SECTION 16

FOLLOW-UP CONTACTS

INTRODUCTION

Follow-up contacts with Women's Health Initiative (WHI) participants occur to address safety issues (Clinical Trial [CT] participants only), collect follow-up data, follow participants for study outcomes, and promote retention. These contacts provide an opportunity for Clinical Centers (CCs) to continue a professional, caring relationship with the participant throughout the duration of the study. The frequency and type of follow-up contacts depend on the study component and include the following:

- Early Adherence and Safety contact (Hormone Replacement Therapy [HRT] and Calcium and Vitamin [CaD]).
- Semi-annual contacts (CT).
- Annual visits (CT) and third-year visit (Observational Study [OS]).
- Annual mail contacts (OS).
- Annual newsletters at six months after anniversary of enrollment (OS).
- Semi-annual newsletters at approximately five and ten months after the anniversary of randomization (CT).
- Non-routine contacts (CT and OS).

Required follow-up tasks for each study component are identified in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*. The target dates for the routine follow-up contacts (visits, phone calls, mailings) and newsletter mailings are based on the randomization date to HRT or Dietary Modification (DM) or enrollment date for OS. Changes in participant involvement due to symptoms or other factors do not alter these target dates. When a participant discontinues any of the interventions, follow-up continues on a semi-annual or annual basis, as appropriate.

This section describes the required and recommended procedures for carrying out routine and non-routine follow-up contacts in all components of WHI.

16.1 Early Adherence and Safety Telephone Contact (HRT and CaD) (Required)

Clinical Center staff make an early phone call to each woman after randomization to HRT or CaD:

- HRT: The call should be made **six** weeks after randomization with a target window of two weeks (± 14 days) on either side of the target date.
- CaD: The call should be made **four** weeks after randomization with a target window of two weeks (± 14 days) on either side of the target date.

The purpose of this contact is to address early adherence and safety concerns. *Form 10 - HRT Management and Safety Interview* or *Form 17 - CaD Management and Safety Interview*, as appropriate, is administered as a phone interview. The purpose of the interview is to check that women in the HRT or CaD are continuing and tolerating the study pills, and that they are having no serious symptoms. The participant's adherence to the pill-taking schedule, by participant estimate, and her willingness to stay on schedule are also assessed. She is supported in her efforts to date, and appropriate referrals are made. This early encouragement has been shown to markedly enhance adherence.

Each CC can decide on the appropriate staff to conduct this phone contact, but the staff must be appropriately trained and certified. Interviewers will refer decisions about possible serious concerns to an appropriate retention specialist as soon as possible. Medical issues should be referred to a Clinic Practitioner (CP).

16.1.1 Preparation for the Telephone Contact

Each week, print the following two reports to identify HRT and CaD participants who need a phone contact:

- *WHIP 0781 - Participants Due for 6-Week Phone Call (HRT).*
- *WHIP 1320 - CaD Participants Due For a 4-Week Phone Call.*

For each participant to be contacted, print *WHIP 0441 - Personal Information Update* and prepare a *Form 10 - HRT Management and Safety Interview* or *Form 17 - CaD Management and Safety Interview*, as appropriate. Prepare to do several phone calls in any one phone session to streamline this activity. It may also be helpful to have participants' files and contact notes available while conducting the calls.

16.1.2 Conducting the Telephone Contact

Start the call attempts near the beginning of the target window to assure that you will be able to contact the participant within the target window (2 weeks on either side of the target six-week date for HRT or the target four-week date for CaD). Frequently, you will not be able to complete all the contacts you set out to do in one sitting. If you are unable to complete a phone call at a particular time and day, try calling at other times and days. A grid for recording the date and time of all phone call attempts is recommended to track this information. (See *Figure 17.1 - Sample Form to Track Contact Attempts*.) Conduct the phone call even if the date is beyond the target window. However, if the date falls within the target window for the first semi-annual contact, conduct the semi-annual contact instead and mark the visit type as semi-annual number one (see *Section 16.4.1 - Missed Contacts*).

16.1.2.1 Introduction and Personal Information Update (Required)

Begin the phone call by introducing yourself and the purpose for the call. The following is an example of what you might say:

"Hello, Mrs./Miss/Ms. (participant's last name). This is (your name) from the Women's Health Initiative at (your CC name). I am calling to find out how you are doing with your study pills and to answer any questions you may have. This will only take about 5-10 minutes. Is this a good time for you to talk?"

If the participant is willing to continue the interview, update and/or confirm her address, telephone number, and other contact information on *WHIP 0441 - Personal Information Update*. If the "father's last name" item is blank on *WHIP 0441*, ask the participant for her father's last name and record it in the space provided. You can inform the participant that this information will be kept confidential and helps the WHI staff to stay in contact with her. (See *Section 16.3.3.6 - Personal Information Update*.)

If the participant says this is not a good time to talk, schedule the telephone contact at a mutually convenient time, ideally, within the target window.

16.1.2.2 Safety Interview (Required)

Complete *Form 10 - HRT Management and Safety Interview* or *Form 17 - CaD Management and Safety Interview*, as appropriate, using the script on the form. Document the participant's responses to the appropriate safety items (e.g., hysterectomy status, specific symptoms, new medical conditions or medications), other concerns, and pill-taking routines. Refer to the interviewing guidelines in *Section 2.11 - Interviewer Procedures* as needed.

Review the participant's responses to the safety and adherence questions. Respond to participant questions and make recommendations based on the following informational resources:

- **HRT**: *Section 5 - HRT, Form 10* form instructions, *HRT Handbook* and the *HRT Question and Answers for CC Staff* in *Appendix G.1.2 - HRT*. If the HRT participant reports any of the conditions, symptoms, or medications listed below, refer her to the CP as soon as possible:
  - Hysterectomy, endometrial hyperplasia, high triglycerides, blood clot to leg or lung, melanoma, heart attack, stroke, or meningioma.
  - Vaginal bleeding or breast changes.
  - Use of anticoagulants or hormones (estrogen, progesterone, testosterone, tamoxifen).
  - Any other serious health questions or symptoms.
- **CaD**: *Section 7 - CaD, Form 17* form instructions, *CaD Handbook*, and *CaD Questions and Answers for CC Staff* in *Appendix G.1.1 - CaD*. If the CaD participant reports any of the conditions, symptoms, or medications listed below, refer her to the CP as soon as possible:
  - Hypercalcemia
  - Kidney problems (such as kidney or bladder stones)
  - Use of > 1,000 IU vitamin D daily
  - Use of calcitriol
  - Any other serious health question or symptoms

Discuss strategies for improving adherence and/or make appropriate referrals to CC staff specializing in adherence and retention issues (e.g., to Intensive Adherence Program). Refer to *Section 17 - Retention* and *Section 17.2.5 - Intensive Adherence Program.*

If the CaD participant indicates problems with tolerating the CaD study pills (e.g., because of its taste, size, or other characteristics) reassure her that she can switch to the other form at her next routine contact. If the participant indicates she is unwilling to wait that long, or has already stopped taking the study pills, explore with her the possibility of switching to the other form immediately. If she is willing to switch, follow procedures outlined in *Section 15.4.5 - Selecting and Dispensing CaD Study Pills.*

16.1.2.3 Concluding the Phone Call

At the end of the call, remind the participant to:

- Continue recording in *Form 53 - HRT Calendar* (if she has a uterus) and to bring the completed form to her next appointment (HRT only).
- Continue taking her study pills every day.
- Bring her study pill bottles (empty or not) and pill organizer with remaining study pills to her next appointment.

Thank the participant for her time *("You are helping us to get the answers to some very important women's health questions"*) and remind her of her next clinic visit or semi-annual contact.

Finally, forward the participant's forms to data entry.

16.2 Semi-Annual Contact (CT only) (Required)

Semi-annual contacts are conducted for all CT participants. The target date for semi-annual contacts is six months after randomization and six months after each randomization anniversary. The target window is ± 2 weeks (± 14 days) on either side of the target date.

The purpose of the semi-annual contact is to:

- Promote rapport with the participant and foster her continued interest in the study.
- Collect updated contact and medical information, including information on potential outcomes.
- Obtain current signatures on release of medical records forms.
- Collect information on safety concerns and symptoms (HRT, CaD).
- Assess and promote medication adherence and dispense a new supply of study pills (HRT, CaD).
- Schedule the next routine visit.

For HRT participants only, an in-person visit is required for the first semi-annual contact (SAV1). For HRT and CaD participants, all subsequent semi-annual contacts may be either an in-person visit, or a telephone call together with mailed forms and study pills as needed. For DM only participants, the SAV1 and all subsequent semi-annual contacts may be a visit, a phone call, or a mail contact. Each CC must decide what method of contact it will use for ongoing CT semi-annual contacts and develop procedures to coordinate and track participants appropriately. Consider when a participant would benefit from a visit rather than a contact so that issues of adherence, retention, and safety can be more directly addressed. Regardless of the method of contact chosen, all required activities must be completed. The "visit" method of contact is outlined below as an example.

16.2.1 Preparation for a Semi-Annual Visit

Print out a semi-annual visit plan *WHIP 0144 - Tasks Required at Visit* for the participant. This will list all the required WHI activities for that contact. Use of a semi-annual contact checklist that lists all WHI-required and CC-specific semi-annual contact activities is recommended (see model in *Vol. 2, Appendix E.4.6 - Model Semi-Annual Contact Checklist*). Each CC can design a checklist to best fit its own operations. Designate one person to review the checklist before the participant leaves the CC to be sure you have completed all the activities.

16.2.1.1 Two Weeks Before a Semi-Annual Visit

Two weeks before the semi-annual visit, mail the participant a first-class packet containing:

a) **Appointment Reminder Letter** that includes:

- Date and time of the appointment, with CC phone number and contact to call if the participant has questions.
- Location of CC.
- Approximately how long the appointment will take.
- Information about the contents of the mailed packet.
- Request to bring her study pill bottles (empty or not) and pill organizer to the CC (HRT, CaD).
- Request to bring her completed *Form 53 - HRT Calendar* (HRT participants with a uterus at the first semi-annual visit only).
- Request to complete and bring in mailed forms, as appropriate.

b) **Self-Administered Forms**, which may include:

- *WHIP 0441 - Personal Information Update (*see *Section 16.1.2.1 - Introduction and Personal Information Update* and *Section 16.3.3.6 - Personal Information Update)*.
- *Form 33 - Medical History Update.*

c) **Other Materials**, such as:

- WHI logo bag for her to return study pills (HRT, CaD).
- Map to the CC and parking validation, as appropriate.

16.2.1.2 Two days Before a Semi-Annual Visit

Prepare ahead for semi-annual visits scheduled in the next few days:

- Ensure a current visit plan, appropriate forms, and participant labels are in each participant's file, including your CC's semi-annual contact checklist.
- Make a phone call to the participant to remind her of the appointment and items she should bring with her.

16.2.2 Conducting the Semi-Annual Visit (Required)

Each CC can organize the flow of the visit to fit its needs as long as the flow meets the following requirements:

- For HRT participants collect study pills and assess adherence, complete *Form 10 - HRT Management and Safety Interview* and collect *Form 53 - HRT Calendar* (HRT participants with a uterus at the first semi-annual visit only) **before** dispensing additional study pills. Note that *Form 10* should be completed at the next **two** routinely scheduled visits or contacts after stopping HRT intervention (see *Section 16.7.1 - Participants Who Have Stopped Intervention*).
- For CaD participants (at SAV2 and beyond), assess study pill adherence and *complete Form 17 - CaD Management and Safety Interview* **before** dispensing additional CaD study pills. CaD participants can choose to switch to the other study pill formulation at each contact. Note that *Form 17* should be completed at the next routinely scheduled visit or contact after stopping CaD intervention (see *Section 16.7.1 – Participants Who Have Stopped Intervention*).
- For HRT and/or CaD participants, refer to the CP any appropriate participant questions, concerns, or information about medical events that might necessitate discontinuing study pills (see *Section 5 - HRT, and/or Section 7 - CaD*). The CP will help evaluate and clear the participant before dispensing additional study pills. If you dispense study pills at the semi-annual contact, dispense only a 6-month supply (see *Section 16.2.2.e - Dispense Study Pills*).
- It is strongly recommended that staff remain blinded to a DM participant's treatment arm. See *Section 4 - Screening*.

16.2.2.1 Reception

When the participant arrives for her semi-annual visit, have her check in with the receptionist. The receptionist should:

- Warmly greet the participant by name and welcome her back to the CC.
- Ask the participant if she has brought her completed forms and study pill bottles (empty or not) and pill organizers as appropriate. Collect and attach the returned forms to the top of her participant file. If she has not remembered the forms, provide her with a replacement set and ask her to complete them while she is waiting.
- State the approximate time needed to complete the visit and explain the visit flow.

- Indicate a comfortable place in the reception area where the participant may wait.
- Notify the clinic staff that the participant is waiting.

Try to limit participant's wait to no more than 10 minutes before she is seen by an interviewer.

The participant's spouse or household members may accompany her to the interview room. If household members are also participants, they must complete separate forms and have separate interviews.

16.2.2.2 Semi-Annual Visit Procedures (Required)

a) Obtain General Medical Releases

Ask the participant to sign several new copies of your CC's *General Medical Release Form* (see model in *Vol. 2, Appendix E.5.1*). Explain to the participant that these new forms will replace the last ones she signed. Many institutions require a signed release within the last 3 to 6 months before releasing any information. Having a recently-signed General Medical Release will simplify future collection of outcome documents.

b) Review Appropriate Forms

Review with the participant the appropriate required forms, as indicated in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*. This form review, in general, should take approximately 30 seconds (see *Vol. 2 – Procedures, Sec. 18.2.3—Review of Forms*). Identify missing pages and remind the participant to complete them. If the participant indicates she has had any events or conditions on *Form 33 - Medical History Update* that necessitate more detailed information for an outcomes investigation, ask her to complete *Form 33D - Medical History Update (Detail)* (see *Form 33* instructions for the algorithm that triggers a *Form 33D* and *Vol. 8 - Outcomes, Section 2 - Ascertainment*).

c) Assess Adherence to Study Pills (HRT, CaD)

Assess the participant's adherence to taking the study pills (this may be an actual or estimated adherence collection.) (See *Section 15.6 - Study Pill Adherence Monitoring*.) Estimate what her adherence has been, and record this on *Form 10* or *Form 17*. Do not let the participant know that you are assessing pill adherence.

d) Complete HRT and/or CaD Management Safety Interview (HRT, CaD)

Complete *Form 10 - HRT Management and Safety Interview* and/or *Form 17 - CaD Management and Safety Interview*, using the script on the form. Each CC can decide on the appropriate staff to conduct this interview, but the staff must be appropriately trained and certified. Interviewers must refer decisions about possible serious conditions or concerns to the CP as soon as possible. Adherence concerns should be addressed or referred to the retention specialist, as appropriate. See *Section 16.1.2.2 – Safety Interview* for guidelines.

e) Dispense Study Pills (HRT, CaD)

If a participant has no findings on *Form 10, Form 17*, other forms, or reports that contraindicate her continuing on study pills (see *Section 5 - HRT* and/or *Section 7 - CaD*), dispense new study pills (if she is to receive a new six-month supply.)

- Follow the procedures described in *Section 15.4 - Medication Dispensing* (note the participant's preference for CaD study pill formulation).
- Inform the participant that you will be giving her a new bottle of study pills and that you will be keeping her old study pills that were dispensed at the last CC visit.
- Offer her a new *HRT Handbook* and/or *CaD Handbook* and review the pill instructions with her.
- Offer her a new pill organizer. (She may benefit from two pill organizers if she takes multiple other pills or needs to track the twice daily dosing of CaD separately).

- Remind the participant to call the CC if she develops new symptoms or concerns with the study pills, loses her study pill bottle, or knows she is going to run out of study pills before her next visit.
- Remind her to bring all her study pill bottles (empty or not) to each routine clinic visit.

For HRT participants, only a 6-month supply of HRT study pills can be dispensed at randomization and at the first semi-annual visit (SAV1). At AV1 and subsequent annual visits, a 12-month supply of HRT study pills can be dispensed (after all required tasks are completed and safety considerations reviewed).

For CaD participants, only a 6-month supply of CaD study pills can be dispensed at AV1 and SAV2 (to ensure that the participant tolerates the formulation she has chosen). Do not dispense any more than a 6-month supply of a particular form of CaD - chewable or swallowable - until the participant has tolerated at least a full-year's worth of that formulation. After a participant has been on one formulation for a full year, a 12-month supply of CaD may be dispensed at annual visits thereafter.

NOTE*:* At semi-annual visits or contacts, you may only dispense a six-month supply of study pills (HRT or CaD). At annual visits you may dispense a six-month or twelve-month supply of pills, as appropriate.

16.2.3 Exit Interview

After completing required procedures and forms, review the semi-annual visit checklist and visit plan to be sure you have completed all required activities or have recorded the reason an activity is not completed. Spend a few minutes talking with the participant to maintain rapport and discuss her further adherence and interest in the study. Record any concerns and how you addressed them in the participant's contact notes. Make sure the participant is aware that:

- Her contribution to WHI is invaluable.
- The CC staff are interested in her safety and her activities with the study.
- She should contact the CC any time she might have questions or concerns.

Schedule an appointment for the next annual visit within the appropriate window (± 2 weeks around the annual visit target date). Explain to the participant that two weeks before the visit she will receive a packet in the mail containing a reminder letter, forms for her to complete, and other appropriate materials (see *Section 16.3.1.2 - Two Weeks Before the Annual (CT) and Third-Year (OS) Visit*).

Inform her of other appropriate annual visit activities, based on her annual visit plan. Relevant activities that might be scheduled and should be mentioned are described in *Section 16.3 - Annual (CT) and Third-Year (OS) Visit (Required)*.

Make sure the participant leaves with the following materials:

- *Form 53 - HRT Calendar* (HRT participants with a uterus at the first semi-annual visit only).
- HRT study pills (HRT) - 6-month supply, as appropriate.
- CaD study pills (CaD) - 6-month supply, as appropriate.
- *HRT Handbook* and/or *CaD Handbook*, if needed (HRT, CaD).
- Appointment card with date for next annual visit and other relevant information about scheduled activities.

Participant retention may be promoted by also sending a personalized thank-you card within a week of the contact.

16.3 Annual (CT) and Third-Year (OS) Visit (Required)

Clinic visits are conducted annually for all CT participants and for OS participants in the third year. The activities of the annual visit will vary according to the trial component. See *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection* for the schedule of activities per contact. The target date for the annual visits is the anniversary of the randomization date for CT and the third anniversary of the enrollment date for OS. The standard window for CT annual visits and OS Year 3 visits is +/- 3 months around the target date for the contact. Selected tasks such as CT Pap, pelvic exams, and mammograms have wider windows. The time limits for collecting tasks are given in *Table 16.1* (see also *Section 16.4.1.2 - Strategies for Managing Missed Contacts*) *WHIP1445 - Task Completeness* uses these windows in its parameters for Standard and Expanded windows.

The purpose of the annual (CT) and third-year (OS) visit is to:

- Promote rapport with the participant and foster her continued interest in the study.
- Collect updated contact and medical information, including information on potential outcomes.
- Obtain current signatures on release of medical records forms.
- Collect information on symptoms and other concerns (HRT, CaD).
- Assess and promote study pill adherence and dispense a new supply of study pills (HRT, CaD).
- Collect interim measurements.
- Schedule the next routine visit (CT).

16.3.1 Preparation for the Annual (CT) and Third-Year (OS) Visit

Print out an annual visit plan report (*WHIP 0144 - Tasks Required at Visit*) for the participant. This will list all the required WHI activities for that visit, including any subsample activities for which the participant has been selected. Run a preliminary CaD eligibility determination before the first annual visit for CT participants to indicate if an invitation to join the CaD trial should be offered. Clinical Centers are required to offer CaD at AV1, however, CaD may also be offered at any time through AV2. Use of an annual visit checklist that lists all WHI-required and CC-specific annual visit activities is recommended (see model *in Vol. 2, Appendix E.4.7 - Model Annual (CT) or Third-Year (OS) Visit Checklist*). Designate one person to review the checklist before the participant leaves the CC to be sure you have completed all the activities.

16.3.1.1 Two Months Before the Annual Visit (CT)

Approximately two months before the scheduled annual visit, take the following steps to obtain appropriate reports on the CT participant:

- **Obtain Mammogram Results (annually for HRT, every other year for DM)**

  Schedule a mammogram at an accredited facility for the participant. If the participant is having mammograms through her own physician or clinic, call her to see if she has had her annual mammogram. If she has not yet had her mammogram, ask her to schedule it and call the CC with the date she is to have the test. If the participant has had her mammogram, write or call for the results. Refer to *Section 12 - Mammography*.

  The CP should review the mammogram report when it arrives at the CC. Record the appropriate information on *Form 85 - Mammogram*. If a repeat mammogram is recommended in less than one year, record this information on *Form 85 - Mammogram*.

The following two reports may be helpful for tracking follow-up mammograms:

- *WHIP 0476 - Mammograms Requiring 6-Month Follow-Up* - lists all participants who have "probably benign findings" on *Form 85* and no follow-up results entered on that same *Form 85*.

- *WHIP 1227 - Referral Follow-Up* - lists women who had abnormal results and/or required follow-up for a given procedure, such as *Form 85 - Mammogram.*

- **Obtain Pap Smear Results (HRT participants with a uterus in years 3, 6, and 9 if performed by personal physician)**

  If a participant chooses to have her personal physician obtain her Pap smear, ask her to have a copy of the lab report sent to the CC. The CP should review the Pap smear reports when they arrive at the CC. Record the appropriate information on *Form 92 - Pap Smear*. Some participants may also insist that their pelvic exams be performed by their personal physician. Reports of these exams should also be obtained (a written report or a verbal report by a clinician is required in years 3, 6, and 9).

16.3.1.2 Two Weeks Before the Annual (CT) and Third-Year (OS) Visit

Two weeks before the annual visit, mail the participant a first-class packet containing:

a) **Appointment Reminder Letter** that includes:

- Date and time of the appointment, with CC phone number and contact to call if the participant has questions.
- Location of CC.
- Approximately how long the appointment will take.
- Information about the contents of the mailed packet.
- Information about joining the CaD trial (eligible CT participants).
- Request to bring all her study pill bottles (empty or not) and weekly pill organizer(s) to the CC (HRT, CaD).
- Request to bring her completed *Form 53 - HRT Calendar* (HRT participants with a uterus at the first annual visit only).
- Request to complete and bring in mailed forms, as appropriate.
- Request to wear light, two-piece clothing for measurements.
- Request not to eat or drink anything but water for 12 hours before her visit if she is to have a fasting blood draw. She should not smoke one hour before her visit nor engage in vigorous exercise eight hours before her visit. She should take any regularly-scheduled medications before her visit, **except** medications for diabetes (she should bring these to the visit to take after her blood draw, unless her primary physician has instructed her otherwise) (Years 1, 3, 6, 9 in CT; year 3 in OS).
- Notification of endometrial subsample participant (Years 3, 6, 9). Pathology results from an aspiration or D & C may be substituted if done during the previous 12 months.
- Notification of 4DFR subsample participant (Year 1 only in DM). See *Section 10.1.3 Follow-up Visit Record Completion*.
- Request to bring in all of her current prescription and over-the-counter medications and supplements (Years 1, 3, 6, 9 in CT; Year 3 in OS).
- Information about other activities that will take place during the visit.

b) **Self-Administered Forms**, which may include (depending on the visit plan):

- *Form 33 - Medical History Update*.
- *WHIP 0441 - Personal Information Update*.
- *Form 35 - Personal Habits Update* (Years 1, 3, 6, 9 in CT).
- *Form 38 - Daily Life* (if needed).
- *Form 60 - Food Frequency Questionnaire* and *Form 61 - How to Fill Out the Food Questionnaire* (DM, OS - if needed).
- *Form 62 - Four-Day Food Record* (assign dates for completion on her form) and *Form 69 - Keeping Track of What You Eat* (DM - if needed).
- *Form 143 - OS Follow-Up* (Year 3 in OS).

c) **Other Materials**

- WHI logo bag (for participant to bring her study pills and bottles, current medications, and current supplements, as appropriate, to the CC).
- #2 pencil for completing any mark-sense forms included in the packet.
- Map to the CC, if appropriate.
- *Invitation to Join CaD* and CaD consent (eligible CT participants).
- At Bone Density sites, include a 30 ml urine container labeled with the participant's ID label and a copy of a Urine Home Collection instruction sheet. (See *Section 11.5.3 - Preparation Before the Visit*).

