITATE COLLECTION OF FASTING BLOOD

Sites should attempt to schedule as many morning visits as possible (depending on participant availability and staffing schedules) to facilitate the collection of fasting blood specimens. However, fasting specimens can be collected at any time of day provided the participant has had nothing to eat or drink except water for the eight hours prior to phlebotomy. When scheduling the visit, site staff should ask the participant if she can fast for at least eight hours prior to her core study visit.

NOTE: Starting at visit 36, fasting specimens for lipid and glucose assays are to be collected once every year at even-numbered visits. The ***Visit Control Sheet*** (VCS) will indicate the date these specimens were last collected. **However, participants should be encouraged to continue to attend ALL visits fasting.**

A copy of the ***Fasting Fact Sheet*** (see **Appendix A** to this section) should be given to each participant at the visit prior to her fasting visit. In addition, reminder phone calls should be made, one to two days prior to the fasting blood draw, to help reinforce compliance with the eight-hour fast.

5. REPORTING OF NON-WIHS CLINICAL LAB RESULTS

Clinical lab results from testing not done as part of a WIHS core visit may be abstracted from medical records for reporting WIHS local laboratory results. This may happen when not enough blood for all specified testing is collected at the WIHS visit via phlebotomy, or when a laboratory error occurs (e.g., specimen is not processed correctly, or is lost). The non-WIHS specimens must have been collected using the same protocol as WIHS collection (see **MOO, Section 10**), and have been tested in a laboratory that also tests the site's WIHS specimens. In addition, the non-WIHS specimens must have been tested within a two week (+/-) window of the participant's core WIHS visit in order to be used. Please note that if the gynecological exam is postponed due to menstruation and the physical exam is done at the time of gynecological exam, and the abstracted clinical lab results are from two weeks prior to the core visit, the abstracted local clinical lab results may be tested as much as four weeks prior to collection of specimens for central lab tests and repository storage. However, this should be a rare occurrence.

Lab results that may be abstracted from medical records include those tests that are run locally. Results should be transcribed to the appropriate local laboratory data collection form (e.g., ***L02, L03,*** etc.).

Specimens for centrally run lab tests (e.g., lipids, HIV RNA, etc.), and those designated for the central WIHS repository must be collected at the WIHS core visit, preferably at the time of the physical examination.

B. ADMINISTRATIVE FORMS

1. MISSED VISIT FORM

If a participant fails to initiate any visit within the visit window, the visit data for that participant is considered missing. Visits may not be conducted outside of the speicified visit windows. Arrange an appointment for the next visit during the appropriate scheduling window and complete a ***Missed Visit Form*** (MVIS) for the missed visit. The purpose of the ***MVIS*** is to gather information about specific efforts to locate women who have missed their WIHS visits and to determine, if possible, the reason(s) for the missed visits. The ***MVIS*** is to be completed only in cases where the participant never showed for the visit. Do not complete the form if the participant had a visit that was only partially completed. Further visits will be labeled with the visit number of the visit period in which they occur.

It may be impossible to complete all study procedures before the end of the calendar-based visit window. For example, a colposcopy exam or laboratory test may not be scheduled or available for several weeks after a visit is initiated. The calendar-based visit system is flexible in this regard and will apply the clinical and/or lab results to the appropriate visit since the classification of visits is based on visit initiation and the protocols used to collect the data. Data freezes will allow sufficient time after the end of the visit window (two to three months) for forms to be entered prior to transfer of data to WDMAC for central editing and compilation.

2. DISENROLLMENT FORM

The ***Disenrollment Form*** (DENR) should be completed when an eligible woman enrolled into the core study, or a specified substudy, disenrolls. This form is to be completed for each WIHS participant who has died and for those who have expressed a desire to withdraw completely from the study or have been deactivated. If a participant indicates that she is too ill or has other limitations that make her unable to complete a full visit, then site staff should let the participant know of the option to complete an abbreviated study visit. (See **Section F** for the ***Abbreviated Visit Protocol***.) The ***MVIS*** or ***DENR*** should continue to be used in all other circumstances.

The ***DENR*** should be entered into Apollo, stapled to the ***MVIS*** and filed in the participant's chart.

If a participant completes a visit and then disenrolls during the same visit window, the visit number should be recorded on the ***DENR*** as the visit number of the next visit window. This will prevent data from being overwritten in the VISITS table of Apollo. However, the ***DENR*** should still be data entered into Apollo during the current visit window.

If a participant is disenrolled from the core WIHS study, they should not participant any longer in any substudy visits post-disenrollment.

NOTE: DO NOT fax ***DENR*** forms to WDMAC. With the implementation of Apollo, this is no longer necessary.

3. TRANSFER FORM

Whenever a participant transfers, either to another WIHS subsite or another WIHS consortium, a ***Transfer Form*** (TRANS) must be completed by the site at which the participant was originally enrolled. It should be noted that a participant is not considered officially transferred to a new site until she attends a visit at that site.

If the participant is transferring to another clinic within the same consortium, the appropriate section of the ***TRANS*** should be completed and forwarded to the site's Data Manager for data entry.

If the participant is transferring to another WIHS consortium, the appropriate sections of the ***TRANS*** should be completed and forwarded to the Project Director at the site to which the participant is transferring. The original site should complete sections A and B and then forward the form to the new site. The new site will assign a new WIHSID number to the participant, and then report this WIHSID to the originating site. The originating site will then update Part C of the form by entering the new WIHSID in Apollo. During the next central edits, all existing records in Apollo will be transferred from the old WIHSID to the new WIHSID.

