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## **SECTION I. OVERVIEW**

### **A. Overview/Study Objectives**

There are two main objectives to Project Viva. The first objective is to examine the effects of specific gestational nutritional factors on fetal growth, length of gestation, incidence of pre-eclampsia, and on cognitive development and blood pressure in infancy. The second objective is to evaluate the associations between women's experiences of racism and violence, their levels of corticotrophin-releasing hormone (CRH) levels, and risk of preterm delivery in the context of sociodemographic factors, health habits, reproductive and medical history, and medical conditions during pregnancy.

### **B. Research Questions**

The hypotheses for Project Viva are:

1. Maternal intake of trans fatty acids is inversely associated with fetal growth, length of gestation and infant cognitive development.
2. Maternal intake of n-3 fatty acids is directly associated with fetal growth, length of gestation and infant cognitive development.
3. Maternal intake of calcium is inversely associated with incidence of pre-eclampsia and blood pressure level in infancy.
4. Maternal intake and red blood cell level of n-3 fatty acids are inversely associated with incidence of pre-eclampsia
5. Maternal experience and fear of violence, and, among African Americans, racial discrimination, are associated with an increased likelihood of preterm delivery.
6. Levels of CRH measured at 26-28 weeks' gestation are elevated among women who subsequently deliver prematurely, compared with women who deliver at term. CRH levels are positively associated with fetal adrenal hormone output, measured as cortisol sulfate and estriol in maternal plasma.
7. Levels of CRH are higher among women who are African American, taking into account maternal socioeconomic position, maternal age, pre-pregnancy weight, prior history of prematurity or spontaneous abortion, and cigarette smoking.
8. Maternal experience and fear of violence, and, among African Americans, racial discrimination, are positively associated with levels of CRH.

### **C. Organizational Structure**

#### **1) Department of Ambulatory Care and Prevention/HPHC/HMS**

Harvard Pilgrim Health Care (HPHC) is the largest health insurer in New England. Harvard Vanguard Medical Associates (HVMA), originally operated as HPHC's staff-model health maintenance organization, provides care to approximately 300,000 members at 14 clinical centers.

The Department of Ambulatory Care and Prevention (DACP) is the academic department of Harvard Medical School based at HPHC. The DACP has special expertise in HMO-based research, including on-site access to the data systems of HVMA and HPHC. With its

combination of research expertise, and access to the diverse population of HVMA enrollees, the DACP provides an optimal environment for Project Viva.

## 2) **Harvard Vanguard Medical Associates (HVMA) Offices**

Project Viva recruitment is being conducted at nine practices of Harvard Vanguard Medical Associates (HVMA) (**Appendix A: Recruitment Sites and Contacts**). Harvard Vanguard Medical Associates has a central administration and, at the start of Project Viva, the study was introduced to several of the central departments of HVMA: the central HVMA OB/GYN Chiefs, OB/GYN Supervisors, Lab Technicians and Lab Supervisors. The central HVMA administration does not play an active role in Project Viva, but they played a key role in refining logistics for the protocols.

Before being initiated at each HVMA practice, the study is introduced to the OB department staff and the Lab supervisor. The OB/GYN departments also have limited involvement in the study operations except that the clinicians are requested to introduce the Research Assistant to the patient at the end of each IOB appointment. The lab staff need to be notified of the additional blood draw for Viva participants (**Appendix B: Viva Blood Draw Protocol**).

As protocols for Viva visits are initiated at the HVMA offices (Visit 1, Visit 2 and Visit 4), the Project Coordinator and Principal Investigator will notify the appropriate staff and send information (**Appendix C: Information for HVMA Clinicians and Staff; Information for HVMA Social Workers**). The Project Coordinator is also in contact with the OB Supervisors to evaluate the recruitment flow and process at each practice.

## 3) **Hospitals**

Post-delivery follow-up will be conducted at two hospitals: Beth Israel Deaconess Medical Center and Brigham and Women's Hospital. Both are located in close proximity to the DACP and are the receiving hospitals for all deliveries from the nine HVMA recruitment practices. Each HVMA practice delivers all of their patients at one of the two hospitals. Quincy, Wellesley, Kenmore, West Roxbury and Post Office Square patients deliver at the Brigham and Women's Hospital; Copley, Medford and Cambridge patients deliver at the Beth Israel Deaconess Medical Center.

At each hospital, Viva has established contacts to assist with the development of the hospital protocol and the distribution of Viva materials to other staff (**Appendix D: Information for Hospital Nurses**).

## 4) **Co-investigators**

Project Viva has been developed in collaboration with a number of co-investigators and consultants from DACP and other institutions. In addition to attending project-wide meetings, these individuals have assisted with the development of study design, the data collection instruments and the analysis plan (**Appendix E: Project Viva co-investigators**).

Project Viva progress reports are sent to the co-investigators every six months. In addition, the co-investigators are expected to participate in project-wide meetings on a regular basis.

## **D. Study Design**

Project Viva is a cohort study of 6,000 pregnant women and their offspring who are members of Harvard Vanguard Medical Associates (HVMA). All participants are recruited from select HVMA practices and deliver at one of two participating hospitals. The project is funded by the National Institutes of Health, the March of Dimes Foundation and the U.S. Centers for Disease Control and Prevention.

Pregnant women are approached during their first prenatal visit (IOB) to determine eligibility.

Women must meet the following criteria to be considered eligible for Project Viva:

- Be less than 22 weeks pregnant at the time of enrollment, as defined by due date or the last menstrual period (LMP), if due date not available.
- Receive prenatal care at one of the selected HVMA practices.
- Plan on delivering at Brigham and Women's Hospital (BWH) or Beth Israel-Deaconess Medical Center (BIDMC).

NOTE: Determination of gestational age: the gestational age for the inclusion criteria is based on a patient's reported due date. The Research Assistant then calculates gestational age back from the expected due date using a pregnancy wheel. If the due date is not known, the Research Assistant calculates gestational age based on LMP. Either due date or LMP must be known for the woman to be considered eligible to participate.

Women will be considered ineligible if they meet any of the following criteria:

- Are planning to terminate the pregnancy
- Are planning to move from the local area before the end of the follow-up period
- Have multiple gestations (twins, triplet, etc.) since they will likely not be comparable to other women, and the limited number would preclude separate analyses.

If a woman is eligible, she is asked to enroll in the study by providing informed consent and completing Visit 1. We will follow participants from their first prenatal visit until six months postpartum. We will also follow their infants from birth until the six-month pediatric visit.

## **E. Study Timeline**

Project Viva will enroll approximately 6,000 subjects over a 3-year period. It is expected that, between all of the sites, there will be approximately 15 recruits per day, or 3,900 recruits per year. We expect approximately 85% of these patients (3,315) will be eligible for the study, and that 65% of the eligible participants (2,155) will enroll per year.

The recruitment numbers will be evaluated at a weekly team meeting. The team will evaluate the number of appointments held, the percentage of eligible patients met, and the percentage of patients recruited. (**Appendix F: Study Timeline**).

## **F. Participant Timeline**

Participation in Project Viva includes four visits: Visit 1 occurs after the first prenatal visit; Visit 2 occurs at 26-28 weeks gestation; Visit 3 occurs after delivery; Visit 4 occurs six months after delivery. During Visit 2, the Research Assistant asks for consent from the mother to enroll her

newborn child after delivery (Informed Consent 2). After delivery, the Research Assistant asks for consent for genetics testing (Informed Consent 3). (**Appendix G: Participant Timeline and Study Domains**).



## **SECTION II. STUDY STAFF**

### **A. Principal Investigator**

The Principal Investigator is responsible for overseeing all scientific and financial aspects of the study. He will meet regularly with all investigators to finalize the study design, monitor data collection, oversee data management, and design and direct data analyses. In consultation with all investigators, he will direct manuscript preparation.

### **B. Project Director**

The Project Director supervises study operations, including oversight of the Project Coordinator and Research Assistants in the areas of training, data collection procedures, quality control activities, and data management. She will participate in finalizing the study design with other investigators, and during the data analysis phase, will also take a lead role in data analyses and manuscript preparation.

### **C. Project Coordinator**

The Project Coordinator is responsible for hiring and training all research assistants, designing efficient systems for data collection and ensuring quality data collection. The Project Coordinator will work with the Data Manager to develop the data management system and will work with the Research Associates to develop study protocols.

### **D. Data Manager and Research Associates**

The Data Manager and Research Associates are responsible for assisting in the development of study operations. The Data Manager will be primarily responsible for overseeing data entry, data management, and quality control of the data. The Research Associates will assist primarily with data collection, including the final design of data collection instruments and, eventually, the creation of analytic data sets.

### **E. Research Assistants**

The Research Assistants are responsible for the recruitment and follow-up of Project Viva participants. The Research Assistants also assist with the development of study protocols, forms and materials. As they are hired, Research Assistants are trained in the Project Viva protocol and standardized interviewing techniques.

Each HVMA office is assigned a Research Assistant who is responsible for overseeing all aspects of Project Viva at that site. In most cases, a second Research Assistant will also be assigned to the site to provide back-up coverage.

The site Research Assistant should act as the main contact person for the site. The site Research Assistant is responsible for ensuring that all appointments are covered, that the site has Viva promotional materials, and that the Viva flyers are put into the IOB packet. The covering Research Assistant should help with recruitment if the site Research Assistant is busy. All schedules and updates should be given to the site Research Assistant who must then communicate any changes to a covering Research Assistant. The site Research Assistant must also keep track of whether there are changes in the HVMA office staffing. If any changes occur,

the Research Assistant must communicate these changes to the Data Manager (**Appendix H: HVMA Midwives at Viva sites; HVMA Physicians at Viva sites**).

Because the site Research Assistant spends a considerable amount of time at the HVMA office, s/he should be sensitive to the working environment of the site. The Research Assistant should be amicable and helpful but should not be overly chatty or disruptive. If there is down time while waiting for appointments, the Research Assistant should look occupied and professional. The Research Assistant should not read a novel or magazine in front of HVMA patients. If asked to do so, the Research Assistant may answer telephones during down time. Otherwise, the Research Assistant should identify a waiting area where the patient can be seen emerging from the exam room but where the Research Assistant will not be in the way of the HVMA staff.

All Research Assistants are given an HVMA name badge and Project Viva business card, both of which should be carried to recruits. Research Assistants should adhere to HVMA dress codes and dress professionally at all times. Blue jeans, sneakers, torn clothing, etc. should not be worn.