Check that *Form 85 - Mammogram* has been completed (CT participants, as appropriate). If not, take steps to get the results and enter them on the form.

16.3.1.3 A Few Days Before the Annual (CT) and Third-Year (OS) Visit

Prepare ahead for the annual visits scheduled in the next few days:

- Ensure a current annual visit plan (*WHIP 0144 - Tasks Required at Visit*), appropriate forms, and participant labels are in each participant's file, including the annual visit checklist.
- Check the participant's file to be sure you have received appropriate reports.
- Make a phone call to the participant to remind her of the appointment and items she should bring with her.
- Ensure Dietary Assessment staff are available to document *Form 62 - Four Day Food Record*, if needed (DM subsample in Year 1).

16.3.1.4 Activities on the Morning of the Annual (CT) and Third-Year (OS) Visit

Each day prepare for the annual exams scheduled for that day:

- Prepare supplies for blood draws, if needed.
- If there are gynecological exams scheduled for that day, set up appropriate equipment (see *Section 4.3.3.3 - Activities on the Morning of SV2*).
- Check that the ECG machine is stocked with paper, has adequate memory space, and all additional necessary equipment is present (Years 3, 6, 9).

16.3.2 Conducting the Annual (CT) and Third-Year (OS) Visit (Required)

Each CC can organize the flow of the visit to fit its needs as long as the flow meets the following requirements:

- Perform the blood pressure measurement before the blood draw (or at least one-half hour after in the opposite arm) and other stressful tests such as ECG, pelvic exam, endometrial aspiration, and mammogram.
- Assess HRT and CaD study pill adherence before completing *Form 10 - HRT Management and Safety Interview* and *Form 17 - CaD Management and Safety Interview*.
- Review the mammogram report before dispensing HRT study pills. Mammograms not scheduled and/or mammogram reports not available by the annual visit need not hold up dispensation of a six-month supply of HRT study pills (a 12-month supply cannot be dispensed if the mammogram report is not available). The mammogram must be scheduled and a report obtained before the next semi-annual contact in order to dispense an additional six-month supply of HRT study pills.
- Review *Form 53 - HRT Calendar* before dispensing HRT study pills (HRT participants with a uterus at the first annual visit).
- Complete *Form 10 - HRT Management and Safety Interview* before dispensing HRT study pills.
- Complete *Form 17 - CaD Management and Safety Interview* before dispensing CaD study pills.
- Refer questions of concern as soon as possible to CP for evaluation and clearance before dispensing HRT or CaD study pills.

16.3.2.1 CaD Review at Annual Visit (Required)

Determine if the participant is eligible and interested in the CaD component of the CT. See *Section 7 - Calcium and Vitamin D Intervention*. CaD screening and randomization procedures include:

- Running a preliminary CaD eligibility determination (Task ID 930).
- Offering a "taste test" of a CaD study pill formulations (see *Section 7.1.4.1 - CaD Study Pill Taste/Swallow Test)*.
- Administering *Form 16 - Calcium/Vitamin D Eligibility Assessment*.
- Reviewing the CaD consent form with appropriate participants.
- Completing *Form 11 - Consent Status*, Task 15 - CaD Consent as needed.
- Running a final CaD eligibility determination and then randomizing the participant to CaD.

16.3.2.2 Reception

When the CT or OS participant arrives for her visit, have her check in with the receptionist. The receptionist should:

- Warmly greet the participant by name and welcome her back to the CC.
- State the approximate time needed to complete the visit and explain the visit flow.
- Ask the participant if she has brought her completed forms and study pill bottles (empty or not) and pill organizers, as appropriate. Collect and attach the returned forms to the top of her participant file. If she has not remembered the forms, provide her with a replacement set and ask her to complete them while she is waiting.
- Indicate a comfortable place in the reception area where the participant may wait.
- Notify the clinical staff that the participant is waiting.

Try to limit the participant's wait to no more than 10 minutes before she is seen by an interviewer.

The participant's spouse or household members may accompany her to the interview room. If household members are also participants, they must complete separate forms and have separate interviews.

16.3.2.3 Annual (CT) and Third-Year (OS) Visit Procedures (Required)

a) Obtain General Medical Releases

Ask the participant to sign several new copies of your CC's General Medical Release form (see model in *Vol. 2, Appendix E.5.1*) Explain to the participant that these new forms will replace the last ones she signed. Many institutions require a signed release within the last 3 to 6 months before releasing any information. Having a recently-signed General Medical Release will simplify future collection of outcome documents.

b) Review of Self-Administered Forms

Review the appropriate self-administered forms, as indicated in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*. Go over each form for completeness. This form review should take approximately 1 minute (see *Vol. 2 – Procedures, Sec. 18.2.3–Review of Forms*). Identify missing pages and remind the participant to complete them. If the participant indicates she has had any events or conditions on *Form 33 - Medical History Update* that necessitate more detailed information on potential outcomes, ask her to complete *a Form 33D - Medical History Update (Detail)* (see *Form 33* instructions for the algorithm that triggers a *Form 33D* and *Vol. 8 - Outcomes, Section 2 – Ascertainment*).

c) CaD Information and Consent (eligible CT participants)

Provide women interested in CaD with a detailed in-depth description of the trial. Provide the participant with an information-sharing session and an opportunity for her to ask questions. Offer her a taste and/or swallow test of the CaD pill formulations, and review and sign the CaD consent. See *Section 7.1.4.1 - CaD Study Pill Taste/Swallow Test*, informed consent, and randomization procedures.

d) Collect Blood Sample (CT at year 1 and subsample in Years 3, 6, and 9; OS at Year 3)

If the participant is designated to have a blood sample collected at this annual visit, direct her to the phlebotomy area and follow guidelines in *Section 11 - Blood and Urine Collection, Processing and Shipment* regarding specimen collection. Participants in HRT may need a specimen sent to the local lab for triglyceride analysis, if the serum appears lipemic. Participants in OS need a specimen sent to the local lab for analysis of hematocrit, white blood count (WBC) and platelet count (or CBC if more convenient) as well as the routine samples to send to McKesson.

Note: All CT and OS participants are required to be fasting at least 12 hours to have their blood drawn.

e) Collect Urine Sample (Bone Density Sites only: CT in Years 1, 3, 6, and 9; and OS in Years 3 and 9)

Collect the urine sample from appropriate CT and OS participants. Process the urine sample as described in *Section 11.5.4 - At the Visit*.

f) Assess Adherence to Study Pills (HRT, CaD)

Assess the participant's adherence to taking the study pills. Be sure to include study pills she may have in a pill organizer. Even if the participant forgot to bring her study pills, you are required to enter an estimated pill count into WHILMA. If your adherence collection is an estimate, give the participant a mailer and ask her to mail her study pills to the CC. (*See Section 15.6 - Medication Adherence Assessment* for procedure.) This task must be done before completing the safety interviews and

dispensing study pills. Do not let the participant know that you are assessing pill adherence. If adherence to study pills is < 80% adherence problems are anticipated. Evaluate whether the participant should be referred to the Intensive Adherence Program (see *Section 15.8 - Intensive Adherence Program* for assistance). For CaD participants, determine if adherence problems may be due to the particular formulation she is taking, and consider switching to the other form at this visit.

g) Complete HRT and/or CaD Management and Safety Interview (HRT/CaD)

Complete *Form 10 - HRT Management and Safety Interview* and/or *Form 17 - CaD Management and Safety Interview*, using the script on the form. Each CC can decide on the appropriate staff to conduct this interview, but the staff must be appropriately trained and certified. Interviewers must refer decisions about possible serious conditions or concerns to the CP as soon as possible. Adherence concerns should be addressed or referred to the retention specialist, as appropriate. See *Section 16.1.2.2* for safety interview guidelines, and *Section 16.7.1* for procedures on completing *Form 10* and *Form 17* when participants stop the intervention.

h) Complete *Form 39 - Cognitive Assessment* (HRT participants 65 years or older at baseline and in years 1, 3, 6, and 9)

Complete the cognitive assessment interview using *Form 39 - Cognitive Assessment*. See *Section 9.11 - Cognitive Assessment* for details.

i) Review Mammogram Report (HRT annually; DM every other year)

Pull the radiologist's mammogram report from the participant's file and review it with her. Explain any terms that might be unfamiliar and answer any questions that she might have. Make referrals, if appropriate. See *Section 12 - Mammography* for guidelines. Mammograms not scheduled and/or available by the annual visit need not hold up dispensation of a six-month supply of HRT study pills. However, the mammogram must be scheduled and a report obtained before the next semi-annual contact in order to dispense an additional six-month supply of HRT study pills.

j) Enter Current Medications and Current Supplements (CT in Years 1, 3, 6, and 9; OS in Year 3)

Ask the participant for all current medications and vitamin/mineral supplements she brought with her. Remind the participant that only supplements taken at least once a week and medications used at least twice a week for the past two weeks will be entered. Enter the medications and supplements into the database (see *Section 4.2.4.6 - Current Medications and Current Supplements Inventory Review* and *Vol. 5 - Data System, Section 7.3 - Direct Data Entry*). Do not enter any WHI open label medications into the current medications inventory. If the HRT participant is taking any hormones (e.g., estrogen, progesterone, tamoxifen, or testosterone), refer her to the CP. The CP may need to communicate with her primary care provider regarding the HRT participant's hormone use.

k) Perform Physical Measurements (CT at year 1 and subsample in Years 3, 6, and 9; OS in Year 3)

Obtain physical measurements of resting pulse, blood pressure, weight, height, (CT annually; OS in Year 3). Obtain height and weight at BD CCs at OS AV6. Obtain waist and hip circumferences (CT in Year 1 and subsample of CT in Years 3, 6 and 9; OS in Year 3). At all other annual visits, leave the hip and waist measurements blank on *Form 80 – Physical Measurements*.

Record results of all physical measurements on *Form 80 - Physical Measurements*. See *Section 9 - Clinical Measurements, 9.1* through *9.5* for guidelines for performing these measurements.

l) Perform Functional Status Measurements (CT subsample in Years 1, 3, 6, and 9)

Obtain functional status measurements of grip strength, chair stand, and timed walk and record results on *Form 90 - Functional Status*. See *Section 9.6 - Functional Status Measurements* for guidelines for performing these measurements.

m) Complete ECG (CT in Years 3, 6, and 9)

Perform an ECG if this is the appropriate year for the CT participant and complete *Form 86 - ECG*. See *Section 13 - ECG Procedures* for guidelines for performing this procedure.

n) Perform Clinical Breast Exam (CBE) (HRT annually, optional for DM participants who have not consented to annual CBE)

Perform a CBE on appropriate CT participants and complete *Form 84 - Clinical Breast Exam*. See *Section 9.7.2 - Performing the Clinical Breast Exam* for a complete description of the procedure. A participant may also review the breast self-exam video if she wishes.

o) Perform Pelvic Exam Annually and Pap Smear in Years 3, 6, and 9 (HRT participants with a uterus)

With the stopping of E+P in tervention on July 9, 2002, pelvic examinations and Pap smears for E+P participants are no longer required, but may be continued for retention purposes, at CC option. When considering this option, keep in mind that these examinations were included in the E+P consent and serve as a retention tool for many participants. CCs should document any examinations that do take place in the CC on the appropriate forms. If an E-plus-P participant prefers to have her future exams done by an outside provider, you are not required to obtain outside provider reports.

Perform a pelvic exam and Pap smear on appropriate HRT participants and complete *Form 81 - Pelvic Exam* and *Form 92 - Pap Smear*. See *Section 9.9.2 - Performing the Pelvic Exam and Obtaining the Pap Smear*.

p) Perform an Endometrial Aspiration (subsample of HRT participants with a uterus in Years 3, 6, and 9)

The routine 6% subsample endometrial aspirations are discontinued with the stopping of E+P intervention on July 9, 2002.

Perform an endometrial aspiration on appropriate HRT participants and complete *Form 82 - Endometrial Aspiration*. Follow the guidelines in *Section 9.10.2 - Performing the Endometrial Aspiration*. If an identified EA subsample participant has had an endometrial aspiration or D & C during the past 12 months, those results may be used to fulfill her subsample requirement. If a participant is in the designated EA subsample and the clinician is unable to gain entry into the uterus (or the participant refuses the EA), a transvaginal ultrasound is required.

q) Document Four-Day Food Record (DM subsample in Year 1)

If the participant is in the designated subsample to complete a 4DFR, a certified dietary assessment staff person must document the 4DFR. See *Section 10.1.5 - Follow-Up Visit Food Record Documentation*.

r) Dispense Study Pills (HRT, CaD)

If a participant has no findings on the safety interview, physical exam, or test results available that contraindicate her continuing on study pills (see *Section 5 - HRT and Section 7 - CaD*), dispense new study pills (a six-month or twelve-month supply, as appropriate):

- Follow the procedures described in *Section 15.4 - Medication Dispensing* (note participant's preference for CaD study pill formulation). Inform the participant that you will be giving her a new bottle of study pills and that you will be keeping her old study pills that were dispensed at the last CC visit.
- Offer her a new *HRT Handbook* and/or *CaD Handbook* and review the pill instructions with her.
- Offer her a new pill organizer, if needed.

- Remind the participant to call the CC if she develops new symptoms or concerns with the study pills, loses her study pill bottle, or knows she is going to run out of study pills before her next visit.
- Remind her to bring her study pill bottles (empty or not) each subsequent visit.

s) Schedule Bone Densitometry (Bone Density Sites: CT in years 1, 3, 6, and 9; OS in years 3, 6, 9)

Schedule and perform a bone densitometry and complete *Form 87 - Bone Density Scan*. If the densitometry cannot be performed by the time of the follow-up visit, schedule the measurement as soon as possible.

t) Complete *Form 33 – Medical History Update* and OS Follow-up Forms (Bone Density Sites: OS in years 3, 6, 9)

The CCC does not mail forms to OS participants at bone density sites during years 3, 6, and 9, so these forms (*Form 33 – Medical History Update* and either *Form 143, 146,* or *Form 149 – OS Follow-up Questionnaire*) must be collected at the clinic visit.

16.3.2.4 Exit Interview

After completing the procedures and forms, review the annual visit checklist and visit plan to be sure you have completed all WHI-required and CC-specific annual visit activities or have recorded the reason an activity is not completed. Forward all forms to data-entry. Spend a few minutes with the participant to maintain rapport and discuss her further adherence and interest in the study. Record any concerns the participant may have and how you addressed them in the participant's contact notes. Make sure the participant is aware that:

- Her contribution to WHI is invaluable.
- The CC staff are interested in her safety and her activities with the study.
- She should contact the CC any time she might have questions or concerns.

Schedule an appointment for the CT participant's next semi-annual visit within the appropriate window (± 2 weeks) or remind her of the target date for a semi-annual contact. Explain to the participant that she will receive a packet of appropriate materials approximately 2 weeks before the target date and discuss appropriate semi-annual contact procedures and forms with her (see *Section 16.2 - Semi-Annual Contact (CT only) (Required*)).

Make sure the participant leaves with all the materials you have given her. These may include:

- HRT study pills (HRT).
- CaD study pills (CaD).
- New pill organizer(s), if appropriate (HRT/CaD).
- *HRT Handbook* and/or *CaD Handbook (*HRT, CaD).
- Appropriate study-wide annual retention item.
- Appointment card with date for the next semi-annual contact and estimated time needed to complete the semi-annual contact activities (if appropriate).

Participant retention may be promoted by sending a personalized thank-you card within a week of the visit.

16.3.3 Post-Visit Review (Required)

Review appropriate lab, pathology, and other reports that arrive after the annual visit. It is recommended that you provide the participant with these findings and required that you follow appropriate alert procedures if critical values are obtained (see *Vol. 1, Section 1 - Study Protocol and Procedures*).

Specific reports may indicate that HRT study pills should be discontinued either temporarily (pending further work-up) or permanently, even if pills were dispensed at the annual visit (see *Section 5.5.3 – Health Problems That May Require Temporary Discontinuation* and *Section 5.5.4 – Health Problems Requiring HRT*

Termination). Note that rules for stopping CaD study pills are not based on reports obtained from annual visit tests. To discontinue HRT study pills after the annual visit, follow the steps below.

- Call the participant with the results (this call must be made by a CC physician or CP, preferably the one who did the exam). Refer the participant to her primary physician. If any findings are suspicious for cancer, the CC physician or CP must call the participant's primary physician (with the participant's consent).
- Send copies of all pertinent reports to the participant's primary physician (with the participant's consent).
- Ask the participant to return her unused HRT study pills. Send a stamped, self-addressed envelope for her to return the study pills to the CC. Enter adherence information into WHILMA (obtain an estimated count at the time of the contact and then enter an actual count when you receive the study pill bottle).
- Instruct the participant to call the CC if the problem is investigated. If found not to be a safety concern, she may be eligible to resume taking HRT study pills.
- Complete a *Form 7 - Participation Status* and/or a *Form 54 - Change of Medications*, as appropriate.

16.3.3.1 Blood Test Results (Required)

Review lab results when returned by the local laboratory if blood was drawn. Follow procedures outlined in *Section 4.2.7.1 - Blood Analysis Results*.

16.3.3.2 Pelvic Exam and Pap Smear Results (HRT) (Required)

Review the pelvic exam and/or Pap smear results when they come in, as appropriate. Complete the remainder of *Form 81- Pelvic Exam* and/or *Form 92 - Pap Smear*. See *Sections 5.4 - Managing Symptoms* and *5.5 - Major Health Problems* for referral information.

16.3.3.3 Endometrial Aspiration Results (HRT) (Required)

Review the pathology results of the aspiration and complete the remainder of *Form 82 - Endometrial Aspiration*. Request slides from the local lab to send to McKesson for central pathology review. (See *Section 5.7 – Endometrial Aspiration Pathological Review*.)

16.3.3.4 Mammogram Report Results (Required)

Review mammogram reports for those mammograms scheduled between the annual and next semi-annual visit and document findings on *Form 85 - Mammogram*. Refer all abnormal findings to the participant's primary physician.

16.3.3.5 Bone Density Scan (Bone Density Sites only) (Required)

Confirm that the bone density scan was completed and complete the remainder of *Form 87 - Bone Density Scan*.

16.3.3.6 Personal Information Update (*WHIP 0441*)

Changes in a participant's address, phone number and contacts should be key-entered into the Members block in WHILMA (see *Volume 5, Section 5.1.2 – Entering a New Participant*). Changes to the alternate contacts that are listed on this report should be key-entered into the original *Form 20 – Personal Information* that was entered in WHILMA at baseline for the participant (See *Volume 5, Section 7.1.3 – Making Corrections to Key-entered Data)*. Do not enter a new *Form 20*.

An item to collect the participant's father's last name" was added to *Form 20* with version 37 of WHILMA. This item will be added to the Personal Information Update report for Version 38 of WHILMA. You can inform the participant that this information will be kept confidential and helps the WHI staff stay in contact

with her. For participants who completed their baseline *Form 20* before the publication of version 37 of WHILMA, you will need to key-enter the "Father's Last Name" into WHILMA after it is collected on the Personal Information Update.

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16.4 Follow-Up Contact Problems for Annual (CT) and Third-Year (OS) Visits

There may be many different reasons why participants might miss a scheduled contact, including:

- Transportation difficulties
- Illness
- Personal stress or life events
- Vacations and travel
- Temporary or permanent moves
- Decreased interest in or dissatisfaction with WHI

Strategies for managing follow-up contact problems for annual (CT) and third-year (OS) visits are detailed in the sections below. Strategies for managing annual mailed contacts in OS are described in *Section 16.5 - OS Annual Mail Contact and Follow-Up of Non-Responders*.

16.4.1 Missed Follow-Up Contacts

16.4.1.1 Strategies for Avoiding Missed Contacts

Strategies for avoiding missed follow-up contacts depend on the type of contact and the participant's availability and willingness to participate. Clinical Centers can refer to *Table 16.3 – Options for WHI Task Completion* for the available options for collecting the critical tasks for each study component.

- **If you are unable to complete a phone contact**, make several attempts to contact the participant at various times and days. Each CC should decide, based on their resources and experience, how many phone call attempts to make for any one participant. If you are unable to contact the participant by phone after several attempts, try to make initial contact by mail using a postcard that asks for current contact information and offers a phone number and CC staff person name for the participant to call with any questions. If you are still unable to contact the participant, begin efforts to locate her. Use *Form 23 - Search to Locate Lost Participant* to record your attempts to locate the participant (*see Section 17.3 - Locating "Hard to Find" Participants*). Although participants can miss the early phone call and still remain active in HRT or CaD, such contacts have been shown in other clinical trials to be critical for promoting ongoing adherence and retention.

- **If the participant cancels a scheduled visit** or fails to show up, reschedule her visit as soon as possible.

- **If the participant is reluctant to complete a required visit** (i.e., annual visits in CT and the semi-annual visit one in HRT, discuss the importance of this visit for safety, getting updated health information, and dispensing additional study pills, as appropriate. Appropriate CC staff should discuss with the participant (and help to resolve) any barriers to making a clinic visit (see *Section 17 - Retention*).

- **If the participant refuses a visit** (whether required or not), attempt to complete the contact as much as possible by mail and/or phone, as appropriate (a phone interview is needed to complete *Form 10 - HRT Management and Safety Interview* or *Form 17 - CaD Management and Safety Interview*). The safety interviews must be completed for HRT and CaD participants before dispensing additional study pills. Initiate a *Form 24 - Retention Worksheet* and refer to appropriate CC staff (see *Section 17 - Retention*), as needed.

- **If the participant refuses any routine contact**, determine her willingness to continue with the intervention and/or follow-up. Appropriate CC staff should discuss with the participant (and help to resolve) any barriers to making a clinic visit (see *Section 17 - Retention*). If she is not willing to continue with the intervention and/or with full follow-up procedures, complete *Form 7 - Participation Status*.

16.4.1.2 Strategies for Managing Missed Contacts (Required)

In general, every effort should be made to get participants who miss a follow-up contact back on their routine schedule. Specifically, if a follow-up contact is missed, the next scheduled contact should be planned such that:

- Missed annual visit tasks are conducted, even if the next scheduled contact is a semi-annual contact (CT).
- Missed year 1, 3, 6, or 9 visit tasks are conducted, even if the next scheduled contact is a year 2, 4, 5, 7, or 8 visit (CT)
- Missed third-year OS visit tasks are conducted up to 15 months after the target third-year date (OS).

In March 2000, the Steering Committee defined the allowable window for collection of data. In general, the time limits extend from several months before the target date for a task up to the window for the next target date. For **CT**, the general time limits are:

- Tasks due every 6 months: -/+3 months
- Tasks due at every 12 months: -/+6 months
- Tasks due less frequently than every 12 months: -6/up to 6 months before the text target date
- Tasks collected only once in follow-up -6/+30

For **OS**, the general time limits are:

- Tasks due for Year 3 Visit: -6/+15 months
- Tasks due for other Annual Contacts: -2/+10 months
- Bone Density tasks: -3/+15 months

The exact time limits for each task is given in *Table 16.1 - Time Limits for Collecting Tasks* (the same table is presented in the Outlook Public Folders under Manual Information). The table gives CT time limits of tasks on page 1 and OS time limits on page 2. The footnotes, described on the bottom of the second page, are similar to the foot notes in Appendix 1-A1 in the protocol. Note that the time limits listed in the table correspond to the "expanded" windows used by *WHIP1445-Task Completeness*. For CT, the "Subsample" column gives the percentage of participants on whom the task is collected.

Initiate a *Form 24 - Retention Worksheet* (recommended) for participants who are not willing to continue follow-up visits (see *Section 17 - Retention*). If follow-up visits have been missed and the participant's status has changed on *Form 7 - Participation Status*, follow reactivation procedures for the next follow-up visit (see *Section 17.4.5 - Reactivation of Participants with Changes in Participation Status*).