If a participant will be transferring to another WIHS consortium for only one visit, then a ***TRANS*** should not be completed. Instead, the new site should complete all study forms using the participant's original WIHSID, and then FedEx the completed study forms to the originating site for data entry.

C. COMPONENTS OF THE FOLLOW-UP VISIT

This section provides an overview of the potential components of the follow-up visit. Other sections provide detailed information and protocols for conducting each of the components of the follow-up visit. For the most part, the same data collection methods used for the baseline visit should be implemented for follow-up visits.

The WIHS follow-up visit may consist of a core interview; physical and gynecological exams; laboratory specimen collection including blood, oral, gynecological, and urine specimens; Neurocognitive Battery administration; and selected substudy interviews. Depending on protocol and participant clinical characteristics, some procedures may not be completed at certain visits. Additionally, the order in which the components are administered may vary depending upon whether or not the participant is participating in the fasting blood collection protocol or will be administered the Neurocognitive Battery at the current visit. The components listed below are all possible procedures that could be done for a given participant. The ***Visit Control Sheet*** *(VCS)* (refer to **MOO, Section 11**) will list which study forms are expected (and therefore indicate which procedures should be done) for each participant at a specific visit.

1. INTERVIEW

   The core interview should be administered to all participants, in the following order.

   - F21: *Sociodemographics*
   - F22HX: *Follow-up Health History*
   - HOSP: *Hospitalization Form*
   - BX: *Biopsy Report Form*
   - F22MED: *Medication Use History*
   - F23: *Obstetric, Gynecological and Contraceptive History*
   - F24BEH: *Alcohol, Drug Use and Sexual Behavior*
   - F25: *Health Care Utilization Questionnaire*
   - F26: *Psychosocial Measures*
   - SDCQ: *San Diego Claudication Questionnaire* (women $\geq$ 40 years of age only; every two years beginning with visit 39 as part of ABI protocol)
   - PAQ: *Physical Activity Questionnaire* (women $\geq$ 40 years of age only; every two years beginning with visit 39 as part of ABI protocol)
   - WAVE: *Women's Adherence and Visit Engagement (WAVE) Study Form*
   - DISC: *Stigma and Discrimination Questionnaire*
   - PSQI: *Pittsburgh Sleep Quality Index*
   - PPSR: *Personal Progress Scale Revised* (HIV+ employed women at UAB-MS, UNC, ATL)
   - SPSR: *Stanford Presenteeism Scale Revised* (HIV+ employed women at UAB-MS, UNC, ATL)
   - ATC: *Ascertainment Tracking Checklist* (if applicable)

2. FOLLOW-UP MEDICAL EXAM

   The follow-up medical exams should be done on all participants as detailed below. ABI will be performed once every two years on women $\geq$ 40 years old. Beginning with visit 41, the components of the exam can be completed in any order.

   Urine Collection for pregnancy testing (all visits) and repository (even-numbered visits).

   ABI: *Arterial Brachial Index Measurement Form* (women $\geq$ 40 years of age only): ABI should be performed before phlebotomy if possible. If the ABI does not precede the blood draw, ensure

at least one hour elapses, and that the blood draw site has clotted, before performing the ABI procedure. See **MOO, Section 38** for a complete description of the protocol.

F07: *Physical Exam*

- Height/Weight/Vital Signs (height measured at even-numbered visits only beginning with visit 21)
- Body Circumference Measures (do not do if participant is pregnant) (measured at even-numbered visits only beginning visit 41)
- Bioelectric Impedance Analysis (do not do if participant is pregnant) (measured at even-numbered visits only beginning visit 41)

F08: *Gynecological Exam*

- Vaginal Exam
- Cervical Vaginal Lavage (record on ***F31***)
- Cervical Exam

L14: *Colposcopy* (if indicated)
L15: *Biopsy* (if indicated)
L16: *Dysplasia Treatment* (if indicated)

3. FRAILTY SUBSTUDY

Beginning with visit 43, functional performance tests will be administered annually at odd-numbered visits to women ≥40 years of age. See **MOO, Section 42** for a complete description of the frailty protocol. Results will be recorded on the form "Functional Performance Tests" (form PBM).

- Repeated Chair Stands
- Grip Strength
- 4-meter Walk

4. PPD/ANERGY SKIN TESTING

NOTE: The ***Mantoux Skin Test Result Anergy Panel*** (L07) was discontinued after visit 11. ***PPD*** testing (L08) was discontinued after visit 16.

5. LABORATORY SPECIMEN COLLECTION

Please refer to the *Schedule of Laboratory Evaluations* (**MOO, Section 10**) for a complete list of lab specimens to be collected at the follow-up visit. Individual specimens collected and plasma cell specimens frozen are recorded on the following forms:

F29a: *Antiviral Usage Assessment for Blood Draw* (if appropriate)
F29: *Blood Specimen Collection Form*
L20: *Repository Specimen Processing Form*
F31: *Specimens Collected During the Physical Exam*

NOTE: Sites should ensure that any antiretroviral medications reported on forms ***F29a*** and ***F22MED,*** are consistent. Any inconsistencies should be resolved with the participant at the time of the visit.