All Research Assistants are required to observe HPHC's video, "Protecting Patient Confidentiality," and to sign the HPHC "Policy on the Confidentiality of Information: Acknowledgement." Research Assistants should be careful not to use participant's names or identifying information when speaking with other Viva staff.

Each day, the Research Assistant should check the daily schedule for Viva appointments. Before leaving for an appointment, the Research Assistant should make sure that he/she has a sufficient supply of Acceptor Folders, Decliner Folders, Visit 2 Folders, Visit 3 Folders, and blood tubes in the recruitment binder to complete the day's appointments. (**Appendix I: Recruitment Materials, Visit 2 Materials, Visit 3 Materials**). An extra packet of recruitment and follow-up materials should be carried by the Research Assistant or left at the site in case additional recruitments arise.

Upon arrival at the HVMA practice, the Research Assistant should approach a medical assistant in the OB-GYN department to determine which room is being used by the clinician for the IOB or ROB to be attended. The Research Assistant should find a good waiting spot and be prepared to start the recruitment at any time.

## **SECTION III. PARTICIPANT RECRUITMENT**

### **A. Recruitment Strategies**

Pregnant women are approached about Project Viva at the end of their Initial Obstetrical appointment (IOB). Although Project Viva knows about IOB appointments several weeks before they occur, Project Viva is not allowed to contact women directly before the IOB because HVMA wants the clinician to be the first point of contact for newly pregnant women.

To disseminate information about the study, Project Viva therefore relies on broader publicity efforts. Project Viva has written articles about the study for the HPHC newsletter. The Research Assistants have been able to get Viva flyers placed in the HVMA elevators and Viva brochures placed in the OB waiting rooms. Some HVMA offices have Viva flyers posted in each OB exam room.

The OB staff have been helpful in providing information directly to pregnant women after an IOB is booked. They place a Viva flyer or brochure in the pre-IOB packet mailed to women (**Appendix J: Viva Flyer**) and at some sites, the Medical Assistants mention Project Viva to women when the IOB is booked (**Appendix K: Telephone Introduction**). The purpose of these publicity efforts is to alert potential recruits to set aside 5-10 minutes after the IOB to hear about the study. Few details about the study are provided at this point since the primary goal is to secure a brief meeting with the participants.

Project Viva is also publicized at the monthly Early Pregnancy Information Class (EPIC) which is attended by many pregnant women before their IOB. Project Viva Research Assistants are responsible for presenting an introductory overview of Project Viva at these classes on a monthly basis (**Appendix L: EPIC Introduction and EPIC Research Assistant Summary Form**).

### **B. Identifying Recruits**

Appointment information for all HVMA practices is stored in a single HVMA Automated Appointment System (AAS). Project Viva has been granted limited access to this system and is able to use it to identify recruitment opportunities, namely IOB appointments.

Project Viva is permitted to recruit at all IOB appointments in AAS except those appointments for women with a “restricted record” or “sensitive condition”. These appointments will appear on the schedule with an indicator of “DO NOT MEET” or a large “X”, and they should not be attended. Please note: these women are free to contact and enroll in Project Viva as long as they initiate recruitment.

Project Viva is provided with an AAS database of upcoming IOB and ROB appointment information on a bi-weekly basis. This AAS database includes complete appointment information for IOB and ROB appointments at the recruitment sites. This AAS database is imported into the Viva Data Management System (DMS) and a copy is stored in the AAS Archive. The DMS searches this AAS database for all midwife and nurse-practitioner IOB appointments and creates a schedule. When the DMS comes across appointments for women with “restricted records” or “sensitive conditions”, it will omit the appointments by printing “DO NOT MEET” by the appointments on the schedule.

At the end of every day (3:00 pm), the Data Manager confirms the next day’s appointments by comparing the DMS Viva schedule with the appointments in the “live” AAS system.

Appointments that have been canceled from AAS are deleted from the DMS. Those that have been rescheduled in AAS are deleted in the DMS. New appointments appearing in AAS (ones that have been scheduled since the AAS database was imported) are added to the schedule. The Data Manager scans all new appointments to ensure that the records are not restricted. If there is a note in AAS indicating that a woman is restricted, the Data Manager writes “DO NOT MEET” on the schedule next to the appointment.

While recruitment generally occurs at IOB appointments, recruitment may occur at a subsequent appointment. This happens if, at an IOB, the woman expresses interest in the study but does not have time to meet. The Research Assistant should assign a Decliner ID number to this recruitee, and should give the woman a brochure about the study. The Research Assistant may either ask the woman to call the study if she’d like to be met again or the Research Assistant may schedule a subsequent meeting time on the spot.

If the woman arranges to meet a Research Assistant at another appointment, the Research Assistant should obtain the woman’s list rec number (HVMA medical record number) from the medical assistant or the Data Manager. The list rec number should then be entered in the Research Assistant’s Lotus Notes calendar next to the established meeting time. If the Research Assistant enrolls the participant during the non-IOB meeting, she must complete a Deleting Decliner IDs Form, and speak to the Data Manager about converting the already-assigned ID number (**Appendix LL: Deleting Decliner IDs**).

### **C. The Recruitment Schedule**

Once the AAS database has been imported into the DMS, daily schedules can be generated by the DMS. These schedules can be generated by site or by date. Because the schedule information is updated on a daily basis, they are generally not printed for more than two days in advance. The Viva schedule includes appointment time, date, clinician, and a space for an ID label.

Each day by 3:00 p.m., The Data Manager places the next day’s schedule for each site in the Viva file cabinet (**Appendix M: Scheduling Instructions**). The Data Manager also posts the next day’s schedule with all sites on the Viva file cabinet. This schedule is marked as FINAL. After the schedule is posted, the Project Coordinator will review all appointments and assign coverage for them if necessary. A schedule for two day’s in advance is posted on the file cabinet and is marked as “DRAFT.”

Each morning, the Research Assistant should pick up his/her schedule for the day and prepare for her appointments. The Research Assistant should also check the schedule for the following day (marked “DRAFT”) to see if she needs coverage for any of her appointments. Each Research Assistant is responsible for covering all appointments at his/her assigned site in addition to any Visit 2 appointments with her initials on the schedule. If coverage is needed, the Research Assistant should make a note on the draft schedule or notify the Project Coordinator directly.

The Project Coordinator will notify the site Research Assistant in person or through voice mail if there are changes to the draft schedule. If a Research Assistant is off-site in the afternoon, she should check her voicemail between 3:00 and 4:30. If coverage is needed, the Research Assistant should contact the Project Coordinator as soon as possible.

The schedule outlines the total number of potential daily recruitments for Viva. At the end of each day, the Research Assistant should return the schedule to the file cabinet with a recruitment

status/ID number for each appointment held. If the Research Assistant is at a site, the schedule may be faxed to the Data Manager. A schedule must be received from each site by the end of each day.

If an appointment is cancelled, rescheduled or not kept, the Research Assistant should indicate this on the schedule so that the appointment can be deleted from the DMS. This ensures that the DMS keeps an accurate count of actual IOBs held each day, thus reflecting the total number of potential recruitees.

If the Research Assistant attends an appointment and is told by the clinician that the woman has miscarried or does not have a viable pregnancy, the Research Assistant should indicate on the schedule that the appointment was cancelled. Because the woman is no longer pregnant, the appointment is not an IOB, and therefore should not be included in the Viva database. The Research Assistant should not assign a decliner ID to these women.

## **Section IV. VISIT 1 (<22 weeks gestation)**

### **A. Initiation of Visit 1**

Visit 1 takes place at the time of a woman's initial obstetric appointment (IOB) with either a Certified Nurse Midwife (CNM) or a Nurse-Practitioner (NP). IOBs are also held with a physician (MD), but the MD IOBs generally occur one month after the CNM/NP IOB. Project Viva does not normally recruit from the MD IOBs.

At the end of each day, the Research Assistant should check the daily schedule for the next day's appointments marked with an "I" (IOB) and her initials and make sure that she is available to meet the appointment. If the Research Assistant is unable to meet the appointment, she should let the Visit 1 Research Associate know so that coverage can be found for the appointment (**Appendix N: Research Assistant Coverage**).

### **B. Preparing for Visit 1**

The time that appears on the schedule is the IOB start time and not the time of the Viva visit. Because CNM/NP IOB appointments generally last 60 minutes, the Research Assistant should plan to arrive at the OB department 30-45 minutes after the start time noted on the calendar.

Some women may have their MD IOB **before** the CNM/NP IOB. In these cases, the CNM/NP IOB appointment appearing on the schedule will last only 15 minutes, not the usual 60. A Research Assistant may miss these shorter IOB appointments but may recruit at them, if possible.

The Research Assistant may call the OB department before leaving for a recruitment to check if the woman has arrived for the IOB. (**Appendix O: Directions to Sites**). If the appointment is not completed the Research Assistant should note "cancelled" on the schedule if the appointment was cancelled, "rescheduled" if the appointment was rescheduled, or "DNK" (for "did not keep") if the appointment was not kept. If the woman is no longer pregnant at the time of the appointment, the Research Assistant should note "not an IOB" on the schedule.

### **C. Visit 1 Protocol (Early Pregnancy Visit)**

Research Assistants should approach recruitees leaving exam rooms after IOB appointments. In most cases, the IOB clinician will have mentioned the study to the patients before the end of the IOB. The Research Assistant should ask the recruitee if she has time to hear about the study (*see Screening Form*). If she does, the Research Assistant should escort the recruitee to a quiet, enclosed room.

If the woman does not have time to hear about the study, the Research Assistant can offer her a brochure for further information. If the woman asks the Research Assistant to meet her at her next appointment (ROB), the Research Assistant should assign the woman a decliner ID number and also fill out the top half of a deleting decliner IDs form. The Research Assistant should then place the deleting decliner form in the "Delete Decliner RA Drop-off" folder in the filing cabinet. (**Appendix LL: Deleting Decliner IDs**).

If the clinician feels that the study is not suitable for the patient, either because of eligibility criteria, because the patient has to go for an immediate ultrasound or some other reason, the clinician may notify the Research Assistant not to approach the woman. This should be coded as "22—Clinician recommendation" on the Screening Form.

Visit 1 is generally administered at a single visit (**Appendix P: Visit 1 Sequence**) but if the woman has limited time, Visit 1 may be split across several visits (**Appendix P: Alternate Visit 1 Sequence**). Alternate scenarios are documented by the Research Assistant in the study folder. For example, if the interview is conducted over the telephone, the Research Assistant should note on the EPI: “phone interview”. (**Appendix P: Recruitment Flow**).