16.4.2 Minimum Procedures Required for a CT Participant to Remain on Intervention (Required)

Although appropriate and complete data collection are critical to the success of WHI, there may be situations in which full data collection at a routine contact is not possible. Minimum requirements for routine contacts, if the participant is unable or unwilling to complete all activities, vary by trial component and are based primarily on safety concerns.

Note that if the semi-annual *Form 33 - Medical History Update* is **not** administered, the next annual visit *Form 33* must show the date of the previous annual visit *Form 33* as the "date of last medical history update" (see appropriate forms instructions).

If a woman completes the minimum requirements listed below, she may continue on intervention even if she no longer attends CC visits and/or can no longer communicate (as long as a proxy respondent answers for her).

Table 16.1
Time Limits for Collecting Tasks
CT

Task	Name	SAVs*	Window**	AVs*	Window**	AV1	Window**	AV3, 6, 9	Window**	Subsample
10	HRT Interview	H[1] (all)	-3 / +3	H[1] (all)	-3 / +3					
17	CaD Interview	C[2](all)	-3 / +3	C[2](all)	-3 / +3					
33	Medical History	X (all)	-3 / +3							
35	Personal Habits					X	-6 / +18	X	-6 / +30	
38	Daily Life					X	-6 / +30	%X	-6 / +30	6%
39	Cog Assessment					%H	-6 / +18	%H	-6 / +30	HRT > 65
44	Current Medications					X	-6 / +18	X	-6 / +30	
45	Current Supplements					X	-6 / +18	X	-6 / +30	
53	HRT Calendar[4]	H (SAV1)	-3 / +3			H	-3 / +18			
60	FFQ			%D (AV2+)	- -6 / +12	D	-6 / +12			33% AV2+
80	Physical Measures			X (all)	-6 / +6					
	Hip/Waist[3]					X	-6 / +18	%X	-6 / +30	6%[6]
81	Pelvic[4]			H (all)	-12 / +6					
82	EA[4]							%H	-12 / +24	5%
84	Clinical Breast Exam			H (all)	-6 / +6					
85	Mammogram			H (all) D (AV2, 4, 6, 8)	-12 / +6 -24 / +6					
86	ECG							X	-6 / +30	
87	BD					BD	-6 / +18	BD	-6 / +30	
90	Functional Status					%X	-6 / +18	%X	-6 / +30	25% > 65
92	Pap[5]							H	-12 / +24	
100	Blood					X	-6 / +30	%X	-6 / +30	6%
101	Urine					BD	-6 / +18	BD	-6 / +30	
950	Pill Dispensing	H (SAV1)	-3 / +3	H (AV2+) C (all)	-6 / +6 -6 / +6	H	-3 / +6			
951	Pill Adherence	H (SAV1)	-3 / +3	H (AV2+) C (all)	-6 / +6 -6 / +6	H	-3 / +6			

See next page for footnotes.

Table 16.1
Time Limits for Collecting Tasks
OS

Task	Name	AVs* excluding AV3	Window**	AV3	Window**	AV6	Window**	AV 9	Window**
33	Medical History	X (AV1) X (AV2) X (AV4+)	-2 / +10 -2 / +9 -2 / +10	X	-6 / + 15[7]				
38	Daily Life			X	-6 / +15				
44	Current Medications			X	-6 / +15				
45	Current Supplements			X	-6 / +15				
48 143 144 145 etc.	OS Follow-up Forms	X (AV1) X (AV4) X (AV5+)	-2 / +10 -2 / +10 -2 / +10	X	-6 / +15				
60	FFQ			X	-6 / +15				
80	Physical Measures			X	-6 / +15	BD (Ht/Wt)	-3 / +15		
87	Bone Density			BD	-6 / +15	BD	-3 / +15	BD	-3 / +15
100	Blood Collection			X	-6 / +15				
101	Urine			BD	-6 / +15			BD	-3 / +15

Key:

X = All participants
H = HRT
D = DM
C = CaD
BD = BD sites
% = Subsample of participants, description in Subsample column
* = applicable contacts given in parentheses ( ).

1 = Active in HRT and 2 routine contacts after stopping (e.g., at next semi-annual and annual contacts)
2 = Active in CaD and 1 routine contact after stopping (e.g., at next semi-annual or annual contact)
3 = Hip/Waist not currently monitored on Task Completeness Report
4 = With Uterus
5 = With Cervix
6 = Same as the 6% blood draw subsample
7 = If Year 4 Form 33 from mailing has been completed, do not collect the Year 3 Form 33.

** = number of months before (-) and after (+) the contact target date.

Time limits are the same as th e expanded windows for *WHIP 1445 – Task Completeness*.

16.4.2.1 Hormone Replacement Therapy (Required)

The following minimum safety procedures must be completed and reviewed for safety concerns before an HRT participant is given HRT study pills. See *Table 16.2 – Follow-up Clinical Examinations/Minimum Safety Requirements for HRT Participants.* It is recommended that safety exams performed by outside providers be done within 6 months of the annual visit. Any abnormal reports should be thoroughly investigated and documented:

- Clinical breast exams are required annually for pills to be dispensed. The CBE may be done at a CC visit or by an outside provider. See *Section 9.7 – Clinical Breast Exam (Required)* and *Table 16.2 – Follow-up Clinical Examinations/Minimum Safety Requirements.*
- Mammograms are required annually. Participants may still receive a 6 month supply of HRT study pills at the annual visit, even if the annual mammogram has not been scheduled. However, the mammogram must be scheduled and a satisfactory report obtained by the semi-annual contact for an additional 6-month supply of HRT study pills to be dispensed. Do not dispense HRTstudy pills if more than 18 months have elapsed since the date of the last mammogram.
- Pelvic exams (for HRT participants with a uterus only) are required annually. See *Section 9.9 – Pelvic Exam and Pap Smear (Required)* and *Table 16.2 – Follow-up Clinical Examinations/Minimum Safety Requirements.*
- Pap smears are required in years 3, 6, and 9 although they can be offered to participants annually. See *Section 9.9 – Pelvic Exam and Pap Smear (Required)* and *Table 16.2 – Follow-up Clinical Examinations/Minimum Safety Requirements.*
- *Form 10 - HRT Management and Safety Interview* is required to be collected annually. This form may be completed at a CC visit or by phone. *Form 10A* may be mailed to participants for semi-annual visits only. (See *Section 5 - HRT* for more details.) A participant who can no longer communicate may continue on HRT study pills only if she has a proxy respondent approved by the CC Consulting Gynecologist and/or Principal Investigator (PI). An approved proxy should be a caregiver to the WHI participant (i.e., someone concerned about and involved with her health care). The required *Form 10* may be completed by an approved proxy at a CC visit or by phone (but not by mail). (See *Vol. 2 – Procedures, Section 16.6 – Follow-Up by Proxy.)*
- The *HRT Handbook* must be offered each time study pills are dispensed.
- A participant may continue on HRT study pills without the completion of *Form 33 - Medical History Update* with the expectation she may resume full participation in future years.

16.4.2.2 Calcium/Vitamin D (Required)

The following minimum safety procedures must be completed and reviewed for safety concerns before a CaD participant is given CaD study pills:

- *Form 17 - CaD Management and Safety Interview* annually. This form may be completed at a CC visit or by phone. *Form 17A* may be mailed to participants for semi-annual visits only. (See *Section 7 - CaD* for more details.) A woman who no longer can communicate may continue on CaD study pills only if she has a proxy respondent approved by a CC physician and/or PI. An approved proxy should be a caregiver to the WHI participant (i.e., someone concerned about and involved with her health care). The required forms may be completed by an approved proxy at a CC visit or by phone (but not by mail). (See *Vol. 2 – Procedures, Sec. 16.6 – Follow-up By Proxy*).
- The *CaD Handbook* must be offered each time study pills are dispensed. A participant may continue on CaD study pills without the completion of *Form 33 - Medical History Update* with the expectation that she may resume full participation in future years.

Table 16.2

Follow-up Clinical Examinations/Minimum Safety Requirements for HRT Participants

Exam/Procedure	Protocol-Defined Frequency	If Participant refuses procedure at CC, What is Acceptable?*	Minimum Safety Requirements (for participants to stay on study pills)*
Clinical Breast Exam (*Form 84*)	Annually	CBEs should be done in the CC. If the participant refuses to have the CBE done at the CC, a written or verbal report of an outside provider exam must be obtained from a clinician. A report of "normal" is acceptable.	Same
Pelvic Exams (women with uteri) (*Form 81*)	Annually	Pelvic exams should be done in the CC. If a participant refuses to have the exam done at the CC, a written or verbal report of an outside provider exam must be obtained. Verbal reports from participants will only be accepted in years 2, 4, 5, 7, or 8. A report of "normal" is acceptable.	If a participant refuses to have the exam done at the CC, a written or verbal report from a clinician for an outside provider exam must be obtained in years, 3, 6, and 9. A report of "normal" is acceptable.
Pap Smears (women with cervices) (*Form 92*)	Years 3, 6, and 9	They may be done annually with the pelvic exam. If a participant refuses to have a pap smear done at the CC, a written or verbal report of an outside provider exam must be obtained.	Same
HRT Safety Interview Management (*Form 10*)	Semi-annually and annually	*Form 10* may be completed at a CC visit or by phone. *Form 10A* may be mailed to participants at semi-annual visits only.	Annually
Mammograms (*Form 85*)	Annually	Mammograms from other institutions are acceptable.	18 months

*Note: If a participant refuses a recommended diagnostic follow-up exam/procedure for an abnormality, study pills may need to be discontinued. *Refer to section 5 – HRT* for specifics.

16.4.2.3 Dietary Modification

A DM intervention participant may continue to attend DM sessions without participating in any follow-up procedures, with the expectation that she may resume full participation in future years.

16.4.3 Guidelines for Restarting Participant who Discontinued Pills for 12 Months or More

16.4.3.1 Restarting HRT

See *Section 5.5.4.1 – Guidelines for Restarting a HRT Participant who Discontinued Pills for 12 Months or More*

Table 16.3 – Options for WHI Task Completion

Form#	Form Name	Current Options					Comments
		CC Visit[1]	Mail	Phone Priority[2]		Outside Provider	
				High	Low		
10	HRT Management and Safety Interview[3]	X	X	X			HRT while on study pills and 2 subsequent contacts (eg., semi-annual and annual) if off intervention
17	CaD Management and Safety Interview[4]	X	X	X			CaD while on study pills and 1 subsequent contact (eg. One semi or annual) if off intervention
100	Blood Collection	X					CT subsample, OS AV3
101	Urine Collection	X					Bone density sites
143-148	OS Exposure Update	X	X		X		
20	Personal Information Update	X	X	X			
33/33D	Medical History Update/Detail	X	X	X			
35	Personal Habits Update	X	X		X		CT only
38	Daily Life	X	X		X		CT subsample (blood subsample), OS AV3
39A/B	Cognitive Status	X					HRT ≥65 only
40	Addendum to *Form 33*	X	X		X		One-time only
44	Current Medications	X			X		
45	Current Supplements	X			X		
60	FFQ	X	X				DM subsample, OS AV3
80	Physical Measurements	X					CT (waist and hip in subsample only), OS AV3
81	Pelvic[3]	X				X	HRT only. Refer to an outside provider only if participant refuses to have it in-clinic (verbal report of a normal exam is not acceptable at AV3, AV6, or AV9).
82	Endometrial Aspiration	X				X	HRT subsample or according to bleeding management procedures in *Vol. 2, Section 5 – HRT*. Refer to an outside provider only if participant refuses to have it in-clinic.
83	Transvaginal Uterine Ultrasound	X				X	HRT only; ultrasounds are done at some CCs, but are not routine in-clinic procedures
84	Clinical Breast Exam[3]	X				X	HRT only (option in DM). Refer to an outside provider only if participant refuses to have it in-clinic.
85	Mammogram[3]	X				X	CT only, mammograms are done at some CCs, but are not routine in-clinic procedures
86	ECG	X					CT only
87	Bone Densitometry	X					Bone density sites only
90	Functional Status	X					Subsample of CT participants 65 or older
92	Pap[3]	X				X	HRT only
WHILMA	Study Pill Adherence	X	X	X			HRT/CaD only, collections can be done in-clinic or by mail (estimates can be done over the phone).

[1]In clinic or at an appropriately equipped remote site.

[2]High phone priority means that the task is a study priority, and you should attempt phone completion as an early option. Low phone priority means that phone completion should be attempted only after all other options to complete the task have been thoroughly exhausted.
[3]Required for staying on HRT study pills.
[4]Required for staying on CaD study pills.

16.5 OS Annual Mail Contact and Follow-Up of Non-Responders

Follow-up data are collected annually from OS participants during the nine years following enrollment. Activities to collect the data consist of a series of mail and telephone contacts during the follow-up period. Data collection attempts by mail (Contacts 1-4) are conducted by the Clinical Coordinating Center (CCC) on an annual basis, except for participant year 3 when the data are collected by the CC during the follow-up clinic visit. For participants who do not respond to Contacts 1-4, data collection attempts by telephone (Contacts 5-6) are conducted by the CCs on an every-other-year basis (participant years 1, 5, 7, and 9).

16.5.1 CCC Responsibilities for Annual OS Follow-Up

A series of mail contacts to collect follow-up data from OS participants is conducted annually by the CCC, except in year 3 when the CC conducts the Year 3 Visit. The CCC is responsible for all printing (through the Government Printing Office [GPO]), assembly, and outgoing postage costs for the mail contacts. The four mail contacts include:

- An initial mailing of the entire questionnaire packet (Contact 1).
- A reminder/thank-you postcard (Contact 2). (Discontinued as of May 1997).
- A second mailing of the entire questionnaire packet (Contact 3).
- A third mailing of the entire questionnaire packet (Contact 4).

Spanish-language versions of the contact materials are mailed to participants whose primary language is Spanish, as indicated either by the "Preferred Language" flag on the Contact Information Screen in WHILMA (see *Vol. 5 - Data Systems*) or by prior completion of a Spanish-language *Food Frequency Questionnaire (Form 60S)*.

16.5.1.1 Mailing of Annual OS Questionnaire Follow-Up Packet 1 (Contact 1)

A follow-up packet is mailed annually by the CCC to all OS participants (except those whose participation status in WHILMA is set to no mail contact, no follow-up contact, deceased, lost to follow-up, or absolutely no follow-up) two months before the participant's enrollment anniversary month. The exception to this schedule is during participant Year 3, when a clinic visit is scheduled. The packet includes a cover letter with a CC telephone number listed (see *Figure 16.1 - Cover Letter for OS Contact 1 (Year 1)* ; a postage-paid, CC-addressed return envelope with business reply information; a *Form 33 - Medical History Update* with the date of the last WHI medical update; and an OS Follow-Up Questionnaire, as appropriate. For Year 1, the *OS Follow-Up Questionnaire* is *Form 48*; for Year 3, it was *Form 143*; for Year 4, it is *Form 144*; for Year 5, it is *Form 145*. There is no *Follow-Up Questionnaire* for Year 2.

The *Form 33* has two labels:

1) **Date Label**: a Date Label with date of the last WHI medical update (last *Form 33* or date of enrollment for Year 1), OS contact number and corresponding barcode, participant year, and participant ID.

2) **Participant ID label:** a Participant Identification Label with participant name, participant ID and barcode, OS contact number, and participant year.

The *OS Follow-Up Questionnaire* (e.g., *Form 48*) has one label, a Participant Identification Label, with participant name, participant ID and barcode, OS contact number, and participant year.

The packet is sent third-class (bulk) mail in a mailing envelope printed with the CC's return address, the CCC bulk mailing permit number, and a request for notification of change of address.

16.5.1.2 Mailing of the Thank You/Reminder Postcard (Contact 2 – Discontinued in May 1997)

During the first year of mailing, a postcard (see *Figure 16.2 - Follow-up Postcard for OS Contact 2*) was mailed by the CCC to all OS participants one month after the mailing of the Contact 1 packet. The postcard served to thank those participants who had completed and returned their forms, and to remind those who had not returned their forms to please do so. Because the postcard did not increase response rates, it was discontinued in May 1997.

16.5.1.3 Second Mailing of Entire Follow-Up Packet (Contact 3)

A second complete follow-up packet is mailed during the participant's enrollment anniversary month (three months after the mailing of Contact 1) to those participants who did not respond to the first mailing (i.e., those who did not complete and return the form sent in Contact 1 and for whom the CC has not indicated receipt in WHILMA). The packet includes: A cover letter (different from the Contact 1 cover letter - *see Figure 16.3 - Cover Letter for OS Contacts 3/4 (Year 1)*) with CC telephone number listed; a postage-paid, CC-addressed return envelope with business reply information printed on the envelope*; Form 33 - Medical History Update*; and *Form 48 - OS Follow-up Questionnaire* (for Year 1).

The packet is sent third-class (bulk) mail in a mailing envelope printed with the CC's return address, the CCC bulk mailing permit number, and a request for notification of change of address.

16.5.1.4 Third Mailing of Entire Follow-Up Packet (Contact 4)

A third packet (identical to the Contact 3 packet) is mailed three months after the enrollment anniversary month (two months after Contact 3) to non-responders only (i.e., those who have not completed and returned the forms sent during earlier contacts and for whom the CC has not indicated receipt in WHILMA).

16.5.2 CC Responsibilities During Annual OS Follow-Up Mailings (Required)

The CCs have several responsibilities during mail Contacts 1-4. These responsibilities consist primarily of:

- Updating WHILMA to reflect that *Form 33* has been completed and returned.
- Making address corrections as soon as they become available.
- Completed forms are returned directly to CCs in the business-reply envelopes provided in the packet. Clinical Centers are responsible for paying the postage for these completed, returned forms.

16.5.2.1 Processing Returned Packets (Contacts 1-4) (Required)

Clinical Center staff are responsible for indicating in WHILMA that packets have been returned to the CC. When a packet is received at the CC, it is important to note its return immediately to prevent additional mailings from being sent to participants.

Return of a packet can be indicated in one of two ways: by using the "OS Receipt Screen" in WHILMA or by data entering *Form 33* and/or the OS follow-up form for that year (e.g., *Form 48*). (See *Vol. 5 - Data System.*)

Option 1: Using the "OS Receipt Screen"

- Remove *Form 33* and/or the OS follow-up form (e.g., *Form 48*) from the envelope.
- Scan the Participant ID barcode on the Participant ID Label on the top of either form.
- Indicate the OS contact number. This can be done in one of two ways:

  a) Scan the OS contact ID barcode on the *Form 33* Date Label, and press **F10** to save the data, or

b) Enter the contact number, which is listed on both the Participant ID Label (on *Forms 33* and *48*) and the Form 33 Date Label (e.g., label reads C3, enter 3), and press **F10** to save the data.

Option 2: Data entry of *Form 33* and/or the OS follow-up form (e.g., *Form 48*).

Using the first option is preferable because receipt of the packet needs to be indicated immediately and the CCC needs to know the OS contact number to evaluate the effectiveness of the various contacts.

Regardless of which option is chosen to indicate the return of the packet, the forms still need to be data entered. Before data entry, complete the top part of the forms. "Date Received", "Contact Type", and "Type of Visit" can be completed by the person opening the packet of forms. For "Date Received", fill in the day the packet is received at the CC. For "Contact Type", indicate "Mail". For "Visit Type", indicate "Annual" and fill in the visit year number, which can be found in the lower right-hand corner of the Participant ID Label (e.g., label reads Y1, record 01 on the form). The form should then be passed on to the appropriate person(s) for review, who should then complete the "Reviewed by" field on the form. Participants who have left entire pages blank on any of the return forms or who have not completed questions 4 through 7 on *Form 33* (these items are necessary to trigger a *Form 33D - Medical History Update (Detail*)), should be telephoned to collect the missing data. Refer to *Volume 8, Section 2 - Ascertainment and Form 33D* Forms Instruction for procedures for participants requiring completion of a *Form 33D - Medical History Update (Details)*.

Incomplete Packets:

If a packet containing only one form is returned, the CC should still indicate that the packet has been returned using the procedures described above (to stop further mailings to that participant). Participants with missing forms will appear on *WHIP 1207 - Returned Packet with Missing Form*, which should be run monthly. Missing forms are those that have *not yet been data entered*. *WHIP 1207* includes the participant name and ID, date packet was received, and a message indicating which form is missing.

Clinical Centers are responsible for following up to collect data on missing forms. To follow-up on missing forms:

1) Check within the CC to make sure that the form is indeed missing. It may have been returned, but not yet data entered.

2) If the form is missing, CCs may use whatever methods they choose to collect the data on the missing form (e.g., they may use telephone, mail, both, etc.).

Names continue to appear on *WHIP 1207* until the missing form has been data entered or until Contact 5 (CC data collection by telephone) is initiated. At that point, if the missing form is *Form 33*, it will appear on *WHIP 1206 - OS Enrolled Members Needing Clinic Follow-Up*. The result of data collection attempts do not appear on *WHIP 1207* once the Contact 5 period has been reached (e.g., if a *Form 33* is completed after Contact 5 starts [but the *OS Follow-Up Questionnaire* is not completed] the follow-up questionnaire will not appear on *WHIP 1207*).

16.5.2.2 Making Address Corrections (Required)

Clinical Center staff are responsible for updating WHILMA to reflect any participant address changes. Each packet mailed out to OS participants has their CC's return address in the upper left-hand corner, with the line "Address Correction Requested" underneath. In the event that the participant's address on the mailing envelope is incorrect, the U.S. Post Office (USPO) will notify someone at the return address printed on the envelope. The USPO will not actually return the envelope, but will provide a photocopy of the envelope and a statement as to why it was not delivered. If the address has been changed, the new address will be provided. If the address has changed and no forwarding address is available, it will be marked "undeliverable". The USPO will charge the CC for each packet that is not delivered ($.50 as of spring, 1996).

For **changed addresses where the new address is provided by the USPO**, update the address in the "Contact Information Screen" in WHILMA immediately. This will prevent future mailings from being sent to the undeliverable address (which would again cost the CC approximately $.50). It is a good idea to try reaching these participants by telephone to determine whether or not the telephone number has also changed. If it has, this information should also be updated in WHILMA.

When a participant has an **undeliverable address and a new address is not available**, set the "undeliverable address" flag on the "Contact Information Screen" immediately (see *Vol. 5 - Data System*). This will prevent future mailings from being sent to the undeliverable address. Initiate a search to find the correct address by contacting the participant and/or by using the information listed on *Form 20 - Personal Information*. Refer to *Section 17.3 - Locating "Hard to Find" Participants* for specific instructions for conducting a search for lost participants. Try to fix the address as soon as possible, so as not to lose permanent contact with the participant. Participants with an undeliverable address will appear on the *WHIP 1211 - Undeliverable Address Report* the next time it is produced (see *Section 16.5.2.3 - Running Monthly OS Follow-up Reports from WHILMA (Required)*).

When the USPO indicates that a participant is "deceased", initiate contact with persons listed *on Form 20 - Personal Information*. If a death is confirmed, complete *Form 7 - Participation Status and Form 120 - Initial Notification of Death* and process according to procedures outlined in *Volume 8 - Outcomes*.

Clinical Centers pay for the cost of USPO updates on address changes and non-deliverables ($.50 per update as of spring, 1996) and for the cost of completed forms mailed from participants to the CC.

16.5.2.3 Running Monthly OS Follow-up Reports from WHILMA (Required)

Several reports are available to help CCs keep track of the status of OS participant follow-up. Detailed instructions for running these reports in WHILMA are given in *Vol. 5 - Data System, Section 9.2 - Reports and Appendix D - WHILMA Reports*.

Every month, each CC should run the following reports:

1. *WHIP 0611 - Members With an Incomplete Address or Long Name/Address*. This report provides a list of participants with problem addresses (e.g., the address is incomplete or will not fit on a mailing label). Participants with address lines that are too long should be fixed immediately. An address line is too long if it appears on this report as more than one line. To fix the problem, use Address Line 2 for the second line of the address, or abbreviate words in the first line so that they stay within the 30-character width limit of the mailing labels.