For reporting results, following is a list of lab tests performed at the follow-up visit and the form numbers that correspond to them:

Form #:	***Lab Test:***
L01	*HIV 1/2 Testing Results* (if HIV-negative or indeterminate)
L03	*CBC and Automated Differential* (even-numbered visits only for HIV-negative)
L03a	*Hand / Manual Differential*
L04	*Flow Cytometry* (baseline visit only for HIV-negative)
L05	*Liver and Renal Function Test/ Partial Chemistries* (even-numbered visits only for HIV-negative)
L12	*(Urine) Pregnancy Test*
C60	*PAP Smear* (as per protocol in MOO Section 9)
NA	*Lipid Panel and Insulin* (collect once per year only at even-numbered visits)
NA	*Glucose* (fasting participants only; collect once per year only at even-numbered visits)
NA	*Hemoglobin A1c (HgA1c)* (collect once per year only at even-numbered visits)

5. NEUROCOGNITIVE BATTERY

The ***Neurocognitive*** (NC) ***Battery*** will be administered to 25% of the cohort per visit beginning at visit 30, i.e., 25% of cohort at each of visits 30-33 for first administration, 25% of cohort at each of visits 34-37 for second administration, 25% of the cohort at each of visits 38-41 for third administration, 25% of the cohort at each of visits 42-45 for fourth administration. Sites will choose which 25% of participants to test at each visit based on convenience, save for those participants who have missed the prior two or more visits (e.g., for visit 30, have missed visits 28 and 29); these participants should be prioritized to receive the battery at visit 30 (or the first of visits 30-33 that they attend).

The ***NC Battery*** will usually be administered during the core visit, and not at a separate visit. The battery should be administered in the following order. (For more information on the NC Battery protocol, see ***MOO, Section 32.***)

- *Neurocognitive Study Introduction*
- IADL: Lawton *Instrumental Activities of Daily Living – Long Form (IALD-LF)* if not previously administered; *Short Form (IADL-SF)* if IADL-LF has been previously administered
- NC06, Section B: *Hopkins Verbal Learning Test – Revised (HVLT-R)* (Immediate Recall trials)
- NC07: *Stroop Task*
- NC01a, Section B: *Cognitive Measures, Standard TMT*
- NC01a, Section C: *Cognitive Measures, SDMT*
- NC06, Section C: *Hopkins Verbal Learning Test-Revised (HVLT-R)* (Delayed Recall and Recognition trials)
- NC08: *Verbal Fluency*
- NC09: *Letter Number Span*
- NC10: *Grooved Pegboard*
- NC02a: *English Word List* (*WRAT-3)* (English- and Spanish-speakers; only if not completed at a previous visit)
- NC04: *Pronunciation Word List (WTAR)* (English-speakers; only if not completed at a previous visit)
- PTSD: *Stress Assessment Questionnaire*
- *Neurocognitive Study Closing Statement*

D. STANDARD FOLLOW-UP VISIT SEQUENCE

The entire follow-up visit is to be administered during a single appointment. There are a few possible exceptions that are described in **Section E** below. However, sites should make every attempt to follow the order described below, keeping in mind that deviation from the protocol should be kept to the absolute minimum. All exceptions should be fully documented by writing a memo to the Data Manager and Project Director citing the participant's WIHSID and an explanation of what happened. This memo should be copied to the participant's study files.

1. ARTERIAL BRACHIAL INDEX MEASUREMENT

   ABI measurement should be done on women ≥ 40 years of age only. ABI should be performed before phlebotomy if possible. If the ABI does not precede the blood draw, ensure at least one hour elapses, and that the blood draw site has clotted, before performing the ABI procedure.

2. PHLEBOTOMY, URINE COLLECTION

   The following data must be collected during the follow-up visit, but flexibility is allowed as to when these occur in the follow-up visit sequence:

   a. Phlebotomy: Beginning with visit 45, phlebotomy will be performed only at even-numbered visits for HIV-negative participants, unless HIV testing is performed using blood. **NOTE: If an HIV-negative participant misses her even-numbered visit, then phlebotomy should be performed at the next odd-numbered visit.** If the participant reports that she has fasted for eight hours preceding the blood draw, phlebotomy should be done before the interview. If the participant reports that she has not fasted, then the blood draw may be done at any time during the visit (i.e., before or after interview or before physical exam). However, if the physical exam is postponed (see **Section F** below), phlebotomy should be drawn on the same day as the physical exam.

      Form ***F29a*** should be administered by the phlebotomist to all HIV-positive participants (regardless of antiretroviral usage history) immediately preceding the blood draw so that the most accurate data on the participant's last antiviral medication dose(s) is captured. If the participant has more than one blood draw (e.g., due to mishandling or clotting of the first sample), the phlebotomist should complete a second ***F29a*** at the time of the second blood draw. Apollo will allow multiple ***F29a*** forms to be data entered for a visit.

      All participants who attend their WIHS visit after having fasted for eight hours should be offered a small snack and drink before being asked to proceed with the rest of their visit.

   b. Urine Collection: One urine specimen must be collected during the follow-up visit. It is recommended that collection occur prior to the gynecological exam.

3. CORE INTERVIEW

   The entire ***core interview*** (as listed in **Section C**) should be administered in that order, at one time, by a single interviewer, at the beginning of the visit before any of the examinations (physical or gynecological).

4. SUBSTUDY FORMS

   All site-specific substudy forms that are not part of the WIHS core interview should be administered after completion of all core interview forms.

5. PHYSICAL EXAM

The ***physical exam*** (which includes the frailty and gynecological exams) should be done after completion of the core interview and any site-specific substudy forms. **The components of the physical exam can be performed in any order.** If the participant is menstruating, the gynecological exam may be postponed to another time within a six-week completion window; however, sites should aim to complete the gynecological exam within two weeks of the core visit, if possible. If the gynecological exam occurs three to six weeks after the core visit, ***F08*** (Gynecological Exam) and the Pap smear can be performed, but no other gynecological specimens should be collected. In all cases where the gynecological exam is postponed, phlebotomy should be performed on the same day as the physical exam.