Research Assistants should be sure to carefully follow the protocol for the Standardized Research Interview (**Section VIII.A**).

At the end of the recruitment, but while the participant is still in the room, the Research Assistant should review the Recruitment Checklist to make sure that all Visit 1 steps have been completed (**Appendix P: Recruitment Checklist**).

#### **D. Visit 1 Forms**

##### **1) Screening (SCR1)**

The Research Assistant should administer page 1 of the Screening Form to determine the woman’s interest in participating in Project Viva. If the woman is interested in the study and has time to determine eligibility and review consent (page 1 successfully completed), the Research Assistant should proceed to page 2 and determine the woman’s eligibility status.

After the Screening Form has been administered, the Research Assistant should either proceed to the Consent form (Acceptor) or thank the woman for her time (Decliner). The final enrollment status, as well as perceived race of the participant, should be coded on page 3 of the Screening Form after the visit is completed.

##### **2) Informed Consent (CON)**

The Research Assistant should give the woman a copy of the Informed Consent and read the Informed Consent script to describe the study in greater detail (**Appendix Q: Informed Consent Script**). After the Research Assistant has answered questions, she should sign two copies of the Informed Consent 1, and ask the recruitee to sign both copies.

If the recruitee intends to deliver at Beth Israel Deaconess Medical Center, or if she is planning to deliver at Brigham and Women’s Hospital but does not consent for cord blood collection, the Research Assistant should cross out the section under “For women delivering at Brigham and Women’s Hospital” and write her initials and the date next to the section. These participants should be assigned a status of 41 on page three of the Screening Form. If the recruitee is delivering at Brigham and Women’s Hospital but does not consent for cord blood collection, the Research Assistant should also itemize the exclusion on an Informed Consent Form Addendum (see *Informed Consent Form Addendum*).

NOTE: If a participant withdraws her consent for cord blood collection at any time after recruit and before delivery, the Research Assistant should notify the Research Assistant in charge of filing cord blood flyers at Brigham and Women’s Hospital as soon as possible.

Other exclusions may also be noted on the Consent Form Addendum but Visit 1 Research Associate should be notified of these cases.

After Informed Consent 1 is signed, the patient is considered enrolled in the study. One copy of the Informed Consent document (and Addendum, if applicable) should be given to the

participant; one copy must be kept for the study files. Informed Consent Form Addendums should be stapled to Informed Consent Forms for filing.

After the Consent Form is completed, the Research Assistant should complete the remainder of Visit 1. All completed forms should be placed in the Acceptor Folder.

**IMPORTANT:** We can not collect any data from women who have not signed the Informed Consent form. If a recruitee would like to take the consent form home to think about participating, the Research Assistant should give the recruitee a copy of the form and a Viva brochure to take home. A recruitee is **not enrolled** unless she has signed the consent form, and therefore she should be given a Decliner ID for this recruit.

### **3) Early Pregnancy Interview (EPI1)**

After consent has been obtained, the Research Assistant should proceed to administer the EPI1. The entire interview is to be administered during a single appointment. The Research Assistant should note on the top of the EPI if another person, for example a husband or partner, is in the room at the time the EPI is administered. For further information about conducting a research interview, the Research Assistant should refer to the protocol for standardized research interviews (**Section VIII.A**).

If the Research Assistant is not able to complete the EPI1 at the time of recruitment, it may be administered over the telephone. If an interview is conducted over the phone, the Research Assistant should make a note of this on the EPI1, and note the date of the interview, not of the visit, as the event date on the label. Interviews conducted after the recruitment date (either by phone or at a subsequent appointment) should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**) and logged in DMS.

If the interview is not conducted at the time of the recruitment, the Research Assistant must still ask two questions on the EPI1 at the time of recruitment, Date of Birth (QA1) and Date Learned Pregnant (QE1). The Research Assistant must then transcribe these fields to other forms. Date of birth will be noted on the blood tubes and Blood Delivery Log, and “Date Learned Pregnant”, along with the LMP from Screener, must be transcribed to the FFQ1 and EPI.

### **4) Early Pregnancy Supplement (EPS1)**

The EPS1 should be given to the participant after the interview has been completed. The Research Assistant must read the instructions at the top of the page verbatim. It should be completed on the spot, while the Research Assistant prepares the other recruitment forms. Because of the sensitive nature of the questions on the form, if questions on the EPS1 are left blank the Research Assistant should not give the form back to the woman to complete. For questions that are left blank, the Research Assistant should write “-9 blank,” the date, and her initials next to each blank question.

If the interview is not conducted at the time of recruitment, the EPS1 may be sent home with the EPQ1 and FFQ1.



## 5) **Locator Form (LOC1)**

The Research Assistant should administer the LOC1 at the time of recruitment. The Locator form collects information that will allow the Research Assistant to contact the participant in the future by phone, mail and e-mail.

The entire LOC1 must be completed at the time of a recruitment, regardless of whether the EPI has been administered.

## 6) **Early Pregnancy Questionnaire (EPQ1)**

At the end of the recruitment, the Research Assistant should place the EPQ1 in the Participant Folder and request that the participant complete the form within two weeks and mail it back to the study PO Box (**Appendix P: Participant Folder Script**). A Business Reply Envelope is provided for this purpose.

Two EPQ1 items may need to be modified before the EPQ1 can be placed in the folder:

- If the participant is less than 18 years old, B8b (pg. 7) and C4b (pg. 9) should be crossed out.
- If the EPQ is version 01/01/2000 or earlier, page 11 should be torn out for all participants.

Note: Prior to 1/23/02, the protocol was as follows: For a full Visit 1, if the participant's race was "White"; "Other"; or "White and Other" ONLY, page 11 was torn out. For an abbreviated Visit 1, when the EPI1 had not been conducted, the Research Assistant would tear out page 11 if the perceived race from the SCR1 was "White or Caucasian".

## 7) **Early Pregnancy Food Frequency Questionnaire (FFQ1)**

At the end of the recruitment, the Research Assistant should place the FFQ1 in the Participant Folder and request that the participant complete and return the form within two weeks. Before the FFQ1 can be placed in the Participant Folder, the Research Assistant must transcribe several dates onto the FFQ1 and review the instructions at the top of the FFQ1 with the participant. The participant's LMP should be transcribed to page 1 of the FFQ1, 3 months before date learned pregnant should be transcribed to page 15 of the FFQ1, and date learned pregnant should be transcribed to pages 15 and 17 of the FFQ1. The form can be mailed back to the study post office box (**Appendix P: Participant Folder Script**). A Business Reply Envelope is provided for this purpose.

If the participant is more than 18 weeks pregnant, the Research Assistant should not give the participant the FFQ1. The Research Assistant should write "Set to Missing, > 18 weeks, was not given" on the form, initial and date the form, and leave it in the acceptor folder. When the forms are data entered, the FFQ1 will be set to missing. The Research Assistant should write ">18 weeks, was not given" as the reason.

## 8) **Early Pregnancy Blood Form (BLD1)**

This form should be completed regardless of whether blood is drawn. If the participant agrees to have blood drawn for the study, the blood form should be partially completed at the time of recruitment, and then fully completed later in the day when the Research Assistant can confirm the number of tubes drawn. If the participant does not agree to have blood drawn for the study, the Research Assistant should complete the entire blood form at the time of recruitment and note the reason why blood is not being drawn.

## 9) Early Pregnancy Primescreen Interview (EPP1)

The Research Assistant should attempt to complete this form if four weeks have passed since the recruitment, and the FFQ has not yet been received. The EPP1 is a shorter version of the FFQ, which should be administered over the phone or at a subsequent visit when the FFQ is set to missing.

If the Research Assistant is able to contact the participant to conduct the Early Pregnancy Primescreen Interview, she should administer the EPP1 and then log the form in the DMS. Interviews conducted either by phone or at a subsequent appointment should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

The Research Assistant should try to contact the participant to administer the Early Pregnancy Primescreen Interview for four weeks. After this time, the Research Assistant should set the form to missing in the DMS.

### E. Visit 1 Follow-up

If the Viva materials are not sent back to the study, the recruiting Research Assistant should follow up with the participant. Call logs are printed on a daily basis to assist Research Assistants in keeping track of Visit 1 follow-up (**Appendix R: Printing Call Logs**). Each day, the Research Assistant should check her personal file (green hanging file) in the file cabinet for any new call logs.

The timeline and steps for Visit 1 follow-up are as follows:

- 10 days after recruitment, the Research Assistant should call the participant to follow-up on FFQ1/EPQ1 if they have not yet been received. The Research Assistant should continue calling the participant until she is able to speak to her.
- 16 days after recruitment, the Research Assistant should hand-write a reminder note on a Viva notecard if the FFQ1/EPQ1 have not yet been received.
- 25 days after recruitment, the Research Assistant should call the woman to follow-up on FFQ1/EPQ1 if they have not yet been received. During this call, the Research Assistant should suggest to the participant that she send in one of the forms (EPQ1) if possible, and then bring the other form (FFQ1) to her next appointment.
- Four weeks after recruitment, if the FFQ1 has not yet been received, the Research Assistant should set the form to missing in the DMS, and should call the participant to administer the Early Pregnancy Primescreen Interview.

Text has been written for each of the follow-up calls and letters (**Appendix R: Follow-up Contacts**). The Research Assistants should not leave messages on answering machines or with other people in the household unless they are asked to do so by the participant. If the Research Assistant is pressed to identify herself to someone else answering the phone, the Research Assistant should acknowledge affiliation with HPHC but should not mention Project Viva or pregnancy.

The Research Assistant may also pursue other strategies to get the forms back from the participant. The Research Assistant may suggest that the participant leave the form in the OB department at her next ROB. If a Research Assistant receives Visit 1 forms at a site after the

recruitment date, she should enter the forms into the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**). The Research Assistant may also attempt to contact the participant via e-mail to remind her to complete and return her questionnaires.

If the participant says that she lost the forms, the Research Assistant may offer to mail her another set of questionnaires. If a Research Assistant needs to mail a participant another set of forms for any reason, she should put the date that she mailed the new questionnaire on the label, not the date of the original visit.

If the Research Assistant has not been able to contact the participant, she should submit an AAS request to find out when the participant's next ROB is and should note that appointment on her personal calendar. If the questionnaires do not come back before that date, the Research Assistant should plan to go to the ROB and try to connect with the participant. The Research Assistant should bring additional questionnaires (and necessary dates – LMP and Date Learned Pregnant) to the ROB in case the participant needs another copy. If the questionnaires are received before the ROB, the Research Assistant should cross this appointment off of her personal calendar and not plan to meet the participant.