   Addresses that are incomplete should be followed up on as soon as possible. If the zip code is missing, try calling the USPO, or if that fails, call the participant to obtain the complete/correct address. If you cannot fix the address right away, set the undeliverable address flag on the "Contact Information Screen" in WHILMA. This will prevent mailings from being sent to an undeliverable address. Incomplete addresses should be fixed within two weeks of appearing on *WHIP 0611*. Participants will continue to appear on this report until either the address has been fixed or the "undeliverable address" flag has been set. Once you have made all of the necessary edits indicated on the report, run the report again to confirm that problems have been cleared.

2. *WHIP 1211 - Undeliverable Address Report*. This provides a list of all (CT and OS) participants with undeliverable addresses in the CC's database. It does not include those with follow-up status 5-7 (no follow-up, deceased, lost to follow-up). Included on the report are the participant's name and (undeliverable) address; member ID; home phone; work phone; note indicating that the workplace should not be contacted, if applicable; best time to call; telephone numbers for other contact; follow-up status; and date marked (i.e., the date the undeliverable address flag was set).

Undeliverable addresses should be updated as soon as possible, since a participant will not receive any mailings (such as OS follow-up data collection packets) until the address is fixed. If the participant does not receive her mailings, the data will eventually need to be collected by CC staff (see *Section 16.5.3 - CC Data Collection for Non-Respondents to OS Mailings*). Also, the sooner you try to get an address correction, the more likely it is that you will be able to locate the participant. Undeliverable addresses should be corrected within one month of appearing on *WHIP 1211*. Participants will continue to appear on this report until the "undeliverable address" flag has been removed or follow-up status changes.

3. *WHIP 1207 - Returned Packet with Missing Forms*. This report lists participants for whom packets have been returned, but either one or both of the forms have not yet been data entered in WHILMA. Use this report to serve as a reminder to data enter the forms that have been returned or to follow-up with participants to collect data on forms that were not returned in the packet.

4. *WHIP 1206 - OS Enrolled Members Needing CC Follow-Up*. The purpose of this report is to provide a list of those participants who do not have a completed *Form 33* following the four CCC mailings (by two months after the mailing of Contact 4). A participant appears on this form if no *Form 33* has been data entered since Contact 1 was initiated and if her follow-up status is not any of the following: no follow-up, deceased, or lost-to-follow-up.

   This report lists participant name, participant ID, home phone number, work number, best time to call, phone of other contact, and follow-up status. As described below in *Section 16.5.3 - CC Data Collection for Non-Respondents to OS Mailings*, CCs should use this report as a prompt to initiate follow-up contacts to participants who have not completed a *Form 33*.

   Participants remain on this report until one of the following occurs: either a *Form 33* has been completed; follow-up status changes; or the next year's contacts begin.

   In addition, the *WHIP 1210 - OS Follow-up Receipt Report*, can be run on an as-needed basis. This report lists packets that have been received and processed (as described in *Section 16.5.2.1 - Processing Returned Packets (Contacts 1-4)* at the CC. The report lists participant name and ID, receipt date, contact number, and employee ID.

16.5.3 CC Data Collection for Non-Respondents to OS Mailings (Required)

During participant years 1, 5, 7, and 9, CCs are responsible for collecting *Form 33 - Medical History Update* data on those participants who have not responded to that year's mailings. (*Form 33* data are also collected by CCs during the participant's Year 3 follow-up visit.) If a participant has not responded to Contacts 1-4 during applicable years, CC staff should initiate telephone contacts to collect the data. This is done through a series of attempts to reach the participant or her proxy to collect the data. Non-respondents needing follow-up data collection are listed on *WHIP 1206 - Members Needing CC Follow-Up* (a report generated monthly by the CC).

Clinical Center OS follow-up data collection activities consist of two types of contacts: a phone contact to ascertain correct address and to collect *Form 33- Medical History Update* from the participant (Contact 5), and, if applicable, a mail or phone contact to trace participants and/or collect *Form 33* data from a proxy (Contact 6).

16.5.3.1 Telephone Contact to Ascertain Correct Address and to Collect Medical History Update (Contact 5) (Required)

If *Form 33* has not been returned by two months after the third mailing of the OS follow-up packet (CCC Contact 4) during participant years 1, 5, 7, and 9, the CC should attempt to reach the participant by telephone. The purpose of this call is to confirm that the correct address is shown in WHILMA and to complete *Form 33 - Medical History Update*. Use the Members Needing CC Follow-Up report to determine which participants require follow-up telephone contacts.

Actual contact is required with the participant at this point to confirm that we have the correct address and phone number for her (e.g., a message left on an answering machine reminding her to mail in the packet is not sufficient since there is no way to confirm that she has even received the packet or the phone call).

When calling, make at least 8 telephone attempts the first month and 4 attempts the second month during the "best times to call" (identified on *Form 20 - Personal Information*). Refer to *Figure 16.4 - Suggested Script for OS Contact 5 Telephone* Contact. If contact is made with the participant, verify the address and complete Form 33 over the telephone. *WHIP 0441 - Personal Information Update*, an update *of Form 20 - Personal Information* can also be completed at this time. Completion of the *OS Follow-Up Questionnaire* (if applicable for that year) is optional, depending on the success in reaching completion goals for that form.

If you determine that the telephone number and/or address have changed, update WHILMA accordingly. If a participant requests a change in her participation status, initiate a *Form 24 - Retention Worksheet* (see *Section 17.2 - Clinical Center Activities for Retention Challenges*). If you find out that she is deceased, complete *Form 7 - Participation Status* and *Form 120 - Initial Notification of Death* and process according to *Volume 8 - Outcomes*.

Clinical Centers have the option of mailing a *Form 33* (and *OS Follow-Up Questionnaire*, if applicable) to participants who, as determined by the phone contact, are willing to complete the form but are unwilling to complete it over the phone.

If telephone attempts fail to make contact with the participant, contact a proxy to determine the location and vital status of the participant (Contact 6). After proxy contact, continue to try to locate and interview the participant, if appropriate. Do not interview the proxy unless the participant is deceased, unable to communicate, or has poor cognitive functioning. (See *Section 16.6 - Follow Up by Proxy*.)

16.5.3.2 Mail/Phone Contact to Trace Participant and/or Collect Medical History Update from Proxy (Contact 6) (Required)

If telephone attempts to make contact with the participant fail, contact a proxy to determine her location and vital status. Use *Form 20 - Personal Information* for information on where to locate proxy contacts. When contacting proxies, use the following order of priority: 1) spouse or partner; 2) nearest relative; 3) friend; 4) physician. Refer to *Figure 16.5 - Suggested Script for Proxy Telephone Contact*.

If the proxy indicates that the participant is able to be interviewed, ascertain the new address and telephone number and continue trying to locate and interview her. If the participant has a new address, update the database with the address correction.

If the participant is deceased, unable to communicate, or has poor cognitive functioning, collect *Form 33* data from a proxy by either telephone or mail. For mail contacts, refer to *Figure 16.6 - Sample Cover Letter for Proxy Contact*. The *OS Follow-up Questionnaire* (e.g., *Form 48, 144, 145*) is not collected by proxy.

The CC is responsible for keeping track of which of their participants require Contact 6.

16.6 Follow-Up by Proxy (Required)

Some follow-up contacts, because of a participant's illness, disability, or death, may need to be conducted by proxy. A proxy "stands in" for the participant and provides information about her health. The proxy should be someone who has frequent contact with the participant and knowledge of her health status.

16.6.1 Designating a Proxy (Required)

Clinical Centers must have IRB approval to correct participant data from a proxy if the participant's consent form does not include explicit approval for contact of personal contacts.

Approval to conduct follow-up contact(s) by proxy should be a careful decision based on the participant's situation and the individual proposed to serve as her proxy. Obtain approval to conduct contacts by proxy from the participant or her legal next-of-kin, if possible. Proxy contacts must be also approved by the CC PI and other CC investigators, consultants, and/or staff, as determined at your CC.

Once a proxy has been identified, establish contact with that person(s) and discuss how that person was identified as the proxy (e.g., listed as a close contact or her personal physician). Determine if s/he has any questions about the study and/or the proxy role. Provide the proxy with relevant information about the study (e.g., consent, information sheets). Ongoing efforts to promote rapport and retention with the participant should also extend to your contacts with the proxy.

Complete a new *WHIP 0441 - Personal Information Update* and *Form 7 - Participation Status*, as appropriate, to reflect the proxy contact information and appropriate follow-up status.

16.6.1.1 For CT Participants Attending Clinic Visits

Clinic staff collect proxy names and contact information from CT participants attending their annual or semi-annual clinic visits. To collect the information, the participant is provided with a copy of the *Proxy Update (Vol. 2, Appendix F, Figure F.3.13)* to review and discuss with staff. This update explains the purpose and role of the proxy. After the woman reviews the update and has had an opportunity to discuss the role of the proxy with clinic staff, she is asked to designate her proxy and provide the proxy's contact information (address and phone number). At the same visit, the participant is given two copies of the *Proxy Update*: one for her and one for her proxy. In addition, she fills in her proxy's name and signs her own name on the *Proxy Letter (Vol. 2, Appendix F, Figure F.3.14)*. The *Proxy Letter* informs the proxy that he/she has been selected by the participant to serve as her proxy. Instruct the participant to either give or mail a copy of the *Proxy Update* and *Proxy Letter* to her selected proxy. Be sure to provide a postage-paid envelope addressed to the proxy if he or she does not live with the participant.

Data enter the proxy contact information in the Personal Information screen in WHILMA. At each subsequent clinic visit have the participant review and update, as appropriate, the proxy contact information as part of her routine Personal Information review.

Participants have the option of refusing to name a proxy or provide contact information.

The *Proxy Letter* instructs the proxy to contact the CC if he/she has questions. It is the CC's responsibility to include their contact information on the letter, either by using a stamp, affixing a label or business card, hand-writing the information, or running the letter through a laser printer.

Local IRB approval of the materials and procedures is required before collection of proxy contact information can begin. If the local IRB requires changes to the materials or procedures, CCs may modify them as requested. Revised materials should be submitted to the CCC for review before use.

The *Proxy Update* and *Proxy Letter* are ordered from the CCC using *Form 172 – Supplies Order*.

16.6.1.2 For OS Participants Attending AV3

Starting in summer 2000, clinic staff should collect proxy contact information from OS participants attending their AV3. To collect the information, use the same procedures described in *Section 16.1.1.1 – For CT Participants Attending Clinic Visits.*

16.6.1.3 For OS Participants Beyond AV3

At the time the procedures to designate a proxy were developed, most OS participants had already attended their AV3. Proxy contact information for these participants is collected through a one-time, first class mailing initiated by the CCC in early 2001. The mailing consists of a cover letter explaining the purpose of the mailing, a copy of the *Proxy Update*, a copy of the *Proxy Letter*, a copy of the Personal Information Sheet imprinted with the participant's information, and a Business Reply Mail envelope imprinted with the CC's address. Participants are asked to make relevant updates to the Personal Information Sheet, as well as to provide proxy contact information, and to send the sheet back to the CC. The proxy contact information and any changes to the personal information are data entered in WHILMA at the CC.

16.6.1.4 For Participants Who Do Not Have a Designated Proxy

If a participant has not designated a proxy, or if the proxy is deceased, cannot be located, refuses contact, or is unable to participate, CCs may (subject to local IRB approval) contact one of the participant's other personal contacts to serve as the proxy.

When using other personal contacts to collect proxy information, in order of data collection preference, contact:

- Spouse or partner
- Other close family member
- Close friend
- Health care provider

16.6.2 Proxy Follow-Up Contact Procedures (Required)

Clinical Centers must have IRB approval to collect participant data from a proxy if the participant's consent form does not include explicit approval for contact of proxies or personal contacts.

Follow-up contacts with a proxy for CT participants should preferably take place by phone or visit, rather than by mail (see *Figure 16.5 - Suggested Script For Proxy Telephone Contact*). Follow-up contacts with a proxy for OS participants can take place by mail (see *Figure 16.6 - Sample Cover Letter for Proxy Contact*), if necessary. When the proxy is first contacted by the CC, discuss how that person was identified as the proxy (e.g., designated by the participant, listed as a personal contact). Determine if s/he has any questions about the study and/or the proxy role. Provide the proxy with relevant information about the study (e.g., Proxy Update, consent forms, study information sheets), as needed. Any ongoing efforts used to promote rapport and retention with the participant should also extend to your contacts with the proxy.

If the participant is alive, each proxy contact should be preceded by a discussion of the participant's ability to resume her own follow-up contacts, depending on her particular situation. If it has not been done, complete a *Form 7 - Participation Status*, to reflect that she is on "Proxy follow-up" and to indicate any changes to her intervention status, as appropriate (see *Vol. 2, Section 16.4.2 – Minimum Procedures Required for a CT Participant to Remain on Intervention* for details on keeping "proxy follow-up" participants on intervention).

If the participant is deceased, details on proxy follow-up outcomes information are described in *Vol. 8 - Outcomes, Section 7 – Fatal Events.*

16.6.2.1 Proxy Follow-Up Procedures for CT Participants (Required)

For CT women who are alive, conduct twice yearly contacts with the designated proxy. The only data to be completed by proxy (if scheduled) are:

- *Form 10 - HRT Management and Safety Interview (HRT).*
- *Form 17 - CaD Management and Safety Interview (CaD).*
- *Form 33 - Medical History Update* and, if appropriate, *Form 33D - Medical History Update (Detail).*
- *WHIP 0441 - Personal Information Update.*
- *Form 950 - Medication Adherence.*

For CT women who are deceased (see *Vol. 8 - Outcomes, Section 7 – Fatal Events*), collect:

- *Form 120 – Initial Notification of Death*
- *Form 33 - Medical History Update* and, if appropriate, *Form 33D - Medical History Update (Detail).*

16.6.2.2 Proxy Follow-Up Procedures for OS Participants (Required)

The CCC does not mail annual follow-up packets to OS participants (or their proxies) if the follow-up status is listed as "proxy" on *Form 7 – Participation Status.* It is the CC's responsibility to contact the proxy and collect the data, preferably by phone. OS participants who are on "proxy follow-up" automatically appear on *WHIP 1206 – OS Members Needing CC Follow-up,* along with the participant's contact information, follow-up status, and date of last *Form 33 – Medical History Update*. To get the proxy contact information, see the participant's Personal Update Screen. CCs should run this report every month to see which of their OS participants require CC follow-up. This report can be run to show participants needing follow-up for all years (i.e., AV1, AV2, AV4, AV5, etc.), for a select year (e.g., AV5 only), or for odd-numbered years only (e.g., AV1 and AV5).

For OS women on proxy follow-up who are alive, collect *Form 33 - Medical History Update, Form 33D – Medical History Update (Detail),* if appropriate, and *WHIP 0441 - Personal Information Update* with the proxy during years 1, 3, 5, 7, and 9 post-randomization. For OS women on proxy follow-up who are deceased, collect *Form 120 – Initial Notification of Death* and *Form 33 – Medical History Update* and, if appropriate, *Form 33D – Medical History Update (Detail).*

For additional information about proxy follow-up of OS participants, *see Section 16.3 – CC Data Collection for Non-Respondents to OS Mailings.*

16.6.3 Using Proxies to Obtain Medical Records

The role of the proxy in obtaining medical records is determined by local state and institutional laws and policies. The designated proxy, especially if she/he is a family member or has medical power of attorney, may be able to sign medical releases. CCs will need to contact their local IRB and medical institutions for information and policies on this issue.

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16.7 Follow-up of Participants with Less than Full Participation Status (Required)

For women with less than full participation status, the general principle is to continue the WHI tasks (see in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*) for the woman's component (HRT, DM, CaD, OS) to the extent possible given her participation status. Specific situations are given below, as examples.

16.7.1 Participants Who Have Stopped Intervention (CT) (Required)

"Stop HRT", "Stop DM," or "Stop CaD" status: For a CT participant who has stopped her intervention(s), continue with the twice yearly CC visit tasks (see *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*, and *Sections 16.2 - Semi-Annual Contact (CT only) (Required) and 16.3 - Annual (CT) and Third-Year (OS) Visit (Required)*). Specifically, continue with all forms and procedures on the visit plan, including safety procedures and forms (excluding *Form 950 - Medication Adherence*), if the participant is willing. If there are no issues that contraindicate resuming the intervention, inquire about the participant's willingness to start the intervention again (see *Section 17.4.5 - Reactivation of Participants with Changes in Participation Status*).

Additional considerations for participants who have stopped HRT or CaD include:

- Collect study pill bottles and enter adherence information into WHILMA when the participant stops her study pills.
- Complete *Form 10 - HRT Management and Safety Interview* at the next **two** routinely scheduled visits or contacts after stopping HRT intervention.
- Complete *Form 17 – CaD Management and Safety Interview* at the next routinely scheduled visit or contact after stopping CaD intervention.

16.7.2 Participants On Partial Follow-up

The suggested procedures for partial or customized follow-up data collection are:

- When forms are mailed, include a cover letter, pencil, and return stamped envelope.
- Follow-up with a reminder phone call.
- Complete forms by telephone.

Certain minimum procedures are required for the HRT and/or CaD participant to continue on intervention even if she elects partial follow-up (refer to *Section 16.4.2 - Minimum Procedures Required for a CT Participant to Remain on Intervention*). If appropriate, as part of a phone call or cover letter, inquire if the participant is interested in resuming intervention (see *Section 17.4.5 - Reactivation of Participants with Changes in Participation Status*) or resuming CC visits.

16.7.2.1 CT Participants (Required)

For a CT participant who refuses further CC visits but will allow phone and/or mail contact, continue with twice-yearly completion of all forms that are scheduled in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection* that can be completed by phone or mail.

The forms to be completed by phone or mail (if scheduled) are:

- *Form 10 - HRT Management and Safety Interview (HRT)*: phone only.
- *Form 17 - CaD Management and Safety Interview (CaD):* phone only.
- *WHIP 0441 - Personal Information Update*: phone or mail.

- *Form 33 - Medical History Update*: phone or mail.
- *Form 60 - FFQ (DM):* mail only.
- *Form 950 - Medication Adherence*: phone estimate of study pill count and then have the participant mail study pills in.

16.7.2.2 OS Participants (Required)

Observational Study women who refuse the Year 3 CC visit should complete *Form 33 - Medical History Update* and *WHIP 0441 - Personal Information Update* by phone.

Annual follow-up mailings will not be sent to OS participants who have requested "partial follow-up with no mail". For a woman in the OS who refuses mail contact but allows phone contact, complete the phone follow-up at years 1, 3 (unless she attends the CC visit), 5, 7, and 9 post-randomization. See *Section 16.5 - OS Annual Mail Contact and Follow-Up of Non-Responders* for suggested procedures.

16.7.3 Participants Who Are Lost-to-Follow-Up

Continue to search periodically for participants who are lost to follow-up. For procedures, see *Section 17.3 - Locating "Hard to Find" Participants.* Observational Study mailings are not sent to women who are "lost-to-follow-up" or who have an undeliverable address.

16.7.4 Participants on No Follow-Up

A letter or postcard (see model in *Figure 16.7 - Postcard for Participants on No Follow-Up*) should be sent or phone call made yearly to inquire if the participant would be willing to "rejoin" the WHI or if she would, at a minimum, complete *Form 33 - Medical History Update*. See *Section 17.4.5 - Reactivation of Participants with Changes in Participation Status.*

16.7.5 Participants on Absolutely No Follow-Up (Required)

No mail or phone contacts or attempts to collect data should be made with participants who have requested absolutely no follow-up.

16.8 Non-Routine Contacts

Non-routine contacts may occur for any WHI participants. These contacts give the CC the opportunity to continue efforts to build rapport and promote retention. Reasons why a participant may contact the CC non-routinely in person or by phone are detailed below along with brief information and references on how to manage such contacts:

- **Questions about the WHI study (perhaps in response to a recent news item):** The nature of the participant questions will determine the approach you take. Refer the participant to a CC staff person or investigator who has understanding of the issues involved with the news item or specific skill in responding to concerned participants (see *Section 17 - Retention*).

- **Questions or concerns about symptoms:** Symptom questions, in most instances, should be referred to the CP. Refer to *Section 5 - HRT and Section 7 - CaD* for detailed information on management of symptoms associated with the HRT and/or CaD interventions. Make reference to the *HRT Handbook* and/or *CaD Handbook*, as appropriate, or offer to send the participant another copy.

- **Questions about diagnostic reports (e.g., endometrial aspiration, mammogram):** Questions about specific findings should be referred to the CP. If the participant is requesting copies of the reports for herself or her health care provider, follow your CC's procedures for making such copies available.

- **Schedule or reschedule CC visits:** Schedule or reschedule routine CC visits as close as possible to the target window for that visit. Discuss with the participant the importance of keeping her visit appointments and thank her for her efforts to reschedule. Refer the participant to the appropriate CC staff person to initiate activities for retention challenges if she has rescheduled visits several times in the past (or has rescheduled the current visit several times) (see *Section 17.2 - Clinical Center Activities for Retention Challenges)*.

- **Report an outcome or other major event:** If the participant reports an outcome at a **non-routine** contact, remind her to record this information on her next routine medical history update. Interim reports of outcomes will not be processed. Follow local procedures for informing the CP of outcomes that may necessitate stopping study pills or reporting serious adverse experiences (see *Vol. 2 – Procedures, Section 5 – HRT* and *Section 7 – CaD*). CCs may also want to develop procedures for informing appropriate staff (e.g., the participant's Group Nutritionist) so that participant rapport and retention can be supported.

- **Provide new address or phone information:** Update the most recent *WHIP 0441 - Personal Information Update* report in the participant's file and provide this information to the appropriate data entry staff person to update the information in WHILMA.

Each of these non-routine contacts should be documented in contact notes contained in the participant's file along with any referrals or actions taken.

Figure 16.1

Cover Letter for OS Contact 1 (Year 1)

[PRINTED ON WOMEN'S HEALTH INITIATIVE LOGO LETTERHEAD]

Thank you for being part of the Observational Study of the Women's Health Initiative! The purpose of the Observational Study is to learn more about women's health and about the causes of disease in women. As a participant in the Observational Study you are asked to fill out forms each year so that we can update information on your health. This information will be used to learn more about the relation between lifestyle habits and health, and may also be used in related research by other scientists interested in women's health. We want the results of this study to represent **all** women, so your continued participation is very important to us.

Please complete the enclosed two forms. *Form 33 - Medical History Update* asks about your recent medical history and *Form 48 - Observational Study Follow-up* asks about your health habits and medication use. When you have completed the forms, please return them right away in the postage-paid envelope.

If you have any questions about the forms or need any help in filling them out, please call your Clinical Center at the telephone number listed on the attached page. For the next several years, we will need to know where to send your newsletter and health forms, so please call us if you move to a different address.

All information you provide will be kept confidential and your name will not be linked with data given to anyone other than the researchers in this study. Participation in this study is voluntary and you may refuse to answer any questions on the forms. However, it is very important that we have complete follow-up information on all participants to make sure that the results of the WHI are accurate and scientific.

We appreciate your continued participation in the Women's Health Initiative. This is an important study that may help us to improve the health of women for generations to come. Every woman counts, so please keep in touch.

Figure 16.2

Follow-up Postcard for OS Contact 2

[Discontinued in May 1997]

A few weeks ago a packet of forms was mailed to you from the Women's Health Initiative. If you have already completed and returned them, thank you very much.

If you haven't returned the forms, could you return them right away? It is very important that we have complete information on all participants so that the results of the Women's Health Initiative will represent the health of **all** women.

If your address on this postcard is not right, please call your Women's Health Initiative Clinical Center. If we don't receive your completed forms in the next several weeks, we will mail you another set.

Thank you for your continued participation in the Women's Health Initiative.

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Figure 16 .3
Cover Letter for OS Contacts 3/4 (Year 1)

[PRINTED ON WOMEN'S HEALTH INITIATIVE LOGO LETTERHEAD]

A few months ago we sent you a packet health forms to complete as a participant in the Observational Study of the Women's Health Initiative. We have not yet received your completed forms. In case the forms were misplaced or not received, new forms and a postage-paid envelope are enclosed.