If the participant delivered or terminated a pregnancy within eight weeks prior to the study visit, then the gynecological exam must be rescheduled to take place at least eight weeks after the delivery or termination date.

Postponement of ***gynecological exam***:

- Physical and gynecological exams occur on different days: Collect phlebotomy specimens on same date as physical exam.
- Participant is menstruating at time of core visit:
    - Reschedule gynecological exam within two weeks. Collect ***F08***, Pap smear and other gynecological specimens at time of gynecological exam. (Preferred practice if participant is menstruating at time of core visit.) OR
    - Reschedule gynecological exam within six weeks. Collect ***F08*** and Pap smear at time of gynecological exam, but not other gynecological specimens.
- Participant delivered or terminated a pregnancy within eight weeks prior to core visit: reschedule gynecological exam to take place at least eight weeks post delivery or termination date. Collect ***F08*** and Pap smear at time of gynecological exam, but not other gynecological specimens.

NOTE: Post-partum or post-termination is the only circumstance that allows a gynecological exam to be scheduled outside the six-week completion window.

Optional Exams – As of visit 23, examinations of the external genitalia and rectum, as well as the bi-manual exam, are optional. Sites may choose to continue offering these exams, but the information obtained from these exams should not be recorded on any of the visit forms.

6. COLPOSCOPY

According to the colposcopy protocol (See **MOO, Section 9**), sites will perform colposcopies as clinically indicated after the gynecological exam has been completed. Ideally, the colposcopy should be performed on the same day as the gynecological exam. If this is not feasible, it is preferred that it be performed within 30 days of the initial study visit, although a maximum of 60 days is allowed.

NOTE: Anergy panel placement was discontinued after visit 11. PPD was discontinued after visit 16.

E. FOLLOW-UP VISIT SEQUENCE WITH NEUROCOGNITIVE BATTERY

The entire follow-up visit with Neurocognitive Battery is to be administered during a single appointment. Sites should make every attempt to follow the order described below, keeping in mind that deviation from the protocol should be kept to the absolute minimum. All exceptions should be fully documented by writing a memo to the Data Manager and Project Director citing the participant's

WIHSID and an explanation of what happened. This memo should be copied to the participant's study files.

1. ARTERIAL BRACHIAL INDEX MEASUREMENT

   ABI measurement should be done on women ≥ 40 years of age only. ABI should be performed before phlebotomy if possible. If the ABI does not precede the blood draw, ensure at least one hour elapses, and that the blood draw site has clotted, before performing the ABI procedure.

2. PHLEBOTOMY, URINE COLLECTION

   The following data must be collected during the follow-up visit, but flexibility is allowed as to when these occur in the follow-up visit sequence:

   a. Phlebotomy: Beginning with visit 45, phlebotomy will be performed only at even-numbered visits for HIV-negative participants, unless HIV testing is performed using blood. **NOTE: If an HIV-negative participant misses her even-numbered visit, then phlebotomy should be performed at the next odd-numbered visit.** If the participant reports that she has fasted for eight hours preceding the blood draw, phlebotomy should be done before the interview. If the participant reports that she has not fasted, then the blood draw may be done at any time during the visit (i.e., before or after interview or before physical exam). However, if the physical exam is postponed (see **Section F** below), phlebotomy should be drawn on the same day as the physical exam. All participants who attend their WIHS visit after having fasted for eight hours should be offered a small snack and drink before being asked to proceed with the rest of their visit.

   b. Urine Collection: One urine specimen must be collected during the follow-up visit. It is recommended that collection occur prior to the gynecological exam.

3. NEUROCOGNITIVE BATTERY

   The entire ***Neurocognitive*** (NC) ***Battery*** (as listed in **Section C**) should be administered in that order, at one time, by a single, certified interviewer, immediately following phlebotomy and consumption of a snack by the participant. In almost all cases, the Neurocognitive Battery should be administered at the beginning of the visit before any of the core interviews or examinations (physical or gynecological). This will ensure that women completing the NC Battery are well-rested, not hungry or thirsty, and in top mental condition for the testing. However, occasionally, a participant who had initially refused the NC battery may decide after completeion of the interview, that they would like to complete the NC battery. This is allowed, though not preferred.

4. PHYSICAL EXAM OR INTERVIEW

   At visits where the NC Battery is administered, sites can choose whether to complete the physical exam or the core interview first.

   Components of the physical exam can be completed in any order. Please see above for circumstances under which the gynecological exam may be given on a day different than the physical exam.

   The entire ***core interview*** (as listed in **Section C**) should be administered in that order, at one time, by a single interviewer. If the interview follows the exams, ensure that the participant receives clear instruction during the interview to not include any diagnoses found during her physical exam at this core visit. Only diagnoses since her last study visit should be reported.

5. SUBSTUDY FORMS

   All WIHS-wide and site-specific substudy forms that are not part of the WIHS core interview should be administered after completion of all core interview forms.

7. COLPOSCOPY

   According to the colposcopy protocol (See **MOO, Section 9**), sites will perform colposcopies as clinically indicated after the gynecological exam has been completed.

F. ALTERNATE FOLLOW-UP VISIT SEQUENCE

The entire interview must be completed on the same day it is started. The ideal sequence is:

1) Administer entire core interview
2) Perform examinations (fraility, physical and gynecological)

In the event that the ideal sequence is not possible, the following two alternative sequences are acceptable:

Alternative Sequence #1

1) Administer core interview forms F21 through F23
2) Perform examinations (frailty, physical and gynecological)
3) Administer remainder of core interview forms F24BEH through end of interview

Alternative Sequence #2

1) Perform examinations (frailty, physical and gynecological)
2) Administer entire core interview

Other than when followed as part of the NC Battery sequence, alternative sequence #2 is the least recommended of the three sequences and is to be followed only when absolutely necessary to allow for a full core visit to occur.