When the FFQ1 or EPQ1 is received the Research Assistant should note on the call log that the forms were received and place the call log in the "Call Logs" file in the filing cabinet. After the FFQ1 and EPQ1 are logged in the DMS a thank you letter is sent with a \$20 gift card to CVS. (**Appendix S: Printing and Sending Thank You Letters**).

The Research Assistant should try to get the forms back during the four weeks following recruitment. After this time, the Research Assistant should set the forms to missing in the DMS. Forms set to missing can later be data entered if they are received.

If the FFQ1 is set to missing, the Research Assistant should attempt to contact the participant to administer the Early Pregnancy Primescreen Interview (**Appendix R: Early Pregnancy Primescreen Call**). The Research Assistant should try to contact the participant to administer the Early Pregnancy Primescreen Interview for four weeks. After this time, the Research Assistant should set the EPP1 to missing in the DMS.

## **Section V. VISIT 2 (26-28 weeks gestation)**

### **A. Initiation of Visit 2**

Visit 2 takes place at a participant's prenatal visit during her sixth month of pregnancy. Ideally, a participant is met between her 26<sup>th</sup> and 28<sup>th</sup> week of pregnancy. If this is not possible, she may be met before this or up until the time of delivery. Because Visit 2 includes a blood draw, Research Assistants should try to meet the participant at the time of her glucose challenge test ("diabetes test"). The diabetes test typically consists of a woman taking a drink, waiting for an hour, and then having her blood drawn. This may or may not be scheduled in conjunction with a 15 minute ROB appointment. If it is not possible to meet the participant at the time of her diabetes test (i.e., the participant has already had it or has not planned it), the visit can take place in the OB department at the time of another ROB appointment.

Project Viva has a newsletter, Viva Views, which is intended to remind the participant about Visit 2 and to encourage her to call the Research Assistant to set up a meeting time for Visit 2. Viva Views is sent to each participant during her 22<sup>nd</sup> week of pregnancy.

The Research Assistant who recruited the participant is responsible for scheduling, though not necessarily conducting, the Visit 2 appointment. A Visit 2 Control Sheet (VCS) is produced by the DMS to help Research Assistants keep track of scheduling these appointments (**Appendix R: Printing Visit 2 Control Sheets**). Each day the Research Assistant should check her personal file in the file cabinet (green hanging folder) for a VCS for each participant who is eligible for Visit 2. A participant is considered eligible if she has an ROB scheduled between her 25<sup>th</sup> and 29<sup>th</sup> week of pregnancy. The VCS includes the participant's first name, Viva ID number, phone number, ROB appointment date/time, V1 form statuses, space to log contacts made, and a space to write in the scheduled Visit 2 meeting time.

The Research Assistant should note the details of all phone calls on the VCS (**Appendix R: Completing Visit 2 Control Sheets and Sample Visit 2 Control Sheets**). As with Visit 1, messages should not be left on answering machines or with people other than the participant, unless the Research Assistant has been instructed to do so by the participant.

If the Research Assistant is able to speak to the participant, a Visit 2 meeting time should be established. Once a Visit 2 meeting has been set up, it should be noted at the bottom of the VCS and on the Research Assistant's personal calendar. The appointment should be noted at the bottom of the VCS in pencil, in case the visit is not done and another visit needs to be scheduled. The Research Assistant should then manually enter the appointment into the DMS (**Appendix M: Scheduling Instructions**). Finally, the Research Assistant should go to the participant's ID number in the DMS, type COMM in the box on the bottom, left-hand corner of the screen, and enter the details of the appointment in the comment box that appears. This should include the appointment date, time, location (clinician name or "lab") and whether or not the appointment is a glucose visit. The comment should be dated and initialed.

If the scheduled appointment is different from the one in the "Visit Information" section of the VCS, the Research Assistant should delete the old appointment from the DMS (**Appendix M: Deleting Appointments from the DMS**).

If the Research Assistant is not able to contact the participant to schedule a meeting time, the Research Assistant should plan to meet the participant at the appointment appearing in the "Visit

Information Section” of the VCS. If this appointment does not appear on the daily calendar, the Research Assistant should not go to the appointment, and should continue to follow-up with the participant to schedule a time to meet. If the Research Assistant is unable to contact the participant to schedule another appointment, she may submit an AAS Request form to the Data Manager to find out the participant’s next ROB (**Appendix NN: AAS Request Form**).

The Visit 1 Research Assistant should cover appointments that she can easily attend. Each day, each Research Assistant should check the next day’s schedule for appointments marked with an “R” (ROB) to make sure that she is available to cover the Visit 2 appointments for participants she recruited (with her initials on the schedule). If the Visit 1 Research Assistant can not cover a Visit 2 appointment, the Visit 1 Research Assistant should let the Data Manager know, so that coverage can be found. (**Appendix N: Research Assistant Coverage**).

After the Visit 2 has been completed, the Visit 2 Visit Control Sheets are given to one Research Assistant who compiles centralized contact information for the study.

## **B. Preparing for Visit 2**

For Visit 2, the Research Assistant should plan to arrive at the OB department at the time that appears on the schedule. This may be the time of a participant’s ROB or it may be the start time of a Viva visit.

Visit 2 packets are prepared for all participants who have received Viva Views (**Appendix T: Compiling Visit Materials**). Before going to a Visit 2, the Research Assistant should check either the VCS or the Visit 1 folder to confirm the status of Visit 1 forms. If the EPI1, the EPQ1, or the EPS1 is “Missing”, the Visit 2 packet should include the appropriate Abbreviated Form/s to be administered at Visit 2.

If a Research Assistant is covering a Visit 2 for someone, the covering Research Assistant should check the ‘COMM’ field in the DMS to determine whether the participant is expecting to meet with someone. The ‘COMM’ field may also be used to learn when and where the participant is expecting to meet.

The Research Assistant should bring the VCS to a Visit 2.

## **C. Visit 2 Protocol (Mid-Pregnancy Visit)**

The Research Assistant should approach the participant at the meeting place listed on the schedule. If the schedule reads “LAB, LAB” the Research Assistant should meet the participant at the site lab.

If Visit 2 has not been scheduled with the participant, the Research Assistant should ask a medical assistant in the OB-GYN department which room is being used by the clinician for the ROB. The Research Assistant should approach the participant at the end of the visit and reintroduce herself to the participant (**Appendix U: Visit 2 Introduction**).

If the participant is able to meet, the Research Assistant should escort her to a quiet, enclosed room and arrange two chairs to face each other. If the woman is with a partner, the Research Assistant should ask the partner if he/she would mind waiting outside while the interview is conducted. If the partner does not want to leave, the Research Assistant should not insist but rather should just proceed with the visit. If the partner remains in the room for the interview, this

should be noted on the PSS2 as the reason the PSS2 was not administered, and the PSQ2 should not be administered.

If the participant cannot meet for Visit 2 at this time, the Research Assistant should make a note of this on the VCS and schedule another time to meet. The Research Assistant should give the participant the take-home questionnaires to complete and bring to the scheduled Visit 2.

If the questionnaires are given to the participant, or if any Visit 2 form is filled out (BLD2, LOC2), the Visit is “Met” and an ID label should be affixed to the daily schedule. If a Visit 2 is “Met”, the label on the folder should be filled out, with the event date equal to the date on the label affixed to the schedule.

If only the take-home questionnaires are given to the participant, and none of the forms in the folder are completed, the folder should be returned to the Visit 2 “To Go” section of the file cabinet and the VCS should have a note indicating the new Visit 2 appointment. The Research Assistant should add the new appointment to the COMM field of the DMS and to her personal calendar.

If the participant does not keep her scheduled appointment, or if the Research Assistant does not give the participant the questionnaires and does not complete any forms, the appointment is “Not Met” and the Research Assistant should NOT affix an ID label to the daily schedule. In this case, the Research Assistant should note on the schedule why the appointment was Not Met (i.e. DNK, rescheduled, missed). If the appointment is rescheduled, the Research Assistant should note the new appointment date on the VCS again in pencil, should return the Visit 2 folder to the “To Go” section of the file cabinet, and should enter the new appointment information into the schedule and COMM of the DMS.

Visit 2 is generally administered at a single visit (**Appendix U: Visit 2 Sequence**). Any variations from the Visit protocol should be documented by the Research Assistant in the study folder. At the end of the visit, the Research Assistant should review the Visit 2 Checklist to make sure that all Visit 2 steps have been completed (**Appendix U: Visit 2 Checklist**).

#### **D. Visit 2 Forms**

##### **1) Locator Update (LOC2)**

The Locator Update initiates Visit 2.

The Mid-Pregnancy visit includes a separate Locator Form to update our contact information, and obtain the name and phone number of a close friend or relative who does not live with the participant.

##### **2) Mid-Pregnancy Interview (MPI2)**

If the Research Assistant is not able complete the MPI2 at the time of recruitment, it may be administered over the telephone. If an interview is conducted over the phone, the Research Assistant should make a note of this on the MPI2, and note the date of the interview, not of the visit, at question II. If the Research Assistant administers an MPI2 on a date other than the Visit 2 event date (by phone or at a subsequent ROB) the MPI2 should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**). If it is completed by phone on the same day as the Visit 2 event date, it does not need to be entered into the log.

At the end of Visit 2, the Research Assistant should make sure to code the status of child consent (Y, N, NY) on the front of the MPI2. In addition, if there are any Addendums to child consent (see below) this should be noted on the front of the MPI2.

### 3) **Informed Consent (CONC)**

The Research Assistant should describe what the child's participation in Project Viva would entail in greater detail to the participant (**Appendix V: Informed Consent (Child) Script**) and then ask the participant to read the Informed Consent (CONC). After the Research Assistant has answered questions, she should sign two copies of the CONC and ask the participant to sign both copies. The CONC should be filled in with "Child of [*participant's first and last name*]" on the first and last page of the form.

If the participant would like to have her child enrolled in the study, but does not give consent for certain aspects (measurements, blood pressure, VRM) of the study, two copies of the Informed Consent Form Addendum should be completed. Note "Child of [*participant's first and last name*]" on the Member's Name line, and modify the addendum line at the bottom to read: "I agree to have my child participant in Project Viva..."