The purpose of the Observational Study is to learn more about women's health and the causes of disease in women. As a participant in the Observational Study, you are asked to fill out a few forms each year so that we can update information on your health. This information will be used to learn more about the relation between lifestyle habits and health, and may also be used in related research by other scientists interested in women's health. We are writing to you again because we want the results of this study to represent **all** women, so your continued participation is very important to us.

Please complete the enclosed two forms. *Form 33 - Medical History Update* asks about your recent medical history and *Form 48 - Observational Study Follow-up* asks about your health habits and medication use. When you have completed the form, please return it right away in the postage-paid envelope.

If you have any questions about the forms or need any help in filling them out, please call your Clinical Center at the telephone number listed on the attached page. For the next several years, we will need to know where to send your newsletter and health forms, so please call us if you move to a different address.

All information you provide will be kept confidential and your name will not be linked with data given to anyone other than the researchers in this study. Participation in this study is voluntary and you may refuse to answer any questions on the forms. However, it is very important that we have complete follow-up information on all participants to make sure that the results of the WHI are accurate and scientific.

We appreciate your continued participation in the Women's Health Initiative. This is an important study that may help us to improve the health of women for generations to come. Every woman counts, so please keep in touch.

You are very important to the WHI, but we haven't heard from you yet. Please respond.

Figure 16.4
Suggested Script for OS Contact 5 Telephone Contact

The caller should telephone until she/he is able to reach the woman. Actual contact is required to confirm that the CC has the right address and phone number.

"Hello Mrs./Miss/Ms._____, this is _____ from the Women's Health Initiative **(name of clinical center)** ."

"Several weeks ago a form packet was mailed to you from the Women's Health Initiative. Did you receive the packet?"

If not received:

"I'm sorry to hear that. Maybe it was sent to the wrong address. Let me check your mailing address so that we can update our files."

(Record correct address, then continue.)

"Because your participation is very important to us and we would like to include your responses in the study results, I would like to go over one of the forms with you over the telephone. Is this a good time for us to complete the form over the phone?"

If no:

"When would you like me to call back?"

(Confirm time, thank participant, terminate call, call back later to conduct interview.)

If yes:

"Great. I will read you the questions over the telephone and record your answers."

Conduct interview: complete Form 33.

"Thank you very much for spending the time to answer these questions over the telephone. We're very glad to have you as part of the Women's Health Initiative.

(Terminate call.)

If yes:

"Good. Because your participation is very important to us and we would like to include your responses in the study results, I would like to go over one of the forms with you over the telephone. Is this a good time for us to complete the form over the phone?"

Figure 16.4 (continued)

If no:

"When would you like me to call back?"

(Confirm time, thank participant, terminate call, call back later to conduct interview.)

If yes:

"Great. I'll read you the questions over the telephone and record your answers."

Conduct interview: complete Form 33.

"Thank you very much for spending the time to answer these questions over the telephone. We're very glad to have you as part of the Women's Health Initiative.

(Terminate call.)

If during a contact it is determined that the participant is deceased, is unable to communicate, or has poor cognitive functioning, end call appropriately (e.g., if she is deceased *"I am so sorry to hear that Mrs./Miss/Ms._____ has passed away. She was an important member of our study."****):***

Go to Contact 6 - Mail/phone contact to collect data from proxy.

If at any point during the contact her participation status changes (e.g., she requests no further telephone contact):

Update Form 7 - Participation Status.

Initiate Form 24 - Retention Worksheet.

Figure 16.5
Suggested Script for Proxy Telephone Contact

Ask to speak to (in order of priority for contact):

spouse or partner

nearest relative

friend

Once contact is established, start at beginning of script.

If none of the above are available, contact the woman's physician.

"Hello, this is _____ from the Women's Health Initiative **(name of clinical center)** . May I speak to ***[proxy name]?"***

If proxy is available, continue.

If proxy is not currently available:

"Can you suggest a time when I may be able to call back and speak with him [her]?"

Confirm time, thank person on phone, call back later to talk with proxy.

If identified proxy continues to be unavailable after several calls, try to contact another proxy.

If participant is deceased:

"We were very sorry to hear that Mrs./Miss/Ms._____ has passed away. As you may be aware, she was an important member of our study, the Women's Health Initiative."

(Continue below.)

If participant is unable to communicate or has poor cognitive functioning:

"We were very sorry to hear that Mrs./Miss/Ms._____ has had a recent decline in her health. As you may be aware, she is an important member of our study, the Women's Health Initiative."

(Continue.)

"Because we want the study to represent **all** women, we would still like to include her in the results. In order to do this, I would like to ask you some questions about her health during the past year. Would this be a good time for me to ask the questions?"

Figure 16.5 (continued)

If yes:

Complete Form 33 - Medical History Update.

"Thank you very much for your help in the Women's Health Initiative. The information you have provided is very important to the results of the study."

If no:

"When would you like me to call back?"

(Confirm time, call back later to conduct interview.)

If husband/partner refuses to participate, thank him/her, terminate the call, and try to contact another proxy.

In order of priority for contact:

spouse or partner

nearest relative

friend

Once contact is established with new proxy, start at beginning of script.

If none of the above are available, contact the woman's physician.

For all participants, Update Form 7 - Participation Status, if it has not already been updated (e.g., regarding the participant's death or poor cognitive functioning).

Figure 16.6
Sample Cover Letter for Proxy Contact

[PRINTED ON WOMEN'S HEALTH INITIATIVE LOGO LETTERHEAD]

(If participant is deceased:)

We were very sorry to learn of your recent loss. As you may be aware, *[participant name]* was a valued participant in the Women's Health Initiative. The purpose of this study is to learn more about women's health and about the causes of disease in women. Therefore, it is important to us to learn about *[participant name]* 's health conditions. The information collected is used to learn about the relation between lifestyle habits and health, and may also be used in related research by other scientists interested in women's health.

(If participant is unable to communicate or has poor cognitive functioning:)

We are very sorry to learn of the decline in the health of your *[wife, sister, etc.], participant name]*. As you may be aware, *[participant name]* is a valued participant in the Women's Health Initiative. The purpose of this study is to learn more about women's health and about the causes of disease in women. All participants in the study are asked to fill out a few forms about their health each year during the length of the study. The information collected is used to learn more about the relation between lifestyle habits and health, and may also be used in related research by other scientists interested in women's health.

Because we would like to keep our information current, we are writing to ask that you complete a form about *[participant name]* to the best of your ability. We want the results of this study to represent **all** women, so including information about her is very important to us.

Please complete the enclosed *Form 33 - Medical History Update*. When you have completed the form, return it right away in the postage-paid envelope.

If you have any questions about the form, or need any help in filling it out, please call

_____ at _____. The information you provide about *[participant name]* will be kept confidential and her name will not be linked with data given to anyone other than the researchers in this study. Participation in this study is voluntary and you may refuse to answer any question on the form. However, it is very important that we have complete follow-up information on all participants to make sure that the results of the WHI are accurate and scientific.

We appreciate your help in the Women's Health Initiative. This is an important study designed to examine the health of a large number of women over a long period of time. The information you provide may help us find ways to improve the health of women for generations to come. Thank you for your support.

Figure 16.7
Postcard for Participants on No Follow-Up

WOMEN'S HEALTH INITIATIVE

1. Have you had any major health problems since we last saw you?
   ☐ No ☐ Yes → Please describe:_____
   _____

2. Is this address label correct?
   ☐ Yes ☐ No → Change to:_____
   _____

3. Are you interested in rejoining the Women's Health Initiative?
   ☐ No ☐ Yes

   I have questions, please call me at:_____
   Best times to call:_____

Please call [CC phone number] or return this postcard to [CC address].

16.9 Follow-up Visits by Guest Participants

At times, it may be more convenient for a participant to have a follow-up visit conducted at a CC where she is not a participant (for example, if a participant is visiting a city where another CC is located at the time she is due for an annual visit). The following steps are needed at both the "visited CC" and the "home CC" when dealing with guest participants. Because of the added burden on the visited CC, these visits should only be done when the participant will not be returning home within a reasonable time period around her annual visit target date. However, if a guest participant "drops in" to a CC and wishes to complete a visit, the visited CC should make all efforts to accommodate her.

The visited CC should follow these steps:

1) Contact the participant's "home" CC to find out what tasks need to be collected at the visit, and to obtain the participant's WHILMA ID number.

2) Record the participant's full name and ID number on all forms.

3) If blood is collected, follow the instructions in *Volume 2, Section 11.4.1.2 - Mailing Instructions for Visiting Participants*. This section offers two options for handling blood specimens. The home and visited CCs should choose the option that is mutually agreeable to both of them. If the CCs choose the second option, the visited CC must contact McKesson to 1) give them the participant ID and the blood sample ID from the *Form 100 – Blood Collection and Processing*, and 2) let them know that the sample ID needs to be linked to the "home" CC in the McKesson database, even though the visited CC will be submitting the specimen as part of its routine blood shipment.

4) Send all forms to the home CC to be entered in WHILMA.

5) Instruct the participant to continue taking study pills from the bottle in her possession (if any). Determine whether the participant needs a new supply of pills and arrange for the home CC to mail a new supply to the participant at her temporary address, if appropriate. Instruct the participant to return her empty pill bottles and unused pills to the home CC at her next visit.

The home CC should follow these steps:

1) Dispense and mail a new supply of study pills to the participant's temporary address, if necessary.

2) When you receive the completed forms from the visited CC, create a new employee ID in WHILMA and call it "other CC". Use that employee ID number for all forms that are received from the visited CC.

16.10 Guidelines for Contacts with Participants' Survivors

These guidelines offer considerations, scripts, and activities for contacts with WHI participants' survivors (e.g., next-of-kin, spouses, or proxies) after a participant has died. These contacts may occur when you:

- try to contact the participant about routine activities (e.g., scheduling an annual visit)
- contact a participant's survivor to provide final medical history information (i.e., *Form 33/33D – Medical History Update*)—this usually occurs because CC staff have previously learned about the participant's death, either from survivors, notification by another participant, reading an obituary, or other sources (e.g., online databases, National Death Index)
- are contacted by a survivor to inform staff of the participant's death
- are contacted by a survivor in response to a routine communication (e.g., *WHI Matters* mailing)
- are contacted by a survivor in response to a written or voice mail expression of sympathy and/or request for final medical history information

16.10.1 WHI Expectations for Staff Contacts with a Participant's Survivor

Except within the scope of one's professional licensure, you are <u>not</u> expected to (nor should you) screen for the severity of a survivor's emotional response (e.g., depression, suicidal ideation) nor are you expected to treat that response. However, all staff should maintain a professional demeanor, convey understanding, and offer to end or postpone the interaction for an appropriate period of time. Refer to *Section 2.11.4.3 – Guidelines for Suicidal Ideation* for guidelines should you have concerns about a survivor's distress.

16.10.2 General Considerations for <u>All CC Staff</u>

Initial contacts with a participant's survivor. As outlined above, the initial contact with a participant's survivor may occur unexpectedly. If a CC learns of a participant's death via a written source (e.g., obituary, written notification), CC staff (e.g., Outcomes Coordinators) should exercise appropriate clinical judgment and consider waiting at least one month after the participant's death before initiating a contact for medical history information.

Generally, all CC staff who routinely make or respond to outside phone calls (e.g., receptionists) should be prepared for possible contacts with participants' survivors. The initial contact, whether initiated by a survivor or a CC staff person, at minimum, should begin with an expression of sympathy and gratitude for the participant's contribution to WHI. It may then be appropriate to refer the caller to an appropriate staff person who can begin the process of obtaining final medical history information. Even if the circumstances of the death are unusual (e.g., suicide), a general expression of sympathy is appropriate. Below is a sample script to use for these initial contacts:

Thank you so much for letting me know. I'm sorry to hear about _____ and offer my deepest sympathy. When did this happen? [Pause and document the date, as needed, for completing *Form 120 – Initial Notification of Death*.] *She was an important part of the Women's Health Initiative study over the years and we will miss her. You can be proud of the valuable contribution she has made to women's health care through her participation in this study.*

We would like to get some information to help complete her health records for the study. Is this a good time to talk with you or someone else about her health history or should I have someone call you at some other time?

Refer the caller to an appropriate staff person to begin an interview for *Form 33 – Medical History Update* (and/or *Form 33D – Medical History Update (Detail)*, as appropriate) or take down contact information and best time to call. Note that the caller may identify another person to give medical history information, ask the CC to wait for a period of time, express concern about providing such information, or refuse to provide this information. You should be prepared to respond to any of these scenarios.

Form 120 – Initial Notification of Death. Regardless of how the initial information about a participant's death is received, CC staff should initiate a *Form 120* and key-enter the available information in WHILMA so that future participant mailings will be stopped. The CC staff person who actually completes the *Form 120* may or may not be the one who had the initial contact with the survivor, based on local procedures. Depending on the circumstances of the initial notification, it may be appropriate to just enter an approximate date of death and who provided the information.

Sympathy note. Upon hearing of a participant's death, mail out a sympathy note or card to the next-of-kin or proxy. This note can contain hand-written text similar to the script above (e.g., expression of sympathy, recognition of participant's contribution to the study, setting the stage for future contact about participant's medical history). There are many good books available that offer examples of standard, but sensitive, sympathy notes to write.

Local resource list. The CC should be sure there is a short local resource list available that staff can offer to a survivor. Rather than trying to determine if a particular resource is needed or appropriate, CC staff should consider just generally offering it to each survivor (e.g., at the end of the contact—"*We have a list of resources that I can mail you.*"). The resource list should include:

- a basic counseling resource that is relatively low cost or sliding scale
- health information resources (e.g., American Heart Association, American Cancer Society)
- crisis line (contact this resource first to make sure it is appropriate)
- additional resources, such as local/regional treatment sites (e.g., emergency rooms), bereavement/counseling services provided by religious organizations or a hospice group (which often offer services even if the participant did not use the hospice organization), web sites (e.g., http://www.aarp.com/griefandloss/, see "Understanding the grieving process" below)

Review this resource list and contact the printed phone numbers at least every 6 months to confirm that the list is still current.

Understanding the grieving process. There are many excellent resources (books, articles, web sites, professionals at your institution and in the community) available for learning more about bereavement and grieving. The most important point to remember is that there is no one "normal" response to loss and a person's response may have very little to do with the current interaction. Manifestations of grieving can take many different forms based on one's previous experience with loss, relationship with the participant, personality, and current life circumstances. A normal affect, anger, crying, withdrawal, denial, and a desire to talk things through are all possible responses. You are not expected to manage these responses beyond maintaining a professional demeanor, conveying understanding, and offering to end or postpone the interaction for an appropriate period of time. Some excellent resources related to grief and bereavement may be found on the World Wide Web, including:

- http://www.aarp.com/griefandloss/: The "Grief and Loss" website for the American Association of Retired Persons. Includes information about common reactions to loss and many other practical resources.
- http://www.centerforloss.com/library/centerforloss/contents.asp: From the Center for Loss and Life Transition in Colorado. This library of brief articles covers information for surviving family and friends as well as those who would like to help or understand the grief process.

CCs may also choose to provide some in-service training in this area.

16.10.3 Considerations for Staff Who Collect Medical History Information from Survivors

As described above in "WHI Expectations for Staff Contacts with Survivors," CC staff members who are responsible for obtaining participants' final medical history (*Form 33 – Medical History Update*) are not expected to make diagnoses about or to treat survivors' emotional health. However, Outcomes Coordinators or other staff who contact survivors for medical history information should have good interactional skills and a very basic understanding of the grieving process. There may be times when you feel very vulnerable to someone else's emotions (e.g., you have just experienced a loss). At these times, it may be appropriate to refer the contact to another CC staff person. Sometimes these contacts can extend longer than expected or just be emotionally draining. If you are the most appropriate person to make the contact, be sure that the call is made when you are not rushed, in a space where you will not be interrupted, and you are prepared operationally and emotionally.

Considerations for making the contact. When you are contacting a participant's survivor to obtain a participant's final medical history information, consider:

- Delay contact for at least one month after the participant's death (use clinical judgment), but avoid contacting survivors around the participant's birthday or on the same day of the death in subsequent months).
- Consider sending out a letter letting the survivor know you will be calling about the participant (so they can gather information) and then follow-up with the actual medical history update call a week or so later.
- Convey professionalism and understanding, particularly if the survivor wishes to delay or postpone the interview or becomes emotional (in which case, you should offer to postpone the interview; see *Section 2.11.4.2. – Special Situations*).
- Initially cover the elements of the basic script above.
- Ensure that the person you are talking with is the appropriate person from whom to obtain this information (*"Are you able to provide this information or is there someone else we should talk to?"*).
- Follow the basic interview script for *Form 33* (and *Form 33D – Medical History Update (Detail)*; see *Form 33* forms instructions in *Vol. 3 – Forms)*.
- If the participant was in HRT and/or CaD, let the survivor know that we need all remaining WHI pills and bottles (including study pills remaining in pill organizers) returned to the CC. Offer to provide a mailer for this purpose.
- Make use of good interviewing skills (see *Section 2.11 – Interview Procedures*).
- If the survivor is angry, very reluctant to talk, or emotional, do not "blame" the person for his or her feelings or engage in debates about possible objections. You might say, *"It sounds like this is not the best time to talk. Thanks for your time today and I am sorry about your loss."* You will need to judge whether or not it is truly appropriate to offer to call back or whether such an offer might be met with an immediate refusal. In the latter case, instead of making the offer to call back, you might want to just end the call and postpone further contact for an appropriate amount of time. When you follow-up again, you may find some reluctant next-of-kin are now willing to talk.
- If encounters turn difficult, always keep in mind that you are doing the best you can and have all good intentions, even if sometimes you feel like you're not saying the "perfect" thing.
- Offer options for obtaining this information if there is ongoing resistance to doing the interview (e.g., mail or fax medical records or death certificate).
- If the participant is angry, reluctant or impatient about a single question or a series of related questions, cite "the office" or the "researcher." Blame the project for objectionable material, not the participant for being objectionable.

Some survivors may be willing to complete *Form 33/33D* by mail, but not over the phone or in-person. In that case, mail the *Form 33/33D* to the survivor. Follow-up for non-response to this mailing should be sensitive to the survivor's possible emotional needs to delay. If a participant's next-of-kin refuses to provide

this information or will not sign a medical release, note this information in the participant's progress notes. Your local Institutional Review Board (IRB) may have additional guidelines to consider. Refer to *Vol. 8, Section 2.2.4 – Reports of Death* for additional information on WHI procedures related to documenting and investigating a participant's death. *Vol. 2, Section 16.6 – Follow-Up by Proxy* also provides some guidelines on identifying and contacting proxies.

16.10.4 Family or Proxy Requests for Information*

Family members, friends, or designated proxies may ask for specific information about the participant who has died. Here is a possible script for responding to such requests:

We are committed to protecting our participants' confidentiality, so I hope you understand that we must follow careful guidelines and procedures before releasing information to people.

After offering this introductory explanation, provide the survivor with the specific guideline below based on the information requested.

- **Clinical trial treatment assignment:** HRT or CaD Treatment assignment may be made available to the legal next-of-kin upon written request during or after study close-out (procedures to be developed). The Dietary Modification is not a blinded trial, and treatment assignment information may be conveyed by staff who are not involved in outcomes ascertainment or adjudication.
- **WHI records**: A participant's blinded WHI records, including consent forms (not medical records obtained outside those generated by WHI) may be made available to the legal next-of-kin upon written request.
- **Results of blood analyses**: Only those analyses that were done at local laboratories (e.g., complete blood count at baseline and OS Year 3) may be made available to legal next-of-kin upon written request. Analyses done at central labs are not contained in the local databases and are logged centrally by an ID number only, so are not available to study participants or their next-of-kin.
- **Follow-up of physical exam findings (e.g., clinical breast exam, mammogram):** When participants have had abnormal or questionable measurements or exams, we often ask them to have further evaluation. Results of those follow-up exams (if performed by WHI) may be made available to the legal next-of-kin upon written request. The survivor may also request the name of the health care provider or clinic that performed outside exams.
- **Study information and findings:** Findings from the WHI are being published on an ongoing basis. Final results of the main study questions will be published after the study has closed, around 2007. The National Institutes of Health maintains a web page of study information and updates a list of selected publications at http://www.nhlbi.nih.gov/whi/index.html.

*****Participant rights (even after death) dictate that information or records about her death may only be released to the legal next-of-kin. Although state laws may vary slightly, in general, legal next-of-kin is defined as:

- husband, if the participant was married
- children, if the participant was single and has children (unless the children are all minors)
- mother and father, if the participant was single (if mother and father are deceased, then her sisters and brothers are considered legal next of kin)
- other (if none of the above apply)

16.11 Guidelines for Participants With Cognitive Decline

These guidelines offer considerations and suggested strategies, not requirements, for working with WHI participants who have experienced some level of cognitive decline. These guidelines are meant to assist, not constrain, CC staff that must balance WHI procedural requirements with participants' capabilities and needs on a case-by-case basis. The ultimate purpose of these guidelines is to support the appropriate ongoing participation of WHI participants.

16.11.1 Identifying Potential Cognitive Decline in WHI Participants

Steady, progressive cognitive decline resulting in significant impairment is not a normal aspect of aging. Health and social problems among older persons are dynamic and may vary over time. Thus, cognitive functioning can vary over time. WHI participants will experience transient changes in their memory, thinking, and behavior depending on current life events and daily stresses, acute illnesses, or specific medications. Most of the time, these changes are troublesome but not disabling. Rarely, WHI participants will have progressive or profound changes in their cognitive status.

Because cognitive deficiencies can vary from minor to severe, your response to them can vary from minimal to substantial. Your response to cognitive decline should be based on a consideration of its severity and significance with respect to functioning. A thorough assessment of cognitive function is beyond the scope of WHI (though is included for WHIMS or WHISCA participants). However, a thoughtful approach to cognitive problems can help staff reduce barriers to WHI participation and identify care participants may need.

Procedures and tools for making an accurate evaluation of a participant's cognitive status and capabilities are complex and beyond the scope of these guidelines. Likewise, CC staff is not expected to formally assess a participant's cognitive status, except for the purpose of collecting data on current WHI forms (i.e., *Form 39 - Cognitive Assessment*). Responses to *Form 39* or other assessment tools are not necessarily an indication of the participant's competency to continue her participation in WHI, nor should WHI be providing primary health care or giving clinical advice based on such information.

CC staff will become aware of a participant's potential cognitive decline in many ways:

- while completing or reviewing *Form 39 - Cognitive Assessment* with an HRT participant, if she has difficulty with answering interview items
- by testing the subsample of participants who are enrolled in WHIMS or WHISCA
- while carrying out WHI tasks and procedures, if the participant seems confused or does not carry out the procedures (e.g., study pill taking) as appropriate
- based on information in medical records or health care provider reports provided to CC clinic staff
- based on information provided by the participant, a family member, or friend about a participant's cognitive changes or their consequences in her day-to-day life

CC staff is encouraged to discuss her/his concerns about a participant's cognitive decline with other appropriate CC staff and investigators to determine if additional information or specific accommodations should be considered.