NOTE: If alternative sequence #2 is utilized, it is very important to remind the participant that the findings of her exam today should NOT be included in her answers during the interview.

G. ABBREVIATED VISIT PROTOCOL

The purpose of an abbreviated visit is to collect important data for the purpose of studying HIV disease progression in WIHS participants who are too ill or have certain other limitations that make them unable to complete the full WIHS visit. The ***Missed Visit Form*** *(MVIS)* or ***Disenrollment Form*** *(DENR)* should continue to be used in all other circumstances.

1. ELIGIBILITY

   Both HIV-seropositive and HIV-seronegative participants may participate in the abbreviated visit protocol. At least one of the following criteria must be met in order for a participant to be considered eligible to complete an abbreviated visit instead of a full core visit:

   (1) Participant is incarcerated or under home detention and has restrictions (time, illness, or regulations) that make her unable to complete a full WIHS core visit. ***Two abbreviated visits per year are allowed under these circumstances.*** The abbreviated visit may be conducted at any point in the visit window under these circumstances.

(2) Participant is too ill (she states when called to schedule visit that she is too ill) to conduct a full WIHS core visit and the close of the visit window is three weeks or fewer away. The purpose of this time parameter is to allow as much time as possible for the participant to complete a full WIHS visit if possible. An abbreviated visit may be conducted before the last three weeks of the visit window if it is expected that the illness will last beyond the visit window. ***Two abbreviated visits per year are allowed under these circumstances.***

(3) Participant has moved out of the area and is unable to return to complete a full core visit every six months. Sites should try to have the participant return to the WIHS clinic to complete a full core visit at least once per year if possible, ***as an abbreviated visit may only be completed once per year under these circumstances.*** Abbreviated visit may be conducted at any point in the visit window under these circumstances.

If the participant cannot return to the clinic to complete a full core visit for two visits in a row, an abbreviated visit can be completed for the first visit, but ***MVIS*** should be filled out for the second visit. Alternatively, if a participant who has moved far away from the clinic may be deactivated (complete ***DENR*** form).

(4) Participant fails to conduct a full core visit after repeated attempts at scheduling and the close of the visit window is two weeks or fewer away. Again, ***an abbreviated visit should only be completed once per year for this purpose***; if the participant cannot complete her full core visit for two visits in a row, an abbreviated visit can be completed for the first visit, but ***MVIS*** should be filled out for the second visit.

If an abbreviated visit is conducted and the participant later completes a full core visit before the visit window has closed, the abbreviated visit data should be discarded.

If the participant is not willing and/or able to complete an abbreviated visit, a ***Missed Visit Form*** should be completed.

2. IMPLEMENTATION PROCEDURES

If a participant is eligible for an abbreviated visit, the reason should be noted (*participant status*) in Question A9 on the ***Abbreviated Visit Form*** (*ABRV*). If someone other than the interviewer made the initial contact with the participant, the relevant information for the abbreviated visit should be relayed to the appropriate interviewer, and the interviewer should contact the participant to determine the participant's ability and willingness to complete an abbreviated visit. This would include determining the appropriate method (by telephone or in-person) and place of interview (the clinic area, hospital, hospice, jail, or in the participant's home). Information pertaining to how and where the visit took place will be recorded in Questions A10 and A10a.

Telephone interviews should be conducted only as a last resort to obtain study data. If the abbreviated visit is conducted over the telephone, the interviewer should ask the participant to have her medications within reach in order to facilitate answering the medication questions without the aid of photo medication cards. If the participant will be seen for exams/specimen collection, the clinician/interviewer conducting these tests should take along a *Medical Record Release* form and ask the participant to sign it. If the participant will not be seen for exams/specimen collection, site staff should mail the consent form to the participant (including a self-addressed stamped envelope) and follow-up by telephone to ensure timely return of the signed form. Abstraction cannot be performed without the participant's signed consent.

As with all WIHS visits, the participant's confidentiality must be maintained. If the confidentiality of the participant cannot be maintained, the visit should NOT be conducted.

3. COMPENSATION

   The exact amount and method of compensation for an abbreviated visit will be a site-specific decision based on discussions with the local Community Advisory Board (CAB).

4. EXAMS/SPECIMEN COLLECTION

   If the abbreviated visit is conducted in person outside of the regular clinic area, the interviewer should be accompanied by a phlebotomist/clinician in the event that the participant is willing and able to provide a urine specimen, have blood drawn and have exams performed. If the abbreviated visit is conducted over the telephone, the interviewer should ask if the participant would be willing to come in to the clinic or be visited at her home by site staff in order to have specimens collected and/or exams performed. If the participant is willing, fasting blood specimens should be collected for abbreviated visits. Specimen collection and/or exams should take place within two weeks of the abbreviated visit interview.

5. MONITORING

   In order to track frequency and to ensure that the protocol is not being administered outside of the eligibility guidelines, all abbreviated visits will be carefully monitored. WIHS site staff should become familiar with the guidelines and make sure that only women who meet at least one of the listed eligibility criteria are being administered the abbreviated visit. The *Abbreviated Visit Protocol* should not be used as a timesaving or convenient option on the part of participants or staff.

   To dissuade sites/participants from overusing the Abbreviated Visit Protocol for the sake of convenience, those women who are eligible to participate in the Abbreviated Visit Protocol via eligibility criteria (3) and (4) will only be allowed one abbreviated visit per year. If a participant cannot complete a full core visit for two visits in a row, an abbreviated visit can be completed for the first visit, but an ***MVIS*** should be completed for the second visit.