If an addendum is completed, the Research Assistant should note "CCFA" on the top of the MPI2 to indicate that there is a Child Consent Form Addendum. The items to be excluded should be crossed out and initialed by the participant on the Consent Form.

One copy of the Informed Consent 2 document (and addendum, if applicable) should be given to the participant; one copy must be kept for the study files. After the Consent Form is completed, the Research Assistant should complete the remainder of Visit 2.

### 4) **Personal Safety Screening Form (PSS2)**

After completing the Mid-Pregnancy Interview, the Research Assistant should administer the PSS2. Because of the sensitivity of the questions in the PSQ2, the Research Assistant should only administer the PSS2 to a participant who is alone. If a spouse or partner (or other family member or friend) refuses to leave the participant alone in the room, the Research Assistant should not administer the PSS2, and should mark NO-PERA on question IV. If the woman is with a child older than 1 year (verbal), the PSS2 should be still be administered, but the Research Assistant should automatically have the questionnaire be self-administered.

If a participant interrupts the PSS2 before question A2, the Research Assistant should give her the Resource Card. Other participants proceeding to the PSQ2 should be given the Resource Card at the end of the PSQ2 (**Appendix W: Scripts for Personal Safety Questionnaire**).

### 5) **Personal Safety Questionnaire (PSQ2)**

After completing the PSS2, the Research Assistant should administer the PSQ2. Depending on a participant's response to QA2 on the PSS2, the PSQ2 should be either self-administered or interviewer-administered.

All Research Assistants are trained on administering the PSQ and should refer to **Section VIII.B** for further information.

**6) Mid Pregnancy Questionnaire (MPQ2)**

In some cases, the participant will have completed the MPQ2 before Visit 2, and will bring it to the visit to give to the Research Assistant.

If the participant did not bring the completed MPQ2 to the visit, the Research Assistant should give it to her at the end of the visit to complete and return. A Business Reply Envelope is provided for this purpose.

If the participant is having her glucose test done, and has time to wait after the Visit 2, the Research Assistant should ask the participant to complete the questionnaire while she waits for her blood draw.

**7) Mid Pregnancy Food Frequency Questionnaire (FFQ2)**

In some cases, the participant will have completed the FFQ2 before Visit 2, and will bring it to the visit to give to the Research Assistant.

If the participant did not bring the completed FFQ2 to the visit, the Research Assistant should give it to her at the end of the visit to complete and return. A Business Reply Envelope is provided for this purpose.

The Research Assistant should review the instructions at the top of the FFQ2 with the participant.

If the participant is having her glucose test done, and has time to wait after the Visit 2, the Research Assistant should offer the participant a pencil, and ask her to complete the FFQ2 while she waits for her blood draw.

**8) Mid-Pregnancy Blood Form (BLD2)**

This form is to be completed regardless of whether blood is drawn or not. It is partially completed at the time of the blood draw and then fully completed later in the day when the Research Assistant can confirm the number of tubes drawn.

**9) Abbreviated Forms**

If the EPI1, EPQ1 or EPS1 was not completed at Visit 1, the Research Assistant should attempt to get abbreviated versions of these forms at Visit 2. When the forms are being compiled for Visit 2, the Research Assistant will check the Visit 1 folder for form status and add the appropriate forms to the Visit 2 folder.

**a) Abbreviated Early Pregnancy Interview (EPI2)**

If the EPI1 was not completed at Visit 1, the EPI2 should be administered at Visit 2. It should be administered before the MPI2. If the EPI2 is administered, the Research Assistant should not read the introductory instructions on the MPI2.

**b) Abbreviated Early Pregnancy Questionnaire (EPQ2)**

If the EPQ1 was not completed at Visit 1, the EPQ2 should be given to the participant to complete during Visit 2. The Research Assistant should give the participant the EPQ2 before the PSQ2.

One EPQ2 item may need to be modified before the EPQ2 can be given to the participant:

- If the participant is less than 18 years old, B4b (pg. 4) should be crossed out



c) **Abbreviated Early Pregnancy Supplement (EPS2)**

If the EPS1 was not completed at Visit 1, the EPS2 should be given to the participant to complete during Visit 2. The EPS2 should be an interviewer-administered question at the end of the EPI1 or the MPI2.

**E. Visit 2 Follow-up**

If the Viva materials are not sent back to the study, the Visit 2 Research Assistant should follow up with the participant. Call logs are printed on a daily basis to assist Research Assistants in keeping track of Visit 2 follow-up (**Appendix R: Printing Call Logs**). Each day, the Research Assistant should check her personal file (green hanging file) in the file cabinet for any new call logs.

The timeline and steps for Visit 2 follow-up are as follows:

- 10 days after Visit 2, the Research Assistant should call the woman to follow-up on FFQ2/MPQ2 if they have not yet been received. The Research Assistant should continue calling the participant until she speaks with her.
- 16 days after Visit 2, the Research Assistant should hand write a reminder note on the Viva Card if the FFQ2/MPQ2 have not yet been received.
- 25 days after Visit 2, the Research Assistant should call the woman to follow-up on FFQ2/MPQ2 if they have not yet been received. During this call, the Research Assistant should suggest to the participant that she send in the one of the forms (MPQ2) if possible, and then bring the other form (FFQ2) to her next appointment.

Text has been written for each of the follow-up calls and letters (**Appendix X: Visit 2 Follow-up Contacts**). The Research Assistants should not leave messages on answering machines or with other people in the household unless they are asked to do so by the participant. If the Research Assistant is pressed to identify herself to someone else answering the phone, the Research Assistant should acknowledge affiliation with HPHC but should not mention Project Viva or pregnancy.

The Research Assistant may also pursue other strategies to get the forms back from the participant. At the time of the Visit 2, the Research Assistant should ask the participant when her next appointment is, and should note it in the Research Assistant's personal calendar. If the questionnaires do not come back before that time, the Research Assistant should plan to go to the ROB and try to connect with the participant. The Research Assistant should bring additional questionnaires to the ROB in case the participant needs another copy. If the questionnaires are received before the ROB, the Research Assistant should cross this appointment off of her personal calendar and not plan to meet the participant.

The Research Assistant may suggest that the participant leave the form in the OB department at her next OB appointment. If a Research Assistant receives Visit 2 forms at a site after the Visit 2 date, she should enter the forms into the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

If the participant says that she lost the forms, the Research Assistant may offer to mail her another set of questionnaires. If a Research Assistant needs to mail a participant another set of

forms for any reason, she should put the date that she mailed the new questionnaire on the label, not the date of the original visit.

The Research Assistant should try to get the forms back during the four weeks following Visit 2. After this time, the Research Assistant should set the forms to missing in the DMS.

When the FFQ2 or MPQ2 is received (logged in the DMS), a thank you letter is sent with a \$5 gift certificate from Babies R Us. (**Appendix S: Printing and Sending Thank You Letters**).

## **Section VI. VISIT 3 (Post-Delivery)**

### **A. Initiation of Visit 3**

Visit 3 takes place in the hospital after a participant has delivered. Visit 3 includes a brief interview with the mother and measurements of her newborn. The measurements that are taken include head, chest, and abdominal circumferences using a tape measure, length using a Shorr Length Board, and blood pressure using a Dinamap automated blood pressure recorder. The Visit 3 interview takes approximately 10-15 minutes and the measurements of the newborn take approximately 25-30 minutes to complete. Because measurements need to be consistent, only a few Research Assistants cover Visit 3 appointments (**Appendix N: Research Assistant Coverage**).

To keep track of Viva participants who are approaching their delivery, the DMS generates a Viva Delivery Log. The Delivery Log is a list of participants who are more than 24 weeks pregnant and have not yet had a Visit 3. Each week, an updated Delivery Log is printed (**Appendix PP: Printing the Viva Delivery Log**). The Research Assistant who prints the new list should give the old list to the Data Manager, who will check AAS for participants who are more than 42 weeks pregnant to see if they are still expected to deliver or if they are no longer in the system. The Data Manager will disenroll participants who are no longer in AAS.

Participants who are planning to deliver at Brigham and Women's Hospital and have consented to having their cord-blood collected will have a purple cord blood flyer placed in their obstetric admissions folder at Brigham and Women's Hospital when they are 26 weeks pregnant. This is to alert the physicians and midwives that cord blood should be collected (**Appendix Y: Printing and Distributing Cord Blood Flyers**).

The hospital Research Assistants are responsible for completing several tasks each morning to initiate the third Viva visit. These tasks are outlined below. As each task is completed, the Research Assistant should initial the V3 checklist on the file cabinet to indicate to the other hospital Research Assistants what has been completed and what still needs to be done each morning (**Appendix PP: Sample V3 Tasklist**).

#### **1) Receiving and Printing the Birth Logs**

Each morning, the birth log is faxed from the Brigham and Women's Hospital for the previous 24 hours. The Beth Israel Deaconess Medical Center birth log is printed by a Research Assistant each morning (**Appendix PP: Printing the Beth Israel Birth Log**). The Research Assistant should initial and stamp the date received or the date printed on both of the logs (**Appendix PP: Receiving the BWH Birth Log**).

#### **2) Checking the Birth Logs**

The Hospital Research Assistants are responsible for checking the birth logs each morning in order to find out if a participant has delivered. Each morning, a Research Assistant should get the Viva Delivery Log from the Viva Birth Log Binder, and compare the first and last name of each woman on the hospital birth log with the first and last name of each participant on the Viva Delivery Log. If there is a match in the first and last names, the Research Assistant should check the gestational age on the Viva Delivery Log. If the gestational age is more than 30 weeks, the Research Assistant should assume this is a Viva delivery. If the woman is less than 30 weeks

pregnant, the Research Assistant should ask the Data Manager to check AAS to see whether the woman who delivered is a Viva participant (**Appendix PP: Comparing the Viva Delivery Log and the Hospital Birth Log**).

If a Viva participant has delivered at either hospital, the Research Assistant should complete the Viva Delivery Log by filling in the delivery date, the hospital, the room number, and both the mother and newborn's hospital ID numbers. The Research Assistant should then initial and date the hospital Birth Logs to indicate that they have been compared with the Viva Delivery Log.

The Research Assistant should then schedule a hospital visit for each participant that has delivered by manually entering the appointment into the DMS. The Research Assistant should print out the daily schedule for each hospital, if appropriate, using the Appointment System Menu in the DMS. The Research Assistant should then put the schedule in the red pre-visit hanging file (**Appendix M: Scheduling Instructions**). At this point, the Birth Logs and Delivery Log should be placed in the Birth Log binders, with the most recent logs on top, and the binders should be returned to the locked file cabinet.