16.11.2 Addressing Cognitive Decline Concerns

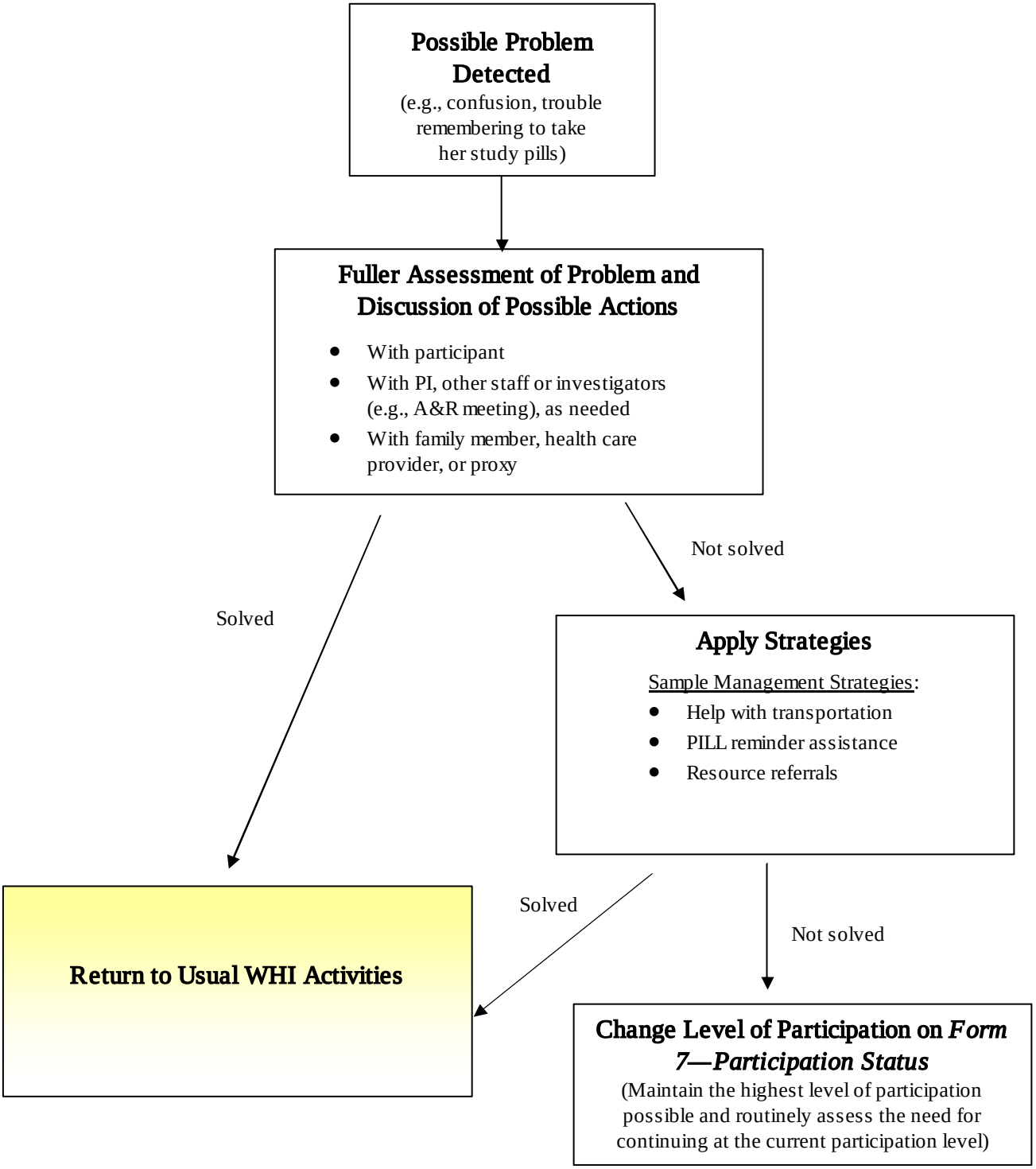
When addressing cognitive decline concerns, it is important to be comfortable with and have some skill in carrying out interactions with such participants. Matters will not be made worse by assessing cognitive function with participants, and it may help. CC staff without comfort or skill in this area should refer these participants to other appropriate staff or investigators. It is preferable, however, that CC staff proceeds with a thoughtful assessment and discussion with the participant.

The primary considerations when ***potential*** cognitive decline is identified include:

- the participant's safety while carrying out WHI activities
- the participant's ability to continue to provide appropriate data on WHI forms

The appropriate steps for addressing cognitive decline concerns are described below in *Figure 1*6.8 - *Algorithm for Addressing Cognitive Decline Issues*.

Figure 16.8 Algorithm for Addressing Cognitive Decline Concerns



16.11.2.1 Assess Specific Concerns

- With the participant (e.g., *Have you noticed any changes in your memory or thinking lately?*)

  In almost all circumstances, it is appropriate for CC staff to be straightforward with participants and directly confront the issue when it is detected (e.g., *At times today, you seem a little confused or forgetful* **or** *Is it getting harder to remember to take your study pills?)*. If the participant identifies issues or circumstances that readily explain the confusion, a notation in her chart may be the only action warranted at this point. If the participant describes (or you note): 1) progressive and significant confusion or memory problems; 2) contacts with health care providers to evaluate her cognitive decline; or 3) tangential or irrelevant responses to your questions, additional steps may be appropriate.

- With your PI and other appropriate WHI staff or investigators

  A group discussion about the participant's situation (for example, at an adherence and retention meeting) can support a full consideration of both the issues and appropriate actions (see "Strategies" below) relevant to her WHI participation. For all participants, the discussion should also include plans for following up on the situation at a future meeting. For participants who are taking HRT or CaD study pills, this group discussion should include a careful consideration of the participant's ability to continue to safely follow the study pill regimen (alone or with assistance), monitor her own health and potential side effects, and complete safety tasks required for continuing on study pills. There may be times when a participant is in imminent danger. For example, immediate action may be warranted if study tests and procedures indicate a WHI alert (see *Vol. 1, Section 1 - Study Protocol and Procedures*), gross misuse of study medication is evident, or a report of domestic abuse is received. For DM Dietary Change participants, the group discussion might include the participant's expressed concerns about driving to the CC for group sessions, how the participant interacts in the group sessions, and how she completes self-monitoring tools and worksheets. Ultimately, the participants' safety and well being supercedes the need to keep people on their assigned regimens.

- With a family member, health care provider, or proxy

  Determine if they are aware of the participant's potential cognitive decline and what, if anything has been done to address this issue.

  It is important to obtain the participant's permission to make such a contact. (e.g., *I'm just a little concerned. Would it be okay if I talk with your [*family member, health care provider, or proxy*] to find out more about this?*). Document this discussion in the participant's chart. The person you contact may be knowledgeable about the participant's changes, aware of her participation in WHI, and able to support or suggest accommodations for her ongoing participation.

16.11.2.2 Carrying out Action Items

Carry out action items based on our discussion of this participant's situation.

- You may decide to continue her participation as before or implement one of the "Strategies" described below.

16.11.2.3 Changing Level of Participation

If concerns continue despite earlier actions, you may need to change her level of participation in WHI.

- If the participant's cognitive decline in WHI continues (e.g., a "temporary" cognitive decline does not resolve, the participant continues to be confused when responding to questions, study procedures or safety measures are not carried out appropriately), a change in participation status may be warranted. Appropriate changes may include stopping intervention, proxy follow-up, or other levels of participation. Discuss the ongoing situation with appropriate investigators and staff (as above) before completing *Form*

7 – Participation Status. Refer to *Section 17 – Retention* for information on addressing retention challenges and making changes in WHI participation levels.

16.11.3 Strategies for Managing a Participant's Cognitive Decline

There are many strategies to consider for managing cognitive decline concerns, depending on the participant's particular situation. These may include:

- Nurture close relationships with the participants, their family members, and their proxies throughout the study, even when no problems exist.
- Provide accommodations (e.g., transportation to the clinic if driving in traffic is upsetting and confusing to her, assistance with remembering to take study pills as in *Section 17 - Retention*) that will help her continue to fully participate in the study. It is important that staff directly confront and address with the participant her need for such accommodations (e.g., *I'm concerned that it may be dangerous for you to drive in heavy traffic.*).
- Provide the participant, her family member, or proxy with a referral to an outside provider, appropriate clinic, or other resource, if they want one. Most CCs already have local resource lists available.
- Actively involve a proxy or caregiver in helping the participant complete study procedures and forms. For more information about proxy procedures, refer to *Vol. 2, Section 16.6 - Follow-up by Proxy*. If the participant's routine procedures include pill taking in the HRT or CaD components, you should make a careful determination of the person's proximity to, ongoing relationship with, and willingness to safely support the ongoing activities of the participant. Note that *Form 60 - Food Frequency Questionnaire* is not to be completed by proxy.
- For participants who have documented or strongly-suspected cognitive decline, CCs will need to ask their local Institutional Review Boards (IRBs) about any requirements for re-consenting participants or reporting this information to an outside provider.
- Document ongoing assessment of the participant's cognitive status, as needed. Such informal assessments may be appropriate over the remainder of the study.

16.12 Procedures and Guidelines for HT/DM/CaD Pre-closeout Contacts

16.12.1 Introduction

The Steering Committee approved the HT Committee's recommendation to develop a pre-closeout plan focused on supporting the HT participant's transition to a personal health care provider at closeout. This document provides required procedures and guidelines that address this transition and support participant adherence and retention through closeout. These procedures are focused on pre-closeout activities for HT and CaD participants. Activities for DM Intervention participants are taking place during regular DM sessions.

Below is a brief overview of the pre-closeout activities:

- Requirements
  - Conduct a Transition Discussion (see below) with HT participants who are still taking study pills at either a visit or phone contact at least 6 months before the closeout contact (for safety reasons).
  - The "spirit" of all pre-closeout contacts should be congratulatory of the participants' achievements combined with a strong emphasis on preserving their commitment to the WHI and improving or maintaining their adherence until the very end of the study.[1] [*Congratulations… Making history… One more year… Still have unanswered questions… We need you!*]
- Recommendations:
  - Conduct Transition Discussion with all other HT and CaD participants.
  - Carry out Adherence and Retention Strategies (see below) with all HT and CaD participants.
- Materials
  - *Potential Questions and Answers* (for use in Transition Discussion and Adherence and Retention Strategies). This Q&A provides CC staff with appropriate responses to participant questions that may come up during this pre-closeout phase. Do not give this *Q&A* to participants; it is intended as a resource for CC staff only.
  - *Dear Dr. Doctor Letter and Information Sheet* (for use in Transition Discussion with HT participants)
  - *WHI Timeline/Milestones Charts* (for use with Adherence and Retention Strategies)

16.12.2 Transition Discussion

Identify those participants without a healthcare provider and discuss with them alternative strategies for healthcare follow up. If the participant has medical insurance, encourage her to find a provider. Use the *Potential Questions and Answers* as a resource during this discussion. If the participant does not have medical insurance, provide contact information for local healthcare agencies that serve uninsured and low

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[1] Critiques of the WHI E+P findings have often focused on E+P adherence (a summary measure that incorporates stop-intervention rates). Despite the fact that sensitivity analyses of the E+P data have confirmed our primary findings, we need to maintain the integrity of the WHI and prevent similar criticism of the E-Alone trial. Currently, only 53.2% of E- Alone participants are at 80% or more adherence, and the stop intervention rate for E -Alone is up to 40%. Therefore, we encourage you to incorporate these adherence and retention strategies into your pre-closeout activities. Don't let this potential opportunity slip by! We can still help some women realize that it is crucial to stay on study pills and to keep taking them regularly during these last visits.

income women. Steps taken to implement this part of the plan may vary by CC, depending on local resources. However, all CCs should:

- Identify participants without plans for healthcare after WHI.
- Create or update your list of local healthcare resources.
- Establish a link with social services to help uninsured participants seek care.

It is strongly recommended that you give HT participants the attached *Dear Dr. Letter and Information Sheet* to take to their healthcare provider (or offer to mail it directly to the provider, if the participant prefers). This material informs HT participants' providers about closeout, mentions the Follow-Up Study, and describes the provider's important role in partnership with the WHI.

Collaboration and partnership with local providers will be critical for supporting activities for the planned HT Follow-up Study. You could say, *"Healthcare providers across the country are watching the WHI very closely; they know that you're making medical history. We hope you'll give this information to your healthcare provider. It describes the important role that participants' providers have in WHI, particularly now that we're in our last critical year before closeout. If you'd like, we can mail this directly to your provider for you."*

16.12.3 Adherence and Retention Strategies

The second message celebrates the substantial contributions the participant has made to WHI in the past and emphasizes how important it is for her to continue in the trial on intervention, if possible, until the study is completed. The pre-closeout contacts offer excellent opportunities for reinforcing with participants the importance of their continued adherence and retention through to the Closeout Visit. Although this discussion may take place over the phone, the best strategy for promoting adherence and retention during pre-closeout contacts is to have an in-person discussion and to provide participants with "take-home" materials that illustrate and elaborate on the key messages.

In addition to the *Timeline/Milestones Charts* (see below for information and recommended talking points), additional materials you may want to have on-hand during this discussion include earlier updates and handouts ("DVT," "HERS," "2000 HRT Update," "2001 HRT Update," "Update on E+P Findings," "Osteoporosis Update", "Your Important Role …" —all available in the Public Folders), particularly those that correspond to the milestones. These handouts may be provided to participants or included in a notebook of relevant materials to have on-hand at the CC. The A&R Working Group is developing other materials suitable for including in a CC notebook; specifically, color PDF files of magazine covers and news articles related to the release of the E+P findings. CCs may also wish to enlarge the "WHI Timeline" or other charts to post in the CC.

Timeline/Milestones Charts

CCs are encouraged to provide HT and CaD participants with the *Timeline/Milestones Charts*. The "WHI Timeline," "HT Milestones," "CaD Milestones," and "Personal Milestones" (for participants to fill in their own milestones) can be used as visual aids when discussing the key adherence and retention talking points. These charts can be used to illustrate the history of WHI, the extended commitment the participant has made to the study, and the fact that we still have a few "milestones" to achieve.

"WHI Timeline" (with special text for DM participants)

- *This "WHI Timeline" shows the long and memorable history of WHI, from 1991—when the National Institutes of Health first began the project, to 1993—when recruitment started up, to 1998 when we last randomized participants into the Diet and Hormone Programs.* [Point to appropriate bubbles.]
- *You joined the study about here.* [Point to appropriate year.] *And we're now about here on the timeline.* [Point to appropriate date.] *You've been a very important participant in this timeline!*

- **For DM participants:** *Your role in the Dietary Study is very important. This is true for Comparison and Dietary Change participants. We need your continued help until the end of the study to find out if a low-fat dietary pattern that includes lots of fruits, vegetables, and grains lowers the risk of breast cancer, colorectal cancer and heart disease in postmenopausal women. The Hormone Program has shown how much WHI can contribute to the world's knowledge of women's health. Soon we will have the dietary results.*
- *A lot has happened, and there are still some exciting events coming up!* [Closeout bubble.] *During this critical time, we hope you know how important it is to keep up your WHI contacts, and provide us with health information. It's also important for as many participants as possible to continue to take study pills regularly.*
- *We're certainly looking forward to sharing these future events—and the final WHI results—with you!* [Last bubble.]
- *What are your thoughts when you look at this timeline?* [Give the participant time to respond and then show her the "Milestones" chart(s).]

"HT Milestones"

- *This "Hormone Trials Timeline" chart shows the history of the study. You probably remember a lot of these milestones.*
- *We've been giving you pretty regular updates on the Hormone Trials, starting even before recruitment ended.* [End-of-recruitment bubble and several update bubbles.]
- *And then here's the BIG news that really hit the headlines!* ["WHI in the News" bubble.]
- *You can see that we're now heading into a critical time for WHI—we call it "closeout."* [Closeout bubble.] *We'll be scheduling closeout visits with all of our Hormone Trials participants during this time. At that closeout visit we'll collect some very important final information, we'll tell you more about your role in the Hormone Trials* [for E-Alone participants, you might mention that we'll be letting them know whether they were assigned to active or placebo pills], *and we'll let you know about future follow-up for Hormone Trials participants.*
- *No matter which part of the Hormone Trials a woman has been in or whether she was assigned to take active or placebo pills, participants like you are making medical history.*
- *This has really been a long commitment on your part, and there are important milestones to come.*
- *Just as our milestones have been and continue to be a part of your life, you are a part of ours.* [Hand participant the corresponding "Personal Milestones" chart]

"CaD Milestones"

- *This "Calcium and Vitamin D Timeline" chart shows the history of the study. You probably remember some of these milestones.*
- *Even before the last participant was randomized to the study* [point to the appropriate bubble], *we were working on ways to help participants "hang in there" with taking pills* [point to the appropriate bubbles as you go along]—*we started having taste-tests so that women had a chance to try out study pills before they joined. And then we developed swallowable pills for those who wanted something different. Can you remind me, did you try both types?* [Give participant time to respond.]
- *You can see that we're now moving into a critical, "closeout" phase for WHI.* [Closeout bubble] *We'll be scheduling closeout visits with all CaD participants during this time. At that closeout visit we'll collect some very important final information, and we'll tell you more about your role in the Calcium and Vitamin D trial, including whether you were assigned to active or placebo pills.*

- *No matter which program women joined or whether they were assigned to take active or placebo pills, all WHI participants—like you—are making medical history.*
- *This has really been a long commitment on your par and there are important milestones to come.*
- *Just as our milestones have been and continue to be a part of your life, you are a part of ours.* [Hand participant the corresponding "Personal Milestones" chart]

"Personal Milestones" (HT or CaD)

- *We thought you might want to note your own milestones—things that have happened in your life while you have been a part of ours—things that have been important to you and your friends and family—achievements, new arrivals, local or national news events.*
- *I hope you'll write in the important events in your life. Are there are couple of milestones that occur to you right now?* [give the participant time to respond and then point to the last bubble] *But don't forget to leave that last "bubble" empty!*
- *We have some important milestones to come! We can't wait to hear about them, right?*

16.12.4 DM Adherence Motivational Postcard (for DM-I only)

The purpose of the *Dietary Adherence Motivational Postcard* is to support DM-I dietary adherence after the end of the Dietary Change Group sessions and until the close-out visit, for participants whose close-out visit is 3 or more months after their last Dietary Change session (10SU). The postcard provides a brief reminder of the WHI Dietary Study research question and asks the participant to continue to follow the WHI low-fat eating pattern through her close-out visit. The postcard also thanks the participant for her important role in the WHI Dietary Study.

The *DM Adherence Motivational Postcard* was shipped to the Clinical Centers in August. It is printed as a 2-sided card, folded in half, so that CCs can apply the participant address label and CC return address. (See *Figure 16.9* below.)

CCs are strongly encouraged to mail, or otherwise deliver, the postcard to DM-I participants whose close-out visit is 3 or more months after their last Dietary Change session (10SU). CCs may use the WHILMA Custom Data Extract System (CDE) to identify these participants and generate mailing labels. Refer to the WHILMA Upgrade Notes for the DM Adherence Postcard (Outlook Public Folders/All Public Folders/WHILMA Resources) for information about using the CDE to manage delivery of the *Dietary Adherence Motivational Postcard*.

Figure 16.9 – Dietary Adherence Motivational Postcard

Your Important Role in the WHI Dietary Study!

Even though your Dietary Change sessions have ended, we still need your help to complete the WHI puzzle and find the answer to the question we have been studying for many years:

Will an eating pattern low in fat and high in fruits, vegetables, and grains reduce the risk of breast cancer, colorectal cancer, and heart disease in postmenopausal women?

Please continue to follow the WHI low-fat eating pattern through your close-out visit.

Thank you for helping to complete the WHI puzzle!

16.13 WHI Close-out

16.13.1 CT Close-out

The CT close-out period begins on October 1, 2004 and ends on March 31, 2005. The CT Close-out visit is conducted for all CT participants, except those with a follow-up status of "no follow-up", "absolutely no contact", or deceased.

The purpose of the close-out visit is to:

- Complete collection of primary outcome data.
- Collect required study forms.
- Collect study pills.
- Collect adherence data from CaD participants.
- Collect adherence data from HT participants (if there are remaining study pills).
- Provide CaD participants with their treatment assignment.
- Recognize the participant's contributions to WHI.
- Present participants with the packet of close-out materials.
- Provide information and invite participation in the WHI Extension Study.
- Obtain signed consent from those willing to participate in the WHI Extension Study.
- Provide information and confirm participant's willingness to have her blood samples shared with non-WHI scientists at for-profit and non-profit organizations (Supplemental Consent).
- Obtain signed Supplemental Consent.

The close-out visit is important for celebrating the participant's participation in the study, encouraging the participant to join the WHI Extension Study, and to sign the Supplemental Consent. There are required tasks that need to be completed at the close-out visit; however, it is up to the CCs to conduct the visit based on available facilities and staffing. The close-out visit may be conducted as an individual visit, in a group setting, or as a combination of the two (for example, an initial group meeting with a limited number of participants and then meeting individually to further discuss and answer personal questions about the Extension Study Consent and Supplemental Consent).

16.13.1.1 Close-out Mailing Packet

One month to two weeks before the visit, mail the close-out mailing packet to the participants via first-class mail. Refer to *Table 16.4 – CT Close-out Mailing Packet Materials*, for materials to include in the close-out mailing packet.

An additional phone call reminder about the scheduled close-out visit may be made one to three days before the scheduled close-out visit.

16.13.1.2 Assemble Close-out Visit Materials Before the Close-out Visit

Print a follow-up visit information report, *WHIP0148*, for each participant. This report lists all the required WHI tasks to be performed at the close-out visit. Also print a copy of the current Personal Information Update.

Before the visit, assemble WHI folders with the materials that are included in the thank-you packet. Refer to *Table 16.5 – CT Thank You Packet Materials*, for a list of the materials to be included in the thank-you packet. To preserve blinding, the staff person who prepares the thank you packet for the participant and who may have access to the *WHIP9758 – CaD Treatment Assignment* should not be the same person who reviews and/or administers the *Form 33 – Medical History Update* to the participant at the close-out visit.

16.13.1.3 Conducting the Close-out Visit

During the close-out period, CCs are not required to collect tasks missed during contacts that were conducted before the close-out window (i.e., before Sept. 31, 2004), but may do so at the CC's discretion if staffing and time permit. Note: do not collecte a missed ECG and transmit it to Epicare after Sept. 31, 2004.

If participants cannot come to the close-out visit or complete all the close-out visit tasks, the priority of tasks to complete are listed below in the order of their priority and the order they should be done:

a) Collect the *Form 33 – Medical History Update* before providing CaD participants with their treatment assignment.
b) Collect *Form 33D – Medical History Update (Detail)* as needed.
c) Collect the Release of Information.
d) Provide CaD participants with their treatment assignment letter.
e) Date the *Form 28 – Treatment Assignment – CaD* with the date the participant is unblinded.
f) Obtain the WHI Extension Study Consent.
g) Obtain the Supplemental Consent.
h) Complete all other close-out tasks.

16.13.1.4 Close-out Visit Procedures

A suggested scenario for the close-out visit is described below. Each CC can organize the flow of the close-out visit to fit its needs as long as the visit includes the following activities.

a. Reception

When the participant arrives for her close-out visit, have her check in with the receptionist. The receptionist should:

- Warmly greet the participant by name and welcome her to her close-out visit.
- Ask the participant if she has brought her completed forms and study pill bottles (empty or not) and pill organizers as appropriate. Collect and attach the returned forms to the top of her participant file. If she has not remembered to bring the forms, provide her with a replacement set and ask her to complete them while she is waiting.
- State the approximate time needed to complete the visit and explain the visit flow.
- Indicate a comfortable place in the reception area where the participant may wait.
- Notify the clinic staff that the participant is waiting.
- Try to limit participant's wait to no more than 10 minutes before she is seen by an interviewer.

b. Questionnaire Review

Review the returned self-administered questionnaires. Identify missing pages and remind the participant to complete them. Ensure a participant barcode label is on the front page of each completed form in the designated place.

There is no close-out contact flag in WHILMA for forms that are collected at closeout. The close-out contact is identified by the *Form 33* that is collected during the close-out period October 1, 2004 through March 31, 2005. This means that if a *Form 33* is completed by the participant before her close-out visit, the *Form 33* must be reviewed with the participant and the "Date Form Finished" question at the end of the form updated with the date of the actual close-out contact. There is no need to update the contact date (the "date received"); the finished date will be used to determine whether the data was collected within the close-out period.

- *Form 33 – Medical History Update.* If the participant indicates she has had any events or conditions on *Form 33 – Medical History Update* that necessitate more detailed information for an outcomes investigation, ask her to complete *Form 33D – Medical History Update (Detail)* (see *Form 33* instructions for the algorithm that triggers a *Form 33D* and *Vol. 8 – Outcomes, Section 2 – Ascertainment*).

- *Form 37 – Thoughts and Feelings, Ver. 6*.
- *Personal Information Update*.
- *Form 55 – Estrogen-Alone Survey, Ver. 2* (only E-Alone participants who were taking study pills at the time the intervention stopped in March 2004).

c. Release of Information

Ask the participant to sign several new copies (2-3) of your CC's *Release of Information*. Explain to the participant that these new forms will replace the last ones she signed.

d. Required Forms to Complete at the Visit

- Complete *Form 85 – Mammogram* (for E-Alone and E+P participants who had their last annual visit between October 1, 2003 and March 2004).
- Administer *Form 10 – HRT Management and Safety Interview* (for E-Alone participants requiring their second *Form 10* since stopping intervention).
- Administer *Form 17 – CaD Management and Safety Interview* (CaD).