6. COMPONENTS OF THE ABBREVIATED VISIT

   The following forms will be used for the *Abbreviated Visit Protocol*:

   ABRV: *Abbreviated Visit Questionnaire*
   F22HX: *Follow-up Health History*
   HOSP: *Hospitalization Form*
   BX: *Biopsy Report Form*
   F22MED: *Medication Use History*
   ATC: *Ascertainment Tracking Checklist* (if applicable)

   If specimens are collected and/or exams are performed, the following specimen/blood/exam forms should be completed as appropriate:

   F07: *Physical Exam*
   F08: *Gynecological Exam*
   L14: *Colposcopy Results* (if indicated)
   L15: *Biopsy* (if indicated)
   L16: *Dysplasia Treatment* (if indicated)
   F29: *Follow-up Blood Specimen Collection*
   F29a: *Antiviral Usage Assessment for Blood Draw*
   F31: *Follow-up Specimens Collected During Physical Exam*
   L01: *HIV Ab* (HIV-negative only)
   L03/L03a: *CBC/Differential* (even-numbered visits only for HIV-negative participants)

L04: *Flow Cytometry*
L05: *Liver/Renal Function Tests* (even-numbered visits only for HIV-negative participants)
L12: *(Urine) Pregnancy Test*
L20: *Repository Specimen Processing Form*
C60: *Pap Smear Form*

8. NOTES ABOUT ABBREVIATED VISITS

When administering the core interview following an abbreviated visit, refer to the *"date form was last administered"* when asking interview questions. For example, when administering at a core visit subsequent to an abbreviated visit for ***F22HX, HOSP, BX,*** and ***F22MED*** (which are administered as part of the abbreviated visit), refer to date of the abbreviated visit; however, for other forms (not administered as part of the abbreviated visit), refer to the date of the last full core visit.

Please note that an asterisk (*) on the ***Visit Control Sheet (VCS)*** next to a visit date indicates that that visit was abbreviated.

H. PARTICIPANT TRACKING PROCEDURES

1. INTRODUCTION

This section of the manual describes methods of finding and relocating individuals selected for participation in a survey. This procedure is often referred to as "tracing" or "tracking."

Longitudinal cohort studies (such as the WIHS) require periodic follow-ups with study participants at specific time intervals to look at changes in behavior, knowledge, attitudes or life circumstances. The ability to follow all study participants over time directly affects the amount of information collected and that, in turn, affects how confident investigators can be that the information accurately reflects patterns of change among study participants. For example, in an "intervention" project (designed to change participant behavior in the period between an initial interview and a follow-up contact), the follow-up interview is just as critical as the initial interview, and information from the first interview is of little use without the second.

Some study populations present greater tracking difficulties than others. The problem of locating, interviewing and retaining participants is increased when participants are concentrated in geographically mobile, youthful, aged or poor populations. Studies focused on such groups require close attention to issues of locating and tracking participants.

This section discusses methods to find and retain participants who are initially hard to recruit, and difficult to locate at follow-up. The focus is on those methods that can be generally applicable, although examples given reflect the adaptation of tracking methods to the particular needs of each study.

2. OBTAINING CONTACT INFORMATION

In a panel or cohort study requiring re-contacts, effective follow-up depends in part on information obtained at the first interview. In addition to giving her current address and phone number, each participant should be asked to supply the name, address and telephone number of at least two relatives, friends, or other contacts (e.g., work colleague, social worker, neighbor or clergy) not living in her household, who will most likely remain in close contact with the participant over time. It is important to assure the participant of the confidentiality of this information and to remind her that these contacts will only be used if the interviewer is unable to locate the participant directly.

3. PROTECTION OF CONFIDENTIALITY

NOTE: It is absolutely crucial to protect the confidentiality rights of participants *at all times*. NEVER divulge the name of the study with anyone other than the participant. Always take extra precautions to ensure that you never divulge a participant's HIV status or any other personal information.

4. INTERIM TRACKING ACTIVITIES

Once obtained, contact information will often need to be updated if the passage of time between initial and follow-up contacts is lengthy, and/or if the study deals with a particularly mobile population. Some studies employ a number of interim steps to remain in touch with participants between initial and follow-up contacts. For example, letters with stamped, addressed postcards enclosed for participants to return with any subsequent change of address can be mailed periodically during lengthy interim periods. Participants should be asked to return the postcard whether or not there are any address changes to report. Those who do not return the postcard should be contacted by telephone to confirm the address and phone number on file. If interviewers or other study staff are unsuccessful in reaching participants, the additional contacts that the participant listed at the initial interview should then be used to locate the participant. As an added incentive for participants to keep in touch with the project, returned postcards can be entered in a lottery with prizes awarded at each recontact phase.

Several projects employ these methods at three-month intervals to increase the response rate between the follow-up interview and subsequent follow-up interviews. Interviewers also make in-person "field" visits to participants' addresses when contact by telephone proves unsuccessful.

5. TRACKING PROCEDURES

Despite a study's best efforts to remain in contact with every participant, inevitably some participants will move without notifying the research team and will need to be traced. Many of those who move remain in the same metropolitan area, perhaps even in the same neighborhood. The first objective of tracking is to verify that the participant has moved and to follow every possible lead to locate her at her new address.

While tracking procedures will vary according to the design and goals of each study and according to available contact information, certain common guidelines can be followed.