The Research Assistant should print out a Visit Control Sheet (VCS) for each new delivery scheduled (**Appendix PP: Printing Visit 3 Control Sheets**). The VCS should be sorted by hospital and placed in the hospital hanging files in the top of the file cabinet. The hospital Research Assistants are responsible for checking the hospital hanging files each morning to see if there are deliveries that need to be covered.

### **3) BWH Deliveries**

If a Viva participant delivered at Brigham and Women's Hospital, the Research Assistant should check the DMS to see if the participant has a recruitment status of "40" in question C1 of the SCR1. If the participant has a status of 40, they gave consent for cord blood collection. The Research Assistant should send an email to Jody Senter at Channing Lab with the names of all the participants who delivered at Brigham and Women's Hospital and who gave consent for cord blood collection. The email should include the participant's name and delivery date (**Appendix PP: Comparing the Viva Delivery Log and the Hospital Birth Log**).

#### **B. Preparing for Visit 3**

For Visit 3, the Research Assistant should plan to go to the hospital before visiting hours start. The Beth Israel Hospital visiting hours are from 2-8 p.m. everyday. The Brigham and Women's Hospital visiting hours are from 1-8 p.m. everyday.

There are two separate folders for Visit 3, one for the mom and one for the child. Visit 3 folders are prepared for all Viva participants who have had a Visit 2 or are close to their delivery date, and for all children of participants who have a logged child consent form (**Appendix T: Compiling Visit Materials**).

The Research Assistant should take a complete mom's folder, child's folder, and two Viva onesies (one of each size) to the hospital. The VCS should be placed in the mom's folder. The other materials the Research Assistant needs for a Visit 3 should be at the hospital inside the measuring cart. The measuring cart should be stocked weekly by the primary hospital research assistant (**Appendix I: Visit 3 Materials**).

### C. Visit 3 Protocol (Post-Delivery Visit)

To make sure that the infants are secure in the hospital, the hospitals have various security precautions that must be followed by the Research Assistants. Because Research Assistants are working with mothers and infants (and other family members) in the hospital, it is important that all Research Assistants follow the outlined security procedures carefully (**Appendix OO: Infant Security**).

At both hospitals, the Research Assistant should check in with the nurse taking care of the participant before meeting with the participant. If the Research Assistant cannot locate the nurse, then she should check in with the nurse in charge of that floor. There is one nurse in charge of each floor at the Brigham and Women's Hospital. If the nurse gives approval, the Research Assistant should proceed to the participant's hospital room.

The Research Assistant should (re)introduce herself to the participant and give the participant the Viva onesie. The Research Assistant should then remind the participant of what Project Viva entails and ask if it would be a good time to conduct a brief interview (**Appendix QQ: Visit 3 Introduction in the Hospital**). If the participant is able to meet, the Research Assistant should conduct the interview (LOC3, DEI3, DES3, PSS3, and PSQ3). After the PSQ, the Research Assistant should review the Child Consent form with the participant.

If the participant is with her partner, the Research Assistant should ask the partner if he/she would mind waiting outside while the interview is conducted. If the partner does not want to leave, the Research Assistant should not insist, but rather should just proceed with the visit. If the partner remains in the room for the interview, this should be noted on the PSS3 as the reason it was not administered, and the PSQ3 should not be administered.

If the participant cannot meet for Visit 3 at this time, the Research Assistant should note "rescheduled" on the VCS and daily schedule, and should schedule another time to meet. If appropriate, the Research Assistant may review the child consent form with the participant and ask if it would be okay to proceed with the newborn measurements.

The newborn measurements can be done in the mother's room or in the nursery. Research Assistants should be sure to carefully follow the protocol for the Newborn Blood Pressure measurements, and the Newborn Head, Chest, and Abdominal Circumference, and Length measurements (**Section VIII.F and Section VIII.G**).

If a participant informs a Research Assistant at the hospital that she would like to disenroll from the study, the Research Assistant should write "Disenroll" on the schedule. The Visit 3 appointment will be cleared as disenrolled, and a Disenrollment Form (DIS) will be expected for Visit 3. The Research Assistant should complete a Disenrollment Form upon returning to the office, with "03" as the event date. This should be noted in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**), data entered, and filed in the Visit 3 folder.

Visit 3 is generally administered at a single visit. Any variations from the Visit protocol should be documented by the Research Assistant in the study folder. At the end of the visit, the Research Assistant should review the Visit 3 Checklist to make sure that all Visit 3 steps have been completed (**Appendix QQ: Visit 3 Checklist and Visit 3 Measurement Checklist**).

## **D. Visit 3 Forms**

### **1) Visit 3 Locator Form (LOC3)**

The Visit 3 Locator Form initiates Visit 3.

The Delivery visit includes a separate Locator Form to update our contact information, obtain the name and phone number of a close friend or relative who does not live with the participant, and obtain information about the newborn's health care.

If the Research Assistant is not able to complete the LOC3 while the participant is still in the hospital, the Research Assistant should call the participant one week after her delivery to administer the LOC3 by telephone. If a LOC3 is conducted over the phone, the Research Assistant should make a note of this on the form, and should note the date of the phone call, not of the visit, at question II. If the Research Assistant administers a LOC3 at a time other than the Visit 3 date, the LOC3 should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

### **2) Delivery Interview (DEI3)**

The Delivery Interview (DEI3) should be completed with the participant in a private room in the hospital. If an adult (non-hospital personnel) is in the room when the DEI3 is administered, this should be noted on the top of the interview.

If the Research Assistant is not able complete the DEI3 while the participant is still in the hospital, the Research Assistant should call the participant one week after her delivery to administer the DEI3 by telephone. If an interview is conducted over the phone, the Research Assistant should make a note of this on the DEI3, and note the date of the interview, not of the visit, at question II. If the Research Assistant administers a DEI3 at a time other than the Visit 3 date, the DEI3 should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

### **3) Delivery Supplement (DES3)**

The Delivery Supplement (DES3) should be given to the participant after the Delivery Interview has been completed. It should be completed on the spot, while the Research Assistant prepares the other Visit 3 forms. If questions on the DES3 are left blank, the Research Assistant should not give the form back to the woman to complete because of the sensitive nature of the questions on the DES3.

If it is not possible for the participant to self-administer the DES3, the Research Assistant may administer the DES3 in the hospital. In this case, the Research Assistant should be sure to use the response card for question A1.

If the DES3 is not conducted at the hospital, the Research Assistant should write "set to M – not given" on the top of the form and leave it in the Visit 3 folder. When the form is data entered, it will be set to missing with "not given" as the reason.

### **4) Personal Safety Screening Form – Visit 3 (PSS3)**

After completing the Delivery Interview, the Research Assistant should administer the PSS3. Because of the sensitivity of the questions in the PSQ3, the Research Assistant should only administer the PSS3 to a participant who is alone. If a spouse or partner (or other family member

or friend) refuses to leave the participant alone in the room, the Research Assistant should not administer the PSS3, and should mark NO-PERA on question IV. If a member of the hospital personnel is in the room, or if the room is being shared with another patient, the PSS3 should still be administered, but the Research Assistant should automatically have the questionnaire be self-administered.

If a participant interrupts the PSS3 before question A2, the Research Assistant should give her the Resource Card. Other participants proceeding to the PSQ3 should be given the Resource Card at the end of the PSQ3 (**Appendix W: Scripts for Personal Safety Questionnaire**).

If the PSS3 is not conducted at the hospital, the Research Assistant should write “set to M – not given” on the top of the form and leave it in the Visit 3 folder. When the form is data entered, it will be set to missing with “not given” as the reason.

#### **5) Personal Safety Questionnaire (PSQ3)**

After completing the PSS3, the Research Assistant should administer the PSQ3. Depending on a participant’s response to QA2 on the PSS3, the PSQ3 should be either self-administered or interviewer-administered.

All Research Assistants are trained on administering the PSQ and should refer to **Section VIII.B** for further information.

If the PSQ3 is not administered, the Research Assistant may recycle this form.

#### **6) Informed Consent for Child (CONC)**

After administering the PSS3/PSQ3, the Research Assistant should review child consent with the participant, and complete the CEN3.

If the participant signed the Informed Consent Form for her child’s participation (CONC) at Visit 2, then the Research Assistant should remind the participant of this, and confirm that the child should be enrolled in the study (**Appendix V: Visit 3 Informed Consent (Child) Scripts**).

If the participant has not yet signed a consent form, the Research Assistant should describe what the child’s participation in Project Viva would entail in greater detail to the participant (**Appendix V: Visit 3 Informed Consent (Child) Scripts**) and then ask the participant to read the Informed Consent (CONC). After the Research Assistant has answered questions, she should sign two copies of the CONC and ask the participant to sign both copies. The CONC should be filled in with “Child of [*participant’s first and last name*]” on the first and last page of the form.

If the participant would like to have her child enrolled in the study, but does not give consent for certain aspects (measurements, blood pressure, VRM) of the study, the items to be excluded should be crossed out and initialed by the Research Assistant on the Consent Form. These exclusions should also be noted on the Child Enrollment Form (CEN) (**see below**).

If the CONC is completed at Visit 3, one copy of the CONC should be given to the participant; one copy must be kept for the study files.

If the Research Assistant is not able to review child consent while the participant is still in the hospital, the Research Assistant should call the participant one week after her delivery to review the CONC by telephone (**Appendix V: Visit 3 Telephone Informed Consent (Child) Scripts**). If the CONC is administered over the phone, the Research Assistant should exclude the

information about the delivery visit when reviewing the form, since this part of the child's participation is no longer applicable. The Research Assistant should cross out the hospital visit information, write "N/A" (for not applicable) in the margin, date and initial the form.

If the participant signed the CONC prior to Visit 3, the Research Assistant should let the participant know that this change was made. If the participant has not yet signed the CONC, two copies of the CONC should be mailed to the participant with a business reply envelope – one to be returned to the study, and one for the participant to keep.

#### **7) Child Enrollment Form (CEN3)**

The Child Enrollment Form (CEN3) enrolls the newborn into the study.

The CEN3 should not be filled out until child consent has been reviewed and the CONC is received.

After the CEN3 is completed, the Research Assistant should proceed to the newborn measurements if the child is enrolled in the study.