Note: *Form 10A* and *17A* may be used throughout the close-out period even though historically, *Form 10A* and *17A* were only used for semi-annual contacts for participants with good adherence. Questions 14–16 (*Form 10/10A*) and 10-16 (*Form 17/17A*) do not need to be answered if the participant stopped intervention before the close-out visit.

e. Adherence to CaD Study Pills – *Task 951* (also for HT if not already collected)

Collect the participant's study pill bottles and pill organizers. Assess the participant's adherence to taking the study pills (this may be an actual or estimated adherence collection). Update any estimated adherence collections with actual adherence (weight).

f. CaD Treatment Assignment

- Complete *Form 28 – Treatment Assignment – CaD*. Complete and date this form on the day the participant is provided her treatment assignment.
- Perform the CaD Unblinding task in WHILMA and print two copies of the report.
- Provide the participant with a copy of *WHIP9785 – CaD Treatment Assignment* and place the second copy in her chart.

g. Thank You Packet

Give the participant the prepared close-out thank-you packet and thank her for her participation. Refer to *Table 16.5 – CT Thank You Packet Materials* for materials to be included in the close-out packet. The Dietary Study materials to be included in the CT thank you packet are described below

- **WHI Dietary Study Summary (for DM-I and DM-C)**

The *WHI Dietary Study Summary* is designed to a) help Dietary Change participants make choices by seeing the similarities and differences between the goals of the WHI Dietary Study and National Dietary Guidelines for the public and b) to provide Comparison participants a brief orientation to the WHI eating pattern without implying WHI recommendations or reviewing the low-fat dietary pattern in any detail.

Talking Points for Staff:

The WHI Dietary Study Summary provides a snapshot of what the WHI low-fat eating pattern looked like. The first page of the handout compares the goals of the WHI Dietary Study to National Dietary Guidelines for the Public. The second page includes two sample menus that provide a few examples of food choices that women in the Dietary Change group made to eat low-fat. This handout does not provide recommendations about what to eat.

For information about managing participant questions about the Dietary Study materials, refer to *Troubleshooting Participant Questions about the Dietary Study Materials* below.

- **WHI Dietary Study Frequently Asked Questions (for DM-I and DM-C)**

The *WHI Dietary Study Frequently Asked Questions* is designed to address DM participant questions about a) the WHI low-fat eating pattern and b) how to proceed until DM study results are known.

Talking Points for Staff:

We recognize that you may have questions about the WHI Dietary Study. The WHI Dietary Study results will be available in early 2006. In the meantime, these "WHI Dietary Study Frequently Asked Questions" provide answers to some frequently asked questions. The first page gives information about the WHI Dietary Study design. On the second page, you'll find information about when the Dietary Study results will be available. The last page gives a reminder to see your personal health care providers (including a registered dietitian) when seeking dietary advice. If you're interested, the last page also describes where to find more information about nutrition.

For information about managing participant questions about the Dietary Study materials, refer to *Troubleshooting Participant Questions about the Dietary Study Materials* below.

- **Troubleshooting Participant Questions about the Dietary Study Materials.**

If a participant asks about when Dietary Study results will be available:

Point the participant to the *'How and when will I learn if...?'* question on the second page of the *WHI Dietary Study Frequently Asked Questions.*

WHI scientists will compare disease rates between the Dietary Change and Comparison groups after all participants have completed their close-out visit (March 31, 2005). This comparison will let us see if the WHI eating pattern reduced the risk of developing breast cancer, colorectal cancer, and heart disease. We will mail the study results to you after all the data have been analyzed. This will be in early 2006.

If a participant asks about what she should eat:

Point the participant to the *'What should I eat?'* question on the third page of the *WHI Dietary Study Frequently Asked Questions.* Avoid offering dietary advice.

Your personal health care providers, including a registered dietitian, can offer guidance about an eating pattern that is right for you. Contacting your personal health care providers for dietary guidance is particularly important if you have a diet-related health condition such as diabetes, heart disease, or are above or below a healthy weight. The Dietary Summary included in your close-out packet provides a snapshot of current national dietary guidelines for the public and how they compare to the goals of the WHI Dietary Study. There are many similarities between the two eating patterns. When the WHI Dietary Study results become available in early 2006, you can also consider them in light of your personal needs to further guide your food choices.

If a participant asks about where to find more information about nutrition:

Point the participant to the *'If I want more information about nutrition, where can I find it?'* question on the third page of the *WHI Dietary Study Frequently Asked Questions.* Do not offer dietary advice.

The American Dietetic Association (ADA) is the nation's largest organization of food and nutrition professionals. The ADA has a Consumer Hotline (1-800-366-1655) where you can listen to brief pre-recorded nutrition messages or get help finding a registered dietitian in your local area. You can find additional food and nutrition information at the ADA website (www.eatright.org). The U.S. government has many health-related resources. For example, the www.healthierus.gov website offers information about a variety of nutrition topics such as healthy eating, food label reading, the USDA Dietary Guidelines for Americans, and the 5 A Day for Better Health program.

h. Consents

Explain and obtain consent for the WHI Extension Study and the Supplemental Use of Specimens. See *Vol. 2, Section 16.14 – WHI Extension Study and Supplemental Use Consent* for details on collecting this consent.

i. CT BMD Scans at Bone Density (BMD) Sites

All BMD cohort CT participants at the three BMD CCs will receive an AV9 BMD or a close-out BMD (if they have not yet had the AV9 BMD). If a participant has had an AV9 BMD within 12 months of the close-out visit, an additional BMD is not required at close-out. A urine sample or height measurement is not required at the close-out visit. Refer to *WHIP0148 – Follow-up Visit Information* to determine if a BMD is required.

j. Exit Interview

Spend a few minutes with the participant to discuss her future involvement with WHI if she is transitioning to the Extension Study. If she has signed the Extension Consent, explain to her when she may expect to receive the first packet of materials for the Extension Study. If she has declined signing the Extension Consent, make sure she is thanked for the participation that she has maintained and celebrate with her the fact that she has made history with a large group of women who have contributed a wealth of information to women's health. Refer to the March 22, 2004, WHI Times for tips for "Saying Goodbye" to participants.

Make sure that the participant is aware that:

- Her participation to WHI has been and remains invaluable.
- She should contact the CC with any questions or concerns that she may have in the future.

Participant retention may be promoted by sending a personalized thank-you card within a week of the visit.

16.13.1.5 Activities for Participants Who Do Not Come to the Close-out Visit

Participants who do not come to the CC for a close-out visits (e.g., "no shows" or "no visit" follow-up) may be contacted by phone or mail to collect the priority tasks. CCs should ensure a thank-you packet is mailed to the participant who does not attend the close-out visit (except those participants with a follow-up status of "no mail", "absolutely no contact", or "deceased").

16.13.1.6 Ancillary Study Tasks at Close-out

Refer to the appropriate ancillary study coordinating center for details on ancillary study tasks required at close-out.

Table 16.4 – CT Close-out Mailing Packet Materials

	CT Documents	Mail	Purpose	Source Location	Title in Public Folders	Manual
1	Close out visit appt. reminder (required)	All	CC includes as cover memo for mailed packet; includes checklist on second page	CC Prints Close-out/Packets/CT Close-out mailing packet	Close-out visit Appointment Reminder.doc	*Vol. 2, App. E.7.1*
2	*Form 33 – Medical History Update* (required)	All	A routine data collection form	CCC/GPO prints	-	*Vol. 3*
3	*Form 37 – Thoughts and Feelings* (required)	All	A routine data collection form	CCC/GPO prints	-	*Vol. 3*
4	*Personal Information Update* report (required)	All	A routine data collection form	CC prints from WHILMA	-	-
5	*Form 55 – Estrogen-Alone Survey* (E-alone) (required for participants on E-Alone at the time E-Alone intervention was stopped)	E-alone	A routine data collection form	CCC/GPO prints	-	*Vol. 3*
6	Cover letter – Extension Study Consent - (non-HT) (required)	Non-HT	A cover letter to attach to the Extension Study consent for non-HT participants	CC Prints Close-out/Packets/CT Close-out mailing packet	Cover letter – CT Pre-visit (non HT) Extension Study Consent.doc	*Vol. 2 App. E.7.2*
7	Extension Study Consent – (non-HT) (required)	Non-HT	Used to obtain informed consent for Extension Study (place a participant barcode label on both copies)	CC Prints Close-out/Packets/CT Close-out mailing packet	Extension Study Consent (non HT).doc	*Vol. 2 App. E.7.3*
8	Cover letter – Extension Study Consent - (HT) (required)	HT	A cover letter to attach to the Extension Study consent for HT participants	CC Prints Close-out/Packets/CT Close-out mailing packet	Cover letter – CT Pre-visit (HT) ExtensionStudy Consent.doc	*Vol. 2 App. E.7.4*
9	Extension Study Consent – (HT) (required)	HT	Used to obtain informed consent for Extension Study (place a participant barcode label on both copies)	CC Prints Close-out/Packets/CT Close-out mailing packet	Extension Study Consent (HT).doc	*Vol. 2 App. E.7.5*
10	Cover letter – Supplemental Consent (required)	All	A cover letter to attach to the Supplemental Consent	CC Prints Close-out/Packets/CT Close-out mailing packet	Cover Letter – CT Pre-visit Supplemental Consent.doc	*Vol. 2 App. E.7.6*
11	Supplemental Consent (required)	All	Used to obtain informed consent for Supplemental consent (place a participant	CC Prints Close-out/Packets/CT	Supplemental Consent.doc	*Vol. 2 App. E.7.7*

			barcode label on both copies)	Close-out mailing packet		

Table 16.5 – CT Thank you Packet Materials

	CT Documents	Visit	Purpose	Source Location	Title in Public Folders	Manual
1	Thank you packet cover letter (required)	All	CC includes as the cover letter for the thank-you packet	CCC/GPO prints Close-out/Packets/CT Thank you packet	Cover letter – CT Thank you packet.doc	*Vol. 2 App. E.7.8*
2	PI thank-you letter (optional)	All	Individualized thank-you letter signed by PI	CC Prints Close-out/Packets/CT Thank you packet	Cover letter – PI Thank you.doc	*Vol. 2 App. E.7.9*
3	CT Close-out Newsletter ("WHI Matters") (required)	All	A newsletter focusing on the legacy of WHI	CCC/GPO prints Close-out/Packets/CT Thank you packet	CT Close-out Newsletter.pdf	-
4	Health Screening Guidelines handout (required)	All	General health screening guidelines for women over 50	CCC/GPO prints Close-out/Packets/CT Thank you packet	Health Screening Guidelines.doc	*Vol. 2 App. F.5.1*
5	Certificate of Appreciation (required)	All	Personalized certificate commemorating woman's participation	CCC/GPO prints template, CC adds participant name Close-out/Packets/CT Thank you packet	Certificate of Appreciation.pdf	*Vol. 2 App. F.5.2*
6	Incentive: mirror/sewing kit (required)	All	CT incentive	CCC	-	-
7	Incentive: jar gripping opener (required)	All	CT/OS incentive	CCC	-	-
8	WHI Dietary Study Summary (required for DM, optional for others)	DM	A handout for DM-I and DM-C participants	CCC prints for DM only; CC prints for others Close-out/Packets/CT Thank you packet	DM Summary.doc	*Vol. 2 App. F.5.3*
9	WHI Dietary Study Frequently Asked Questions (required for DM, optional for others)	DM	A handout of FAQs for DM-I and DM-C participants	CCC prints for DM only; CC prints for others Close-out/Packets/CT Thank you packet	DM FAQ.doc	*Vol. 2 App. F.5.4*
10	CaD Fact Sheet (required for CaD, optional for others)	CaD	A handout about CaD	CCC prints for CaD only; CC prints for others Close-out/Packets/CT Thank you packet	Calcium Fact Sheet.doc	*Vol. 2 App. F.5.5*
11	WHIP9758-CaD Treatment Assignment (required)	CaD	Unblinding letter for CaD participants	CC prints from WHILMA Close-out/Packets/CT Thank you packet	WHIP9758-CaD Treatment Assignment.pdf	-

12	WHI Folder	All	Holds thank you packet materials	CCC/GPO prints	-	-

16.13.2 OS Close-out

Close-out data are collected from OS participants using procedures similar to those used during the annual OS follow-up. Data collection attempts by mail (Contacts 1-4) are conducted by the CCC (see *Vol. 2, Section 16.13.2.2 – CCC Responsibilities for OS Close-out* for details). For participants who do not respond to the mailed contacts, data collection attempts by telephone are conducted by the CCs (see *Vol. 2, Section 16.13.2.3 – CC Responsibilities During OS Close-out (Required)* for details). OS close-out mailings begin April 2004 (first Contact 1s) and end in April 2005 (final Contact 4s). Follow-up phone calls to collect *Form 33 – Medical History Update* from non-respondents and to collect *Form 33D – Medical History Update (Details)* can continue through July 2005.

All OS participants, except those who are deceased or on "absolutely no contact" status should receive a close-out packet, since it contains extra information and expresses appreciation for her participation. The CCC sends mailings to all OS participants except those with a follow-up status of "no mail", "proxy", or "absolutely no contact". For participants on "no mail" or "proxy" follow-up, or with undeliverable addresses, the CC should make every attempt to provide them with the close-out materials. The forms may be completed at any time during the close-out period.

The purpose of the OS close-out packet is to collect close-out data, thank the participant for her years of participation, provide summaries of study results to date, and provide an introduction to the "WHI Extension Study". See *Table 16.7 – OS Close-out Mailing Packet Materials* for materials included in the close-out packet.

All CCC mailed packets are sent third-class (bulk) mail in a mailing envelope printed with the CC's return address, the CCC's bulk mailing permit number, and a request for notification of change of address.

Table 16.6 – Timing of OS Close-out Data Collection shows the approximate dates for completion of OS close-out data collection by enrollment month.

Table 16.6 – Timing of OS Close-out Data Collection

Enrollment month	Contact 1 mailing mo(CCC)	Contact 3* mailing mo (CCC)	Contact 4 mailing mo (CCC)	Phone follow-up (CC)	Approx 33D collection (CC)
June (any year)	April 04	July 04	Sept 04	Nov 04	May 04
July	May 04	August 04	Oct 04	Dec 04	June 04
August	June 04	Sept 04	Nov 04	Jan 05	July 04
Sept	July 04	Oct 04	Dec 04	Feb 05	Aug 04
October	August 04	Nov 04	Jan 05	March 05	Sept 04
November	Sept 04	Dec 04	Feb 05	April 05	Oct 04
December	Oct 04	Jan 05	March 05	May 05	Nov 04
January	Oct 04	Jan 05	March 05	May 05	Nov 04
February	Nov 04	Feb 05	April 05	May/June 05	Dec 05
March	Nov 04	Feb 05	April 05	May/June 05	Dec 05
April	Dec 04	Feb 05	April 05	May/June 05	Jan-July 05
May	Dec 04	Feb 05	April 05	May/June 05	Jan-July 05

*Contact 2 (a thank you/reminder postcard) was discontinued several years ago.

16.13.2.1 Timing of the "Regular Annual OS Mailing" During the Year Preceding Close-out

Mailings and related activities during the year prior to close-out are conducted on the usual schedule. That is, the last pre-closeout Contact 1s are mailed in March 2004. Contact 3s and 4s for these women occur in June 2004 and August 2004. CC phone follow-up with these participants should occur in October 2004.

Forms that were mailed out as part of the previous year's mailing (i.e., not a close-out mailing) and are received within the close-out window will NOT be counted as the close-out mailing. For example, if an AV8 set of forms is mailed in March and is received at the CC in April, it will count as an AV8, not as a close-out form. That participant would receive a close-out packet toward the end of the close-out year.

To help distinguish close-out forms from pre-close-out follow-up forms (which CCs will continue to receive through approximately September 2004), a "CO" for close-out appears on the forms' participant ID labels. The *Form* 33 will have 2 labels: 1) a date label with the date of the last *Form* 33, OS contact number (1, 3, or 4), and corresponding barcode CO (for close-out) and participant ID; and 2) a participant ID label with participant name, participant ID, and barcode, CO (for close-out) and OS contact number. To help distinguish which participants are non-respondents needing follow-up to the close-out mailing, a "close-out flag" appears on *WHIP1206 – OS Members Needing CC Follow-up*.

16.13.2.2 CCC Responsibilities for OS Close-out

The CCC is responsible for the printing (through the GPO), assembly, and outgoing postage costs for the mailed close-out data collection contacts. The mailed contacts include:

- An initial mailing of the entire close-out packet (Contact 1)
- A second mailing of the entire packet (Contact 3)
- A third mailing of the entire packet (Contact 4)

Spanish language versions of the contact materials are mailed to participants whose primary language is Spanish, as indicated by the "Preferred Language" flag on the Contact Information Screen in WHILMA.

- **First Mailing of the Close-out Packet (Contact 1)**

  Initial mailings to participants start in April 2004. Contact 1 mailings are sent two months prior to the enrollment anniversary (i.e., those mailed in April are to women who enrolled in June). To allow adequate time for completion of *Form 33D* and outcomes processing, the close-out mailing year for Contact 1 is shortened from 12 months to 9, that is, the mailing year ends in December 2004 instead of March 2005 (see *Table 16.6 – Timing of OS Close-out Data Collection*). All participants will receive a mailing during the close-out period; the last 5 months worth of Contact 1 mailings (i.e., January – May mailings) will be sent October – December 2004.

- **Second and Third Mailing of the Entire Follow-up Packet (Contact 3 and 4)**

  A second complete follow-up packet (Contact 3) is mailed the month after the participant's enrollment anniversary month (three months after the mailing of Contact 1) to those participants who did not respond to the first mailing (i.e., those who did not complete and return the form sent in Contact 1 and for whom the CC has not indicated receipt in WHILMA). The final few months of the close-out period (i.e., January – May) will be shortened to two months (January and February). The last Contact 3 mailings will be sent in February 2005 (see *Table 16.6 – Timing of OS Close-out Data Collection*).

  The third packet (Contact 4) is mailed three months after the enrollment anniversary month (two months after Contact 3) to those participants who have not completed and returned the forms sent during earlier contacts and for whom the CC has not indicated receipt in WHILMA. The last Contact 4 mailings will be sent in April 2005 to allow for adequate time for completing of *Form 33D* and outcomes processing (see *Table 16.6 – Timing of OS Close-out Data Collection*).

16.13.2.3 CC Responsibilities During OS Close-out (Required)

The CCs have several responsibilities during the close-out mailing of Contacts 1-4. These responsibilities, which are similar to those used during OS annual follow-up, consist primarily of:

- Updating WHILMA to reflect that *Form 33* has been completed and returned. The procedures for processing returned packets during the close-out period are identical to those used during annual follow-up. See *Vol. 2, Section 16.5.2.1 – Processing Returned Packets (Contacts 1-4) (Required)* for procedures.
- Making address corrections as soon as they become available. See *Vol. 2, Section 16.5.2.2 – Making Address Corrections (Required)*.
- Completed forms are returned directly to CCs in the business reply envelopes provided in the packet. Clinical Centers are responsible for paying the postage for these completed, returned forms.
- Running monthly reports from WHILMA to identify participants who do not respond to the mailed contacts (see *Vol. 2, Section 16.13.2.4 – CC Data Collection for Non-Respondents to OS Close-out Mailings (Required)* for more details). This activity will continue through July 2005.
- Follow up with non-responders listed on *WHIP1206* to collect *Form 33s*. See *Vol. 2, Section 16.13.2.4* below.
- Continue attempting to locate and collect *Form 33* from all participants listed on *WHIP1591 – Participants Who Are Lost-to-Follow-up*, as per current procedures (see *Vol. 2, Section 17.3 – Locating "Hard to Find" Participants*).
- Collect *Form 33D – Medical History Update (Details)* data by phone or mail consistent with current procedures. Collection will start upon receipt of the first *Form 33*, around May 2004, and will continue through collection of the final *Form 33* in July 2005.

16.13.2.4 CC Data Collection for Non-Respondents to OS Close-out Mailings (Required)

During close-out, CCs are responsible for collecting *Form 33 – Medical History Update* on those participants who have not responded to the close-out mailings. CCs are required to follow-up with all non-respondents during close-out, regardless of their follow-up year. This includes those on "no mail", "proxy" or "no follow-up", and those with an undeliverable address. If a participant does not have a completed *Form 33* in WHILMA by the seventh month after the mailing of Contact 1 (i.e., five months after her enrollment anniversary), staff should initiate telephone contacts to collect the data. This is done through telephone attempts to reach the participant or proxy to collect the data. Non-respondents needing follow-up data collection are listed on *WHIP1206 – Members Needing CC Follow-up* (see *Vol. 2, Section 16.5.2.3* for WHILMA procedures). See *Vol. 2, Sections 16.5.3.1 – Telephone Contact to Ascertain Correct Address and to Collect Medical history Update* and *16.5.3.2 – Mail/Phone Contact to Trace Participant and/or Collect Medical History Update from Proxy* for details on collecting data from non-respondents.

If a participant did not receive a mailed packet (e.g., because she had an "undeliverable address" or is on "no mail" or "proxy"), CCs are encouraged to send her a copy of the newsletter, a certificate of appreciation, and a thank you bookmark following the phone contact, even if she does not agree to complete the *Form 33*. A small supply of these close-out items have been provided to CCs for this purpose. The report for personalizing the certificate of appreciation (*WHIP9757*) is included in the June 2004 WHILMA upgrade.

Telephone calls to non-responders, whose first mailings were sent in December 2004, may be made one month after the Contact 4 mailing, rather than waiting for two months. To get a list of these respondents, run *WHIP1206* at 5 or 6 months after the first mailing (rather than the default of 7 months) to ensure adequate time for follow-up. For these participants, *WHIP1206* should be run in May or June 2005, following the Contact 4 mailing in April.

16.13.2.5 OS BMD Scans at Bone Density (BMD) Sites

AV9 BMD scans can be scheduled up through September 30, 2004. No BMD scans should be scheduled after October 1, 2004 (the start of CT close-out visits). Starting in April, 2004, the CCC will be mailing forms to the bone density participants, instead of having them mailed by the CCs.

Table 16.7 – OS Close-out Mailing Packet Materials (Mailed by CCC)

	OS Documents	CCC Mails	Purpose	Source Location	Title in Public Folders	Manual
1	Thank-you cover letter – contact 1 (required)	All	Included as the cover letter for packet (contact #1)	CCC/GPO prints Close-out/Packets/OS Close-out Mailing Packet	Cover letter – Oscovfin2.doc	-
2	Thank-you cover letter – contact 3 -4 (required)	All	Included as the cover letter for packet (contact #3-4)	CCC/GPO prints Close-out/Packets/OS Close-out Mailing Packet	Cover letter – Osfincov34.doc	-
3	*Form 33 – Medical History Update* (required)	All	A routine data collection form	CCC/GPO prints	-	-
4	*OS Follow-up Questionnaire* (required)	All	A routine data collection form corresponding to participant's follow-up year: Form 146 and Form 149 for AV6 Form 147 for AV7 Form 148 for AV8 No Form for AV9 or AV10	CCC/GPO prints	-	-
5	OS Extension Study announcement ("Breaking News") (required)	All	Announcement of the Extension Study for OS participants	CCC/GPO prints Close-out/Packets/OS Close-out Mailing Packet	WHI Extension Study Announce.doc	-
6	Certificate of Appreciation (required)	All	A personalized certificate of appreciation	CCC/GPO prints template and CCC adds participant name Close-out/Packets/OS Close-out Mailing Packet	Certificate of Appreciation.pdf	*Vol. 2 App. F.5.2*
7	Close-out Newsletter (required)	All	OS newsletter describing OS participants as a group and informing them of planned mailing of study results	CCC/GPO prints	-	-
8	Thank-you gift: Magnifying bookmark – contact 1 (required)	All	OS thank-you gift (for contact 1)	CCC	-	-
9	Incentive: Jar gripping opener contact 3-4 (required)	All	OS/CT thank-you gift (for contacts 3-4)	CCC	-	-
10	#2 pencil (required)	All		CCC	-	-

11	Business reply return envelope with CC address (required)	All		CCC	-	-

16.13.3 Proxy Close-out (CT and OS Participants)

For CT and OS participants on proxy follow-up, contact the proxy by phone or mail to collect the close-out *Form 33* and, if necessary, *Form 33D*. If the *Form 33* is sent by mail, include a thank you letter letting the proxy know that the study is coming to an end, as well as any supplemental information that the proxy might be interested in seeing and/or sharing with the participant, such as the CT or OS close-out newsletter, the health recommendations, and the thank you gift. If the forms are collected by telephone, follow the call with a thank you packet.