Start with the most obvious, least time-consuming step, and proceed logically from there. Begin with the telephone. Call the participant's number if you have it and use telephone directories and directory assistance if you don't. Follow every lead you have at the outset or receive along the way. This includes:

- calling phone numbers of the participant for home and work, if available;
- calling listed contacts;
- making field visits to obtain information from neighbors, local stores or other community contacts, etc;
- speaking directly with the mail carrier for the participant's neighborhood;
- contacting the participant's employer or physician; and/or
- utilizing data sources like the Department of Vital Statistics or the Department of Motor Vehicles.

Thoroughly document every contact attempt you make whether successful or not. This will assist other staff members who continue the search after you and prevent needless repetition. If your efforts are finally unsuccessful, it will assure supervisory staff that every possible avenue has been pursued.

The process of tracking missing participants utilizes the resources and follows the guidelines listed above. Begin with the most obvious step first and follow an order based on previous tracking experience while following the most productive lead at all times.

6. TELEPHONE TRACKING PROCEDURES

The first step is to call the phone number on file. Working numbers should be called at varying times of day and on different days of the week before proceeding to the next step. Phone numbers that are not usable need to be documented as disconnected, wrong numbers, not in service, etc. Check the documentation of previous contacts to correct any typographical errors.

If there is no telephone number on file, or if the listed number is not usable, the next step is to consult a current telephone directory. Look up numbers for the same name and address or, failing that, the same last name and address. In addition, record numbers for slight variations in name and address. These may be nearby relatives or the result of spelling variations, given name variations, etc., and can be checked out by calling these numbers if other leads prove fruitless.

If this fails to produce a usable number, try Directory Assistance. Dial 411 or 1 + (area code) 555-1212 for long distance numbers. Operators will often tell you that there is a non-published number for a participant at a verified address, indicating that the participant is likely to be living at that address, and can be traced in the field.

When communicating with the operator, always spell the last name and verify the address. For example, “last name of Doe, D-O-E, first name, Mary, located at 9 Galen Street in Watertown. Could you please verify the address?” Directory Assistance should supply you with <u>two</u> telephone numbers at each call. Tell the operator at the outset that you will need two telephone numbers, and to ensure that you are not cut off before you make the second request, ask for the first listing verbally.

Operators sometimes make mistakes or are reluctant to scan a long list of names for a specific address. If you have a particularly uncooperative operator, you can always hang up and call again. Most likely, you will reach a different operator.

If you are unable to contact the participant by telephone, next **telephone the contacts the participant listed at the initial interview**, following the same procedures listed above. If you reach a contact person who does not know where the participant is, ask if s/he has any suggestions as to who might know the participant's whereabouts, and offer to tell the initial contact that you will recontact her/him if you do locate the participant.

7. POSTAL TRACKING PROCEDURES

Recontacting participants by mail is often a cost-effective method of maintaining contact and acquiring information on changes of address compared to telephone or field contacts. Such a postal contact is often a first option in reaching the participant to explain the purpose of the study and invite participation. Studies have found that participants are more likely to open stamped rather than metered mail. Also, Priority or Express mail will be more costly, but will draw attention to the mailing and may convey importance to the participant or contact person.

The inclusion of **<u>stamped</u> return envelopes** with pre-printed cards enables participants to provide information on change of address, change of phone number, and preferred times to be contacted.

Special letters can even be sent to participants without listed phone numbers requesting that they send in their telephone number or a telephone number where they may be reached at certain specified times. Understandably, many participants are reluctant to send unpublished numbers on open postcards through the mail, so the pre-printed cards with postage-paid return envelopes elicit a better response. Some participants prefer to send in a **work** telephone number, or prefer to call the office directly. The letter should always tell participants to call in **collect.** Whenever possible, a 1-800 toll free telephone number is preferable.

All participant letters are stamped with **"Address Correction Requested."** This indicates to the post office that the letter should not be forwarded, rather it should be returned to the sender with a forwarding label attached. Unfortunately, this request is not always honored. In situations where the participant has taken out a restraining order, the postal service will not provide this information. Forwarding information is usually kept on file at the post office in the zip code area of the place of former residence for up to **one year** after the participant moves.

8. FIELD TRACKING PROCEDURES

For those cases in which no contact has been made after all the above steps have been taken, the next stage is field tracking. The steps for field tracking are as follows:

Go to the last known address of the participant. If the participant is not home, but someone else is there, verify the participant's residence or obtain a new address and/or telephone number for the participant if possible. If the participant still lives at the address, ask when the participant is likely to be home, and leave a message that you will recontact her.

If no one is home, leave a message in an envelope addressed to the participant placed **under the door**, but not where it advertises the participant's absence, since this can be irritating to residents. **[Remember, do not place anything directly in the participant's mailbox! It is against the law!]** Then contact neighbors, bystanders, the landlord, building superintendent, public housing project office, management company, near-by shops, etc. It is likely that someone nearby may know where the participant or a friend or relative lives now.

REMEMBER: **When you speak with these individuals, you should NEVER divulge the name of the study, only the name of the organization you represent.** Divulging the study name could compromise the participant's confidentiality and this would be a breach of the rights of all human subjects involved in research studies.

If these avenues fail to produce any information or if the information given proves to be useless, the next step is to visit the homes of any contact persons listed by the participant who you have not been able to reach by telephone. As always, fully document any contacts made, leads to be followed and the results of leads followed.

For tracking personnel, it is important to be easily identifiable by participants and the general public when working in the field in order to minimize confusion and eliminate suspicion. Always carry your identification card from the organization you represent. The best way to display the identification card is to have it pinned to your outer garments. You should also carry with you a **Letter of Introduction** from the organization you represent which may be presented to participants, contacts, or police officers as necessary. This letter should explain that you are working on a research project in the community and should include the name of the funding agency. It should guarantee the confidentiality of information gathered and provide a name and number to call collect (if it is out of the local office area) to verify your status.