If the Research Assistant is not able to review child consent while the participant is still in the hospital, the Research Assistant should call the participant one week after her delivery to review the CONC by telephone. If the CONC was signed at or after Visit 2, the Research Assistant should complete the CEN3 after this phone call, and note the date of the call at Question II. If the CONC is mailed to the participant to be signed and returned, the Research Assistant should set the CEN3 to missing in the DMS. The CEN3 should not be completed until the CONC is received. The date the CONC is received should be noted at question II.

If the Research Assistant completes a CEN3 at a time other than the Visit 3 date and the child is enrolled (CEN3 QA1 = Full or partial participation), the Research Assistant should complete a Missed Visit Form and place it in the Child's Visit 3 folder. The CEN3 should then be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

#### **8) Newborn Blood Pressure (NBP3)**

The Newborn Blood Pressure Form (NBP3) is for the Research Assistant to record the newborn blood pressure measurements, including systolic and diastolic blood pressure, pulse and state of the newborn.

All Research Assistants are trained on conducting the blood pressure measurements, and should refer to **Section VIII.F** for further information.

If consent was obtained for newborn blood pressure, other newborn measurements were taken, but the blood pressure was not measured, the Research Assistant should check "NO" on question 1 and write the reason the measurement was not taken in question 3.

If the Research Assistant is not able to complete the CEN3 while the participant is still in the hospital, none of the newborn measurements should be taken.

#### **9) Newborn Anthropometry (NAN3)**

The Newborn Anthropometry Form (NAN3) is for the Research Assistant to record the newborn



head, chest, and abdominal circumference measurements.

All Research Assistants are trained on conducting the anthropometry measurements, and should refer to **Section VIII.G** for further information.

If consent was obtained for newborn anthropometry, other newborn measurements were taken, but the anthropometry measurements were not taken, the Research Assistant should check “NO” on questions A1, A3, and A5 and write the reason the measurements were not taken in question A9.

If the Research Assistant is not able to complete the CEN3 while the participant is still in the hospital, none of the newborn measurements should be taken.

#### **10) Newborn Length Form (NLG3)**

The Newborn Length Form (NLG3) is for the Research Assistant to record the newborn length measurement.

All Research Assistants are trained on conducting the length measurement, and should refer to **Section VIII.G** for further information.

If consent was obtained for newborn length, other newborn measurements were taken, but the length was not measured, the Research Assistant should check “NO” on question A1 and write the reason the measurement was not taken in question A4.

If the Research Assistant is not able to complete the CEN3 while the participant is still in the hospital, none of the newborn measurements should be taken.

#### **11) Not Met Form – Visit 3 (NMF3)**

The Not Met Form (NMF3) is to be completed for all enrolled Viva participants who are not met at the hospital after delivery. Possible reasons that participants would not be met include: they were discharged over the weekend, a clinician recommended that they not be met, or a Research Assistant was not available to meet the participant.

The NMF3 should be filled out by the Research Assistant that tried to meet the participant (if an attempt was made), OR the hospital Research Assistant (if the participant was discharged over the weekend or a Research Assistant was not available).

#### **12) Missed Visit Form**

The Missed Visit Form should be completed if a participant is enrolled in the study and a visit window closes before the visit is met (the visit is “missed”).

### **E. Visit 3 Follow-up**

If the participant was met at the hospital and all Visit 3 forms were administered, no follow-up is necessary for Visit 3.

However, if the Research Assistant does not meet with the participant at all for Visit 3 (participant was discharged over the weekend, a hospital Research Assistant was not available, etc.), the Research Assistant should follow-up with the participant to conduct the LOC3, DEI3 and CEN3 over the phone. Before contacting a woman that has delivered, the Research Assistant should ask the Data Manager to check AAS to confirm that the woman who delivered is a Viva

Participant. The Research Assistant should then send a Viva onesie to the participant.

The timeline for Visit 3 follow-up is as follows:

- Immediately after delivery, the Research Assistant should fill out a NMF3 for the participant and send the participant a Viva onesie with a Visit 3 card;
- One week after delivery, the Research Assistant should call the participant to administer the LOC3, DEI3 and CEN3 over the phone.

## **Section VII. VISIT 4 (Six-Month Visit)**

### **A. Initiation of Visit 4**

Visit 4 takes place at an HVMA office 5 ½ to 8 months after delivery. Visit 4 includes a take-home questionnaire, an interview, and measurements of the mother and her child. The measurements include mother and child blood pressures using a Dinamap automated blood pressure recorder, mother and child weights using a SECA mother/baby scale, and child length using a Shorr Length Board. In addition, two vision tests are performed on the child, the Visual Recognition Memory test (VRM) and the Visual Acuity test (VRA). Visit 4 takes approximately 60 minutes to complete. Because measurements need to be consistent, only a few Research Assistants cover Visit 4 appointments (**Appendix N: Research Assistant Coverage**).

Project Viva has a newsletter, Viva Views, which is intended to update the participant about Project Viva and to remind the participant about Visit 4. This edition of Viva Views is sent to all eligible participants every three months. Participants are eligible to receive Viva Views if they have delivered and have not yet received the newsletter.

A Visit 4 contact log is produced by the DMS to help Research Assistants keep track of scheduling Visit 4 appointments. A contact log is generated for each participant 5 months after her delivery date. The contact logs are printed on a weekly basis and are distributed to the Visit 4 Research Assistants according to site coverage (**Appendix R: Printing V2 and V4 Contact Logs**). Each week, the Research Assistant should check her personal file in the file cabinet (green hanging folder) for a contact log for each participant who she should begin contacting to schedule a Visit 4. The contact log includes: the participant's first and last name, phone number, child enrollment and consent form status, whether cord blood was collected, the last four digits of the participant's ID number, space to log contacts made, and a space to write in the scheduled Visit 4 meeting time and place.

To assist the Research Assistant in explaining the visit and setting up an appointment, a script has been developed that outlines the major points to be covered (**Appendix RR: Visit 4 Initiation Call**). The Research Assistant should note the details of all phone calls on the contact log. Unlike at previous visits, a Research Assistant may leave a message on an answering machine or with people other than the participant if she has attempted to contact the participant several times and repeatedly failed to make contact. The Research Assistant should be careful, however, not to leave too many messages (**Appendix RR: Script for Leaving a Message to Schedule a Visit 4**).

If a Research Assistant is able to speak to the participant, a Visit 4 meeting time should be established. Before confirming an appointment with a participant, a Research Assistant should verify that space and coverage are available at the appropriate site. Calendars for each site are available in Lotus Notes. Once a Visit 4 meeting has been set up, it should be noted at the bottom of the contact log and in the appropriate site's Lotus Notes Calendar. The appointment should be noted at the bottom of the contact log in pencil, in case the visit is not done and another visit needs to be scheduled (**Appendix RR: Scheduling Visit 4 Appointments**). The contact log should then be given to the Research Assistant who will be covering the appointment. All contact logs with scheduled appointments should be kept in a contact log binder in chronological order.

If the participant is not able to come to one of the available HVMA sites for the full Visit 4, the Research Assistant may set up a phone interview with a participant. A phone interview takes approximately 20 minutes to complete. If a Research Assistant schedules a phone interview, she should write “Phone” as the site on the bottom of the contact log.

Appointments are generally scheduled two weeks in advance. To remind participants of upcoming Visit 4 appointments, and to further prepare them for the visit, a packet is sent to each participant a week before her appointment time. Packets are usually sent each Monday for the following week’s appointments. Each packet contains a letter from the Research Assistant with important information about the visit, such as the appointment date, time and location, what to bring to the visit, contact information to reschedule appointments, and directions to the appropriate site. In addition, a Six-Month Questionnaire is sent to each participant with instructions to bring the completed questionnaire to her upcoming visit (**Appendix TT: Preparing and Sending Visit 4 Packets and RA Letters**).

To remind participants of upcoming Visit 4 phone interviews, a reminder card is sent to each participant a week before the phone appointment to confirm the date and time of the interview (**Appendix TT: Preparing and Sending Visit 4 Packets**).

Most participants have enrolled their children in Project Viva prior to the initiation of Visit 4. If, however, a participant has not yet enrolled her child in the study, the Research Assistant should determine whether or not the participant would like to include her child in the visit when scheduling the appointment (**Appendix RR: Visit 4 Initiation Call**). If the participant chooses not to include her child in the visit, a visit should be scheduled for the mother component only. For mother-only visits, the Research Assistant should send a modified reminder letter to the participants (**Appendix TT: Mother-only RA Letters**). At the visit, the Research Assistant should only administer the forms with Mom IDs.

## **B. Preparing for Visit 4**

Each afternoon, the Research Assistant should check the Lotus Notes Calendars to determine the following day’s appointments. A Research Assistant should call each participant the night before the appointment to confirm the appointment date and time (**Appendix RR: Visit 4 Confirmation Calls**).

Visit 4 folders are prepared for each Viva participant who has scheduled an in-person or phone visit. The folders are prepared a week before the scheduled appointment date (**Appendix T: Compiling Visit 4 Materials**).

Before going to a Visit 4, the Research Assistant should check the contact log to confirm the status of child consent forms and child enrollment. If the child enrollment status is missing, the Visit 4 folder should include a Child Enrollment Form. Even if a participant is not planning on enrolling her child in Project Viva, the Research Assistant should complete a Child Enrollment Form. At the end of Visit 4, all Viva participants should have an updated child enrollment status. The only exception to this rule is for “Missed Visits.” If a Visit 4 is “missed,” child enrollment status should not be updated.

The Research Assistant should confirm that the appropriate forms are added to the Visit 4 folder as indicated in the following chart:

| <b>V3 Child Enrollment Status (From Contact Log)</b> | <b>V2 Child Consent Status (From Contact Log)</b> | <b>Does participant want to include child in study?</b> | <b>Add the following to the Visit 4 folder:</b>              |
|--|---|---|--|
| Blank  | Logged  | Yes or No   | CEN  |
| Blank  | Blank, Expected or No                             | Yes   | CEN, 2 copies of Child Consent Form                          |
| Blank  | Blank, Expected or No                             | No  | CEN  |
| No   | Blank, Expected, No or Logged ( <i>rare</i> )     | Yes   | CEN, 2 copies of Child Consent Form                          |
| No   | Blank, Expected or No                             | No  | No additions   |
| Full or Partial                                      | Blank, Expected, No or Logged                     | Yes   | No additions   |
| Full or Partial                                      | Blank, Expected, No or Logged                     | No  | Disenrollment form or Missed Visit form, depending on reason |

If a Research Assistant has any questions about child enrollment at Visit 4, she should consult with the Field Supervisor.