If the participant is in the CaD Study and is on active intervention status, contact the proxy and let him/her know that the participant should stop taking her study pills.

There are no study-wide plans for providing deceased participants' proxies with close-out information, though Clinical Centers may send this information to proxies (depending on individual or family circumstances) if they wish.

If a CC sends information to a proxy, enclosing a cover letter acknowledging the special role of proxies is recommended.

16.13.4 Close-out Events (CT and OS Participants)

Centers may choose to plan group close-out events for participants. As opposed to group visits, these events are generally celebratory in nature. As long as the goal is participant appreciation, and activities and messages are neutral, all participants in the CT and OS may attend together. In accordance with the Project Office (12/3/03 memo from the Project Office, posted in Public Folders/Close-out folder), close-out participant events may be billed to the contract when reasonable expenditure of costs is likely to result in proportional relative benefit toward fulfillment of contractual objectives. The NHLBI concurs that small expenditures per participant may be incurred for CT participants to encourage retention. No further NHLBI approval is required for costs not exceeding $5.00 per CT participant. Any event for CT participants should have an opportunity for the dissemination of technical information, such as study findings. For OS participants, an informational meeting without incentives requires no further NHLBI authorization. Centers are encouraged to work with local businesses and community organizations to enhance the funds available for events or incentives. Real or apparent endorsements must be avoided in all cases.

16.13.5 Outcomes

One purpose of the close out contact is to complete ascertainment of primary outcome data, including collection of *Form 33* and *33D* (if required), procurement of medical records documentation and adjudication. It is not necessary to collect missing *Form* 33s because the current *Form 33* will capture any missed outcomes. Investigation and adjudication of outcomes is conducted during the close-out period and continues until the August 15, 2005 WHILMA database closure. Outcome priorities remain unchanged during the close-out period, therefore, prioritize CT over OS outcomes with the ultimate goal of having all outcome cases adjudicated and data entered on or before the August 15, 2005 database freeze.

16.13.6 Data Management

All WHI study forms must be entered into WHILMA no later than August 15, 2005.

16.13.7 Records Retention

WHI requirements indicate data and forms on participants who have signed an Initial Consent must be kept after the study has ended. *Form 2/3s – Eligibility Screen* on participants who did not sign an Initial Consent may only be discarded after they have been data entered. *Form 2/3s* on participants who have signed an Initial Consent may not be discarded. CCs are not required to keep records onsite.

16.13.8 Equipment

Participant visits for the Clinical Trial and Observational Study of the Women's Health Initiative are scheduled to end March 31, 2005. At that time, WHI clinical centers will no longer require certain items of equipment, such as scales, ECG machines, optical scanners, centrifuges, freezers, freezer alarm systems, cameras, furniture, refrigerators, microwave ovens, PCs, etc.

Some of the equipment was purchased by your institution and some was provided by the Clinical Coordinating Center (CCC) at Fred Hutchinson Cancer Research Center (FHCRC). Refer to Equipment Letter deated September 9, 2003 in Public Folders/Close-out folder for how to dispose of equipment.

16.14 WHI Extension Study and Supplemental Use Consents

16.14.1 Obtaining Consents for CT and OS Participants

Obtaining a participant's signed consent for enrollment in the WHI Extension Study and for the Supplemental Consent may be done by mail or in-person, as per local IRB requirements. CCs will mail the Extension Consent and the Supplemental Consent Forms to participants, either in the CT close-out visit packet or a separate OS mailing. CT participants who will not receive a close-out visit packet (i.e., participants with a follow-up status of no visit, proxy follow-up, etc.), may be sent an OS consent mailing packet. Ensure the correct Extension Study consent is used (i.e., HT consent for HT participants, and non-HT consent for all other participants). Refer to *Table 16.8 – OS Consent Packet Materials* for items to include in the mailings. Make sure that participant barcode labels are affixed to any consent forms that are mailed out. If the consent is collected by mail, refer to *Vol. 2, Section 16.14.4 – Collecting the Consents by Mail*.

Ideally, consents should be obtained after the close-out tasks are collected from both CT and OS participants. Each CC is responsible for obtaining consent for its own participants. The two consent forms are presented to all participants, with the exception of those with an "absolutely no contact" or deceased follow-up status. To obtain consent from participants on "proxy" follow-up, see *Vol. 2,Section 16.14.5 – Obtaining Consent Forms from CT or OS Participants on Proxy Follow-up*. Participants may choose to participate in the extension study and choose not to sign the supplemental consent. It is also acceptable for the participant to sign the supplemental consent and not participate in the extension study.

It is up to each CC to decide which staff members are in the best position to participate in the informed consent process. There is no training certification required of staff who will be consenting participants. However, it is expected that any staff involved in providing the consents will be fully knowledgeable of the consents' content, as well as the consenting requirements at their institution.

Extension Study Consent

In the spring of 2004 the National Heart, Lung, and Blood Institute approved a five-year extension study of all WHI participants to collect health information through 2010. The WHI Extension Study will help investigators learn more about long-term changes in women's health. All women who participated in WHI will be invited to join the Extension Study.

Two different informed consent forms have been developed for the Extension Study, depending on which component of the WHI the participant was in.

- The Extension Study (Non-HT) Consent is for women who participated in any WHI component other than the Hormone Trial (including OS).
- The Extension Study (HT) Consent is for women in the Hormone Trial, even if they also participated in other components of WHI.

Supplemental Consent (for use of stored specimens by non-WHI researchers at private or non-profit organizations)

When WHI began, participants consented to provide samples of their blood for future research by WHI investigators. These on-going studies have included genetics research to learn how differences in blood, blood proteins, and DNA might be associated with disease risk or health outcomes. The use of participants' blood samples for these studies by WHI investigators can continue under the existing WHI consent. However, we are now asking participants to sign a new, "Supplemental" consent so that WHI stored specimens can be made available to non-WHI researchers at private or non-profit organizations.

Since participants consented to join WHI, huge technological advances have been made in the ways scientists can analyze blood, proteins in the blood, and DNA. Scientists in settings outside of WHI and even outside of traditional academic and medical settings have been involved in making these scientific

advances. In some cases, scientists at private and for-profit organizations and companies have the best access to the experience and state-of-the-art technology needed to conduct these newer types of studies. The WHI would like to collaborate with these scientists so that further advances in science can be made and important public health questions can be answered. This collaboration is consistent with our promise to participants that we are using their health information and specimens to answer many important questions about women's health.

The Supplemental Consent, which discusses the sharing of WHI participant blood samples with scientists at for-profit and non-profit organizations outside of the WHI, must be obtained before the samples can be shared. All participants should be approached to sign the Supplemental Consent Form (*Vol. 2, Appendix E, Figure E.7.7)* regardless of which study arm they participated in.

16.14.2 Extension Study Consent Collected in the CC

16.14.2.1 Extension Study Talking Points

Background:

The National Heart, Lung, and Blood Institute has approved a five-year extension study of all WHI participants so that important health information can be collected through 2010. The WHI Extension Study will help investigators learn more about long-term changes in women's health. Women in the WHI Hormone Trials (even if they participated in other WHI CT components) will be asked to sign a "WHI Hormone Program Extension Study Consent." All other participants (including OS women) will be asked to sign the "WHI Extension Study Consent."

These talking points are intended for staff who will be discussing the WHI Extension Study with participants for the purpose of obtaining informed consent. This document can also serve as a resource for other WHI staff who may be asked about the Extension Study. Staff should read both the WHI Extension Study Consent and the WHI HT Extension Study Consent in addition to this document. More detailed procedures on carrying out the informed consent process with WHI participants (including HIPAA considerations) can be found in the "WHI Close-out Procedures" document and from your local IRB.

Key Points

Regardless of whether your clinic chooses an individual or group format to properly inform and educate women about the Extension Study, the following points should be covered :

- The purpose of the WHI Extension Study is to continue to learn about the health of postmenopausal women for an additional 5 years. Thousands of WHI participants are expected to participate in this study.
- You will **not** be asked to come into the WHI clinical center for visits. Each year you will be sent an annual health update (Medical History Update for all participants; an additional Hormone Questionnaire for HT participants) to complete and send back through the mail.
- FOR HT PARTICIPANTS ONLY: You will also be asked to have a mammogram each year for the first two years and to give us permission to obtain copies of the mammogram report.
- You might be asked to sign a medical release form to get more detailed information about health changes you have experienced.
- Any information you provide will be kept confidential. Only WHI staff will have access to this information. For safety reasons, Food and Drug Administration staff may also examine these records.
- No identifying information will be included in study reports; your health information will be grouped with information from other participants.
- There is no promise or guarantee that you will receive any personal benefit from the study. You should contact your own health care provider about any personal health issues or questions you may have.
- There are no risks to completing the health update forms.
- The study is completely voluntary and you may withdraw at any time.

Additional Points

The following additional points are appropriate to incorporate into your discussions with participants about why the WHI Extension Study is important.

For HT Participants:

- Women, health care providers, and scientists throughout the world are asking how women's risk for certain diseases change after they stop hormones. We need long-term data from WHI Hormone Program participants like you--women from the Estrogen-Plus-Progestin and the Estrogen-Alone studies and those who were the active and placebo groups of both studies--to get answers to these questions.
- Many women and their health care providers are evaluating and re-evaluating their hormone choices since they heard about the WHI Hormone Program findings. Just as you contributed to those important findings, your future choices about hormones--what types of medications, if any, you take--can help us learn more about the health effects of these choices.
- We have tried to make participation in the Extension Study as easy as possible—you will not need to come in for clinic visits or exams. The data for this study will come from forms that we send in the mail.
- To ensure your safety and learn more about breast health after women stop hormones, we will ask your permission to obtain your mammogram reports during the first two years of the study. We may also check in with you by phone to get information about where these mammogram reports or other health records are located. However, you do not need to come in to the clinical center anymore.

For DM Participants:

- The health effects of your past dietary choices may continue for years after the WHI Dietary Study has ended. This is true whether you were in the Comparison group and may not have changed the way you eat, or you were in the Dietary Change group and were asked to eat less fat and more fruits, vegetables, and grains.
- We invite you to continue with the WHI by joining the WHI Extension Study so we can answer questions about these longer term effects of diet.
- Your participation in this new phase of the WHI will help advance knowledge about the effect of diet on health in women.
- We recognize that the choice is yours and invite your questions.

For CaD Participants:

- The WHI Extension Study will allow us to answer additional important questions about the health effects of taking calcium and vitamin D. For example:
    - How long do women need to take calcium and vitamin D to prevent diseases like colon cancer and osteoporosis?
    - Does calcium and vitamin D prevent breast cancer?
    - If there are benefits or risks to taking calcium and vitamin D, how long do they last after women stop taking these supplements?

16.14.2.2 Review of Extension Study Consent

After reviewing the talking points, have the participant read (if she did not receive it ahead of time) or review the Extension Study (Non-HT) Consent or the Extension Study (HT) Consent. Following the reading of the consent form, allow ample time to answer any questions she may have. Refer to the "Extension Study FAQ" (Public Folders) to help answer her questions. If questions come up that are not in the FAQ, refer the participant to the appropriate staff (i.e., CP or PI) for further clarification.

If the consent process is being done in a group setting, smaller groups are advised to stimulate discussion. It is also recommended that women have the opportunity to ask their questions privately.

If the participant needs more time to consider if she wants to sign the consent, provide her with a postage-paid return envelope to return the consent at a later time.

16.14.2.3 Signing of the Extension Study Consent

Ask the participant to sign and date two copies of the consent form in the appropriate places. Sign and date one or two copies of the form as a WHI representative and witness, as required by your CC's IRB. Ensure participant barcode labels are on each copy of the consent form. Give one copy of the consent form to the participant to take home with her and keep one copy for her clinic file.

After the participant signs the form, thank her for her time. Let her know that she will be receiving a WHI newsletter in the mail about once a year. Remind her that she will start receiving her annual data collection packet within a year. Provide her with a number to call or postage-paid postcard to use for notification of a change of address.

After the participant signs the consent form (or declines), thank her for her years of dedication to WHI. Then initiate discussion of the Supplemental consent (see *Vol. 2, Section 16.14.3 – Supplemental Consent*).

Complete and data enter *Form 111 – Extension (Non-HT) Consent Status*, or *Form 112 – Extension (HT) Consent Status*.

16.14.3 Supplemental Consent (for use of stored specimens) Collected in the CC

16.14.3.1 Supplemental Consent Talking Points

Background:

When WHI began, participants consented to provide samples of their blood for future research by WHI investigators. These on-going studies have included genetics research to learn how differences in blood, blood proteins, and DNA might be associated with disease risk or health outcomes. The use of participants' blood samples for these studies by WHI investigators can continue under the existing consent. However, we are now asking participants to sign a new, "Supplemental" consent so that WHI stored specimens can be made available to non-WHI scientists.

Since participants consented to join WHI, huge technological advances have been made in the ways scientists can analyze blood, proteins in the blood, and DNA. Scientists in settings outside of WHI and even outside of traditional academic and medical settings have been involved in making these scientific advances. In some cases, scientists at private and for-profit organizations and companies have the best access to the experience and state-of-the-art technology needed to conduct these newer types of studies. The WHI would like to collaborate with these scientists so that further advances in science can be made and important public health questions can be answered. This collaboration is consistent with our promise to participants that we are using their health information and specimens to answer many important questions about women's health.

It is well understood that the field of DNA and genetic research is growing quickly and can be very complicated to understand. Even those who have significant health and/or science backgrounds can find themselves perplexed at times when answering specific questions related to DNA and genetics. It is recommended that staff review the basics so that they can feel as comfortable with the material as possible. A useful website to serve as a resource to staff is www.nlm.nih.gov/medlineplus/cloning/html.

An in-person discussion about the Supplemental Consent can be done individually or in groups, depending on the CC's specific needs and resources. These talking points are intended for staff who will be having discussions with participants for the purpose of obtaining informed consent. The talking points can also serve as a resource for other WHI staff who may be asked about the Supplemental Consent, how their samples are used, or genetics research in WHI. An optional participant video, introducing the concept of sharing WHI blood and DNA samples with outside scientists, has also been developed for CC use. It is recommended that

women view the video to help them better understand the Supplemental Consent form and to generate some enthusiasm for this opportunity to advance our knowledge of this growing field. The video will help answer potential questions and may cut down on staff time. The video may be shown individually or in a group setting.

In addition to these talking points, staff should read the Supplemental Consent and refer to the Supplemental Consent FAQ for suggested responses to participant questions that may come up. More detailed procedures and guidelines on carrying out the informed consent process with WHI participants (including any HIPAA considerations) can be found in the "WHI Close-out Procedures" document and from your local IRB.

Regardless of whether an individual or group format is used to inform and educate women about the Supplemental Consent, the following points must be covered (see "Supplemental Consent Talking Points" (Public Folders) for more details):

Key Points to Cover in Discussions with Participants about the Supplemental Consent:

- The use of blood samples by WHI scientists can continue under the original existing consent. This new "Supplemental Consent" is specifically asking for permission to share blood and DNA samples with non-WHI scientists at private or non-profit organizations, starting in 2006.
- Collaboration with these non-WHI scientists may lead to even more ways of analyzing samples and to faster development of new tests to diagnose and/or predict diseases.
- The National Heart, Lung, and Blood Institute (NHLBI) and our Institutional Review Board (IRB) will carefully review all research proposed by scientists from outside organizations according to high standards and ethical principles. No samples will be made available until these proposals are approved.
- Only those blood and DNA samples that have already been collected and are already stored will be made available to these non-WHI scientists. No additional blood or DNA will be needed, and you will not be asked to give more blood samples.
- All individual data in the WHI is kept confidential. No results of blood or DNA (genetic) studies done using your samples will be provided to you, or your family, doctor, or insurance company.
- The results of this type of research are reported on and applied to groups as a whole. We will not know what the DNA research shows for an individual person's health.
- Consenting to this supplemental use of blood does not mean that you are consenting to or will have genetic testing. You must speak with your own health provider if you are interested in having genetic testing.
- There will be no direct benefit from these studies to your own personal health, but this research will hopefully result in new tests and treatments to prevent or cure diseases.
- At any time, you may withdraw consent for any use of your blood or just for this supplemental use, without affecting your participation in other parts of the WHI.
- There are no costs to you or your insurance for any blood or DNA research using your WHI samples.
- Your blood and DNA samples will be stored at a central site listed under a code number only. No personal identifying information will be included on your samples.
- WHI has been granted a Certificate of Confidentiality from the US Federal Government to make sure that your confidentiality is protected.

16.14.3.2 Review of Supplemental Consent

Following the video, have the participant read the Supplemental Consent (*Vol. 2, Appendix E, Figure E.7.7*) (or review it, if she received it ahead of time). Following the reading of the Supplemental Consent form, allow ample time to answer any questions she may have. Refer to the "Supplemental Consent FAQ" (Public folder) to help answer her questions. If questions come up that are not in the FAQ, refer the participant to the PI for further clarification.

If the consent process is being done in a group setting, smaller groups are advised, to stimulate discussion. It is also recommended that women have the opportunity to ask their questions privately, if possible.

If the participant needs more time to consider the consent, provide her with a postage-paid envelope to return the consent at a later time. Make sure that the consent form copies that she takes with her have participant barcode labels affixed to them.

The field of DNA and genetic research is growing quickly and can be very complicated to understand. Even those who have significant health and/or science backgrounds can find themselves perplexed at times when answering specific questions related to DNA and genetics. It is recommended that staff review the basics so that they can feel as comfortable with the material as possible. A useful website to serve as a resource to staff is www.nlm.nih.gov/medlineplus/cloning/html.

As fields emerge and grow and technology advances, new situations and questions can arise. Not every question will have a clear answer at this point, since we don't know exactly how the field will evolve. It is important to understand that all WHI researchers and future collaborators will make every reasonable effort to uphold the toughest ethical standards for research with human subjects, including blood and DNA research.

16.14.3.3 Signing of the Supplemental Consent

Ask the participant to sign and date two copies of the consent form in the appropriate places. Sign and date one or two copies of the form as a WHI representative and witness as required by your CC's IRB. Place a participant barcode label on each copy of the consent form. Give one copy of the consent form to the participant to take home with her and keep one copy for her participant file.

If the participant declines to sign the form, thank her for her time.

Complete and data enter *Form 113 – Supplemental Consent Status* indicating the consent status.

16.14.4 Collecting the Consents by Mail

Use *WHIP0870 – OS Extension Consent Batches Screen* and *WHIP0148 – Follow-up Visit Information* to identify OS and CT participants, respectively, who are due for consenting. *WHIP9762 – Close-out and Extension Consent Tracking* can be used for tracking both CT and OS participants who have not completed the consents. See WHILMA upgrade notes Ver. 5.5 for detailed instructions on using WHILMA to identify OS participants and for tracking consents.

Once participants are identified as needing a consent mailing, mail the first consent packet, (see *Table 16.8 – OS Consent Packet Materials* for mailing packet contents). A second packet, identical to the first, can be re-sent to non-responders 2 months after the first two. CCs have the option of sending a third mailing, two months after the second mailing to non-responders. If there is still no response, the CC may try to contact these participants by telephone to discuss the possibility of then signing one or both consents. The amount of effort that goes into locating and obtaining consents from non-responders is at the CC's discretion.

Complete and data enter *Form 111 – Extension (Non-HT) Consent Status* and *Form 113 – Supplemental Consent Status* for all participants indicating the consent status.

16.14.5 Obtaining Consent Forms from CT or OS Participants on Proxy Follow-up

To obtain consent from CT or OS participants on "proxy" follow-up, start first with a contact with the designated proxy. Confirm with the proxy that the participant is competent to consider and sign the Supplemental Consent Form. Discuss also her ability to consider and sign the Extension Study Consent Form, and confirm with the proxy that he/she would be willing to continue completing annual health forms for the participant. If the proxy agrees that you can proceed with one or both consents, contact the participant and initiate the consent process.

Note that a proxy cannot sign either the Supplemental Consent Form or the WHI Extension Consent Form, unless he or she is the participant's power of attorney. Your local IRB may provide additional guidance on obtaining consent from participants on "proxy" follow-up.

16.14.6 Signing of the *Form 114 – WHI Genetic Studies Consent Status*

The *Form 114 – WHI Genetic Studies Consent Status* is completed only when a participant requests one of the following changes in her WHI genetic studies consent status.

- The participant requests that her blood not be used for WHI genetic studies; or
- The participant who previously asked that her blood not be used for WHI genetic studies on *Form 11 – Consent Status* now agrees to allow her blood to be used in WHI genetic studies.

This is not a routine task and the participant should not be prompted or asked about her previous WHI genetic studies consent status.

Table 16.8 – OS Consent Packet Materials

	OS Documents		Purpose	Source Location	Title in Public Folders	Manual
1	Cover letter for mailed consent packet (required)	All	A cover letter that introduces the Extension Study and Supplemental Use consents and Summary Worksheet	CC Prints Close-out/Packets/OS Consent mailing packet	Cover letter – OS Mail Consent Packet.doc	*Vol. 2 App. E.7.10*
2	WHI Consent Summary Worksheet (required)	All	Participant records her intention to either sign or decline signing of the Extension Study and Supplemental Use consents	CC Prints Close-out/Packets/OS Consent mailing packet	Consent Summary Worksheet.doc	*Vol. 2 App. E.7.11*
3	Cover letter - Extension Study Consent (non-HT) (required)	All	A cover letter to attach to the Extension Study consent mailed to OS participants	CC Prints Close-out/Packets/OS Consent mailing packet	Cover letter – OS Mail Extension Study Consent.doc	*Vol. 2 App. E.7.2*
4	Extension Study Consent (non-HT) (required)	All	Used to obtain informed consent for Extension Study (place a participant barcode label on both copies)	CC Prints Close-out/Packets/OS Consent mailing packet	Extension Study Consent (non HT).doc	*Vol. 2 App. E.7.3*
5	Cover letter – Supplemental Consent (required)	All	A cover letter to attach to the Supplemental Use consent mailed to OS participants	CC Prints Close-out/Packets/OS Consent mailing packet	Cover letter – OS Mail Supplemental Consent.doc	*Vol. 2 App. E.7.6*
6	Supplemental Consent	All	Used to obtain informed consent for the Supplemental Consent (place a participant barcode label on both copies)	CC Prints Close-out/Packets/OS Consent mailing packet	Supplemental Consent.doc	*Vol. 2 App. E.7.7*
7	Business reply return envelope with CC address (required)	All	For participant to return her signed consent forms to the CC	CC prepares	-	-

16.15 Post Close-out DM-C Newsletter (for DM-C only)

The purpose of the DM-C newsletter is to honor the WHI protocol commitment to provide an overview of the DM Intervention to DM Comparison participants at the time the WHI Dietary Study results become publicly available.

The newsletter will be written in light of the WHI results, hence is not yet completed. The four page newsletter will provide a snapshot of the DM Intervention: the dietary goals; design of the group sessions; and a summary of session content. It will offer a few choice-based behavior-change tips, such as self-monitoring and paying attention to serving sizes. The newsletter will provide a recommendation to see ones personal health care providers (including a registered dietitian) for dietary advice and offers guidance about where to find more information about nutrition, if a participant is interested.

The DM-C newsletter is designed for DM Comparison participants only. The CCC will mail the newsletter and a WHI Dietary Study update to all DM Comparison participants after October 1, 2005.

SECTION 16

FOLLOW-UP CONTACTS

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