NOTE: Again, this letter should never divulge the name of the study or anything about the nature of the information that is being collected. The term "longitudinal women's health study" is sufficient to describe the study without divulging the exact nature of the study.

Approach a contact's home in a manner that will encourage trust and cooperation. Use an introductory protocol in order to ensure **consistency and standardization** among tracking staff across all sites. Always begin by introducing yourself by name as a representative of your institution and show your identification card. Be sure the contact understands who you are and whom you represent. Give a short explanation of the general purpose of the study.

Example: "This is a nationwide longitudinal women's health study. We are collecting data on the general health of hundreds of women all across the country at six-month intervals. We ask women a variety of questions about all areas of their lives in order to see relationships between these topics and their overall health."

Be sure to tailor your explanation to each person's level of interest. Some will be put off by a lengthy description, while others will require one before they agree to help. If you project ease and confidence in yourself and in the study, this will be shared by the contact person. If you are nervous and/or feel ill at ease, you are much less likely to win the contact's cooperation. Always be prepared to return at a more convenient time if you have caught the person at a bad time. Try to **make an appointment for a recontact** before you leave, and be sure to keep it if you do, or arrange with your supervisor to have someone else cover for you.

If you get to the neighborhood and the address does not exist, go to a nearby home to see if the participant/contact is known in the neighborhood at a different address, or if a dwelling previously existed at that address. You can also visit the nearest police station, fire station or post office to obtain directions and information about changes in street names or numbers.

If you are unable to get into an apartment building because of tight security, contact security personnel or building management personnel for assistance in ascertaining where the contact is and how to leave a message for her/him. Again, if necessary, show your **Letter of Introduction** and provide a name and a number to call collect to verify your status.

Periodically a challenging situation may arise. A contact may be suffering obvious personal hardship, such as a serious illness or a recent bereavement. These situations will require tact and good judgment. While it is not your role to counsel or provide assistance, if a contact requests advice or help, **be sure to have a list of referrals and resources for most health, legal and social needs at your discretion**. Always remember that you are a representative of your organization and that any information you receive is confidential and cannot be passed on to anyone outside the staff who works on your project.

SAFETY ISSUES: Never visit a home when it is dark without an appointment. Make sure your supervisor is aware of any early or late appointments and make arrangements for signing off with your supervisor at the end of the appointment. Always carry the office phone number and the telephone number of someone who will be available by telephone in case you need to consult with her/him while you are in the field. The police can be reached in most metropolitan areas by calling 911. In other areas, make sure you carry emergency numbers with you and that they are easily accessible.

If you are threatened with physical harassment or violence, withdraw immediately and report the incident in writing to your supervisor using an incident report form.

Incident reports should also be used to report the following:

- any physical injury to you or to a contact person which occurs in the course of your visit;
- any damage to property caused by you during the visit; and/or
- any accident, theft or other event during the visit which could be considered the responsibility of the organization you represent.

In tracking hard-to-find populations for longitudinal surveys, field visits have proved to be an invaluable step in assuring a high response rate. This method, while costly and time consuming, has proved most successful in winning the trust and cooperation of both participants and contact persons.

9. OTHER RESOURCES

Public record searches can provide information on the whereabouts of a participant. Vital statistics and voter registration records are public, and do not require consent forms in order to review them. Both agencies should be called before requesting specific information to determine what procedures are required to initiate a search. Make sure to get the name of the person who gives you the specific protocol, in case there are any questions later on in the process. The Voter Registration Office can provide updated address information when given name, date of birth and social security number, but only if the participant has re-registered within the same voting district.

APPENDIX A: FASTING FACT SHEET

Beginning with Visit 13 (October 1, 2000), the WIHS study has asked all participants to fast before coming in for your study visit. By fasting, we will be able to measure your fasting glucose, insulin, and lipid levels. These blood tests are best done when you have not eaten for at least eight hours. If you have fasted, your blood will be drawn before the interview begins and then you may eat a snack. If you have not fasted, the same amount of blood will be drawn, but the interview may be completed first.

The reason for testing women who have fasted is to help us better understand the **lipodystrophy syndrome**. Symptoms of this syndrome may include the redistribution of body fat, and a tendency to develop diabetes, high cholesterol and high blood pressure. The redistribution of fat may change the shape of the body so that the belly becomes larger and the hips become smaller. It seems that the syndrome is related to taking HIV medications; however, not everyone who takes HIV medications gets lipodystrophy and those that do may only have part of the syndrome. We are doing this study to learn more about who gets it and why.

Study participants are encouraged, but not required to fast. We will ask you when you last had something other than water to eat or drink. We need this information to be accurate so it is very important that you tell us the truth.

Fasting means not eating any calorie-containing food or drink in the past eight or more hours. Although many beverages such as black coffee, plain tea and diet soft drinks have no calories, they contain other ingredients that may affect some of the measurements. This means that if you have a morning appointment, **you should not eat anything or drink anything except plain, non-carbonated water** after midnight or 1:00 AM the night before your appointment.

IF YOU HAVE CONCERNS ABOUT THE SAFETY OF FASTING, YOU SHOULD DISCUSS THIS WITH YOU MEDICAL PROVIDER.

You should take all of your regular medications, according to your usual schedule. Medications may be taken only with water during your fast. If your medications are supposed to be taken with food, ask your medical provider if it's okay to take them with only water for that morning. If your provider says no, you should not fast for the visit.

You will not receive any additional money for fasting, but you will be provided with a snack or a meal after the blood draw.

Thank you for your help with this important test.