The Research Assistant should take a complete Visit 4 folder, signed mom and child consent forms (pulled from the consent form files), the Visit 4 Contact Log, and parking and incentive money to each visit. The other materials the Research Assistant needs for a Visit 4 should be in the Visit 4 room. Each Visit 4 room should be stocked as needed by the primary Visit 4 Research Assistant for that site.

The Research Assistant should plan to be at the appropriate Visit 4 site 20-30 minutes before a scheduled appointment to set up for the visit. To set up for a visit, a Research Assistant should confirm that the room is clean, the toys are washed, the blood pressure cuffs are available, and the room is adequately stocked (**Appendix RR: Preparing for a Visit 4**).

### **C. Visit 4 Protocol (Six-Month Visit)**

The Research Assistant should meet the participant and (re) introduce herself. The Research Assistant should escort the participant to the Visit 4 room, and arrange two chairs to face each other.

If the participant is with a partner or other adult, the Research Assistant may allow the partner to stay in the room for the Locator Forms, vision testing and mom and child measurements. The Research Assistant should, however, ask the partner if he/she would mind taking the child outside for about 20 minutes while the interview is being conducted. If the partner does not want to leave, the Research Assistant should not insist but rather should just proceed with the visit. If the partner remains in the room for the interview, this should be noted on the PSS4 as the reason

the PSS4 was not administered, and the PSQ4 should not be administered.

The Research Assistant should review the flow of the visit with the participant (**Appendix RR: Visit 4 Flyer**). The Research Assistant should be sure to inform the participant that if she or her child needs to take a break at any time, she should let the Research Assistant know.

Visit 4 is generally administered at a single visit (**Appendix RR: Visit 4 Sequence**) but if the participant has limited time, Visit 4 may be divided among an in-person and phone visit (**Appendix RR: Alternate Visit 4 Sequence**). The Research Assistant should document all alternate scenarios in the participant's study folder. For example, if the interview is conducted over the telephone, the SMI should note: "Telephone administered".

If the participant is not able to come to an available HVMA site for an in-person visit, the Research Assistant should conduct a phone visit (**Appendix RR: Visit 4 Phone Sequence, Visit 4 Phone Interview Script, and After Phone Visit 4 Letter**).

After a visit, the Research Assistant should clean all forms and should break the Visit 4 folder down into three folders: the Mom V4 folder, the Child V4 folder, and the TE folder (**Appendix RR: After a Visit 4 At a Site**).

The date on the folder label should equal the "event date" entered into the DMS. The date of the Visit 4 is the date that the first form was complete. This could be the date that a phone visit was conducted, the date of an in-person visit, or the date that an SMQ4 was received in the mail. The date of the TE folder is the date that the Project Viva Ages 1-4 consent was reviewed with the participant.

#### **D. Visit 4 Forms**

##### **1) Informed Consent Form Addendum (Adult and Child)**

A review of the Project Viva Informed Consent Forms and the Informed Consent Form Addenda (Adult and Child) initiates Visit 4.

The consent form addenda update the original consent forms to include the mother's weight and blood pressure and the child's visual acuity testing, length and weight measurements. In addition, the Informed Consent Form (child) clarifies that only one set of five blood pressure measurements, rather than the two outlined in the original consent, will be collected.

The Research Assistant should describe the modifications itemized in the Informed Consent Form Addenda (Adult and Child) to the participant (**Appendix RR: Viva Amended Consent Scripts**). After the Research Assistant has answered questions, she should sign two copies of each addendum and ask the participant to sign both copies of each. The Research Assistant should write the participant's full name on the top of both copies of the Informed Consent Form Addendum (adult). The Research Assistant should write "Child of [*participant's first and last name*]" on the top of both copies of the Informed Consent Form Addendum (child).

One copy of each signed Informed Consent Form Addendum should be given to the participant; one copy of each must be kept for the study files. After the addenda are signed, the Research Assistant should complete the remainder of Visit 4.

If a participant refuses to sign the addenda, the Measurement Form – Mother (MSM4) should be completed with "No Consent" checked for the blood pressure and weight measurements. The

Measurement Form – Child (MSC4) should be completed with “No Consent” checked for the weight and length measurements and the Vision Form (VIS4) should be completed with “No Consent” checked for the VRA measurements.

## 2) **Locator Form (LOC4)**

Visit 4 includes a separate Locator Form to update our contact information.

If the Research Assistant is not able to complete the LOC4 in person, it may be administered over the phone. If a LOC4 is conducted over the phone, the Research Assistant should make a note of this on the form, and should note the date of the phone call, not of the visit, at question II. The LOC4 is typically administered at the time of the Visit 4, whether the visit is in person or over the phone. However, in the rare case that a Research Assistant administers a LOC4 at a time other than the Visit 4 date, the LOC4 should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

## 3) **Child Locator Form (CLOC)**

Visit 4 includes a separate Child Locator Form to confirm the child’s date of birth and to obtain information about the child’s health care.

If the Research Assistant is not able to complete the CLOC in person, it may be administered over the phone. If a CLOC is conducted over the phone, the Research Assistant should make a note of this on the form, and should note the date of the phone call, not of the visit, at question II. The CLOC is typically administered at the time of the Visit 4, whether the visit is in person or over the phone. However, in the rare case that a Research Assistant administers a CLOC at a time other than the Visit 4 date, the CLOC should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

Please note: The Child Locator Form should have a mom ID label not a child ID label (i.e. “M10000-1” not “C10000-1”). This is because the CLOC should be administered to all participants, not only those participants who have enrolled their children in Project Viva.

## 4) **Vision Form (VIS4)**

The Vision Form (VIS4) is for the Research Assistant to record the results of the Visual Recognition Memory test (VRM) and the Visual Acuity test (VRA).

All Research Assistants are trained on conducting the VRM and VRA tests, and should refer to **Section VIII.H** for further information.

The VIS4 is a child form and should have a child label. If the child enrollment status (found on the most recent CEN) is not “Full” or “Partial”, none of the visual tests should be completed.

If the participant did not sign the Informed Consent Form Addendum (child) the VRA should not be completed, and the Research Assistant should code “NO CONSENT” at question C1.

## 5) **Measurement Form – Mom (MSM4)**

Measurement Form - Mom (MSM4) is for the Research Assistant to record the mother’s measurements, including systolic and diastolic blood pressure, pulse, and weight.

All Research Assistants are trained on conducting the blood pressure and weight measurements, and should refer to **Section VIII** for further information.

If the participant did not sign the Informed Consent Form Addendum (adult) the mother's measurements should not be completed, and the Research Assistant should code "NO CONSENT" at questions A1 and A4.

#### **6) Measurement Form – Child (MSC4)**

Measurement Form - Child (MSC4) is for the Research Assistant to record the child's measurements, including systolic and diastolic blood pressure, pulse, and state of the child, the weight and length.

All Research Assistants are trained on conducting the blood pressure, weight, and length measurements, and should refer to **Sections VIII.F and G** for further information.

The MSC4 is a child form and should have a child label. If the child enrollment status (found on the most recent CEN) is not "Full" or "Partial", none of the child measurements should be taken.

If the participant did not sign the Informed Consent Form Addendum (child) the length and weight measurements should not be completed, and the Research Assistant should code "NO CONSENT" at questions A4 and A5.

#### **7) Six-month Interview (SMI4)**

The Six-month Interview (SMI4) should be completed with the participant in a private room. If a partner or other adult is in the room when the SMI4 is administered, this should be noted on the top of the interview.

If the Research Assistant is not able to complete the SMI4 at the time of the visit, it may be administered over the telephone. If an interview is conducted over the phone, the Research Assistant should make a note of this on the SMI4 and note the date of the interview, not of the visit, at question II. If a Research Assistant administers an SMI4 at a time other than the Visit 4 date, the SMI4 should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

The last section of the SMI4 determines which Six-month Supplement (SMS) the Research Assistant should give to the participant. After completing the SMI4, the Research Assistant should place a blue-highlighted label on the appropriate SMS and give it to the participant to complete.

#### **8) Six-month Supplements (SMS4)**

There are four Six-month Supplements: Breast Only, Formula Only, Weaned, and Mixed. If a participant has ever breastfed her child and is not currently feeding her child any formula (as determined by the last section of the Six-Month Interview) she should receive the Breast Only supplement (SMSB). If the participant never breastfed her child, she should receive the Formula Only supplement (SMSF). If the participant has ever breastfed her child, is currently feeding her child formula, and is not currently breastfeeding her child, she should receive the Weaned supplement (SMSW). Finally, if the participant has ever breastfed her child, is currently feeding her child formula, and is currently breastfeeding her child, she should receive the Mixed supplement (SMSM).

The Six-month Supplements are intended to be completed by the participant at the time of the



visit, in the presence of a Project Viva Research Assistant. If the participant does not have time to complete the SMS4 at the time of the visit, or if the visit is completed over the phone, a SMS4 may be given (mailed) to the participant to complete and mail back. A Business Reply envelope should be given to the participant for this purpose.

If a SMS4 is received on a date other than the Visit 4 date, it should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

#### **9) Personal Safety Screening Form (PSS4)**

After completing the Six-Month Interview and Supplement, the Research Assistant should administer the PSS4. Because of the sensitivity of the questions in the PSQ4, the Research Assistant should only administer the PSS4 to a participant who is alone. If a spouse or partner (or other family member or friend) refuses to leave the participant alone in the room, the Research Assistant should not administer the PSS4, and should mark NO-PERA on question IV. If the woman is with a child older than 1 year (verbal), the PSS4 should be still be administered, but the Research Assistant should automatically have the questionnaire be self-administered.

If a participant interrupts the PSS4 before question A2, the Research Assistant should give her the Resource Card. Other participants proceeding to the PSQ4 should be given the Resource Card at the end of the PSQ4 (**Appendix W: Scripts for Personal Safety Questionnaire**).

If the visit is conducted over the phone, the PSS4 should not be administered, and the Research Assistant should write, “set to M – phone interview” on the top of the form and leave it in the Visit 4 folder. When the form is data entered, it will be set to missing with “phone interview” as the reason.

#### **10) Personal Safety Questionnaire (PSQ4)**

After completing the PSS4, the Research Assistant should administer the PSQ4. Depending on a participant’s response to QA2 on the PSS4, the PSQ4 should be either self-administered or interviewer-administered.

All Research Assistants are trained on administering the PSQ and should refer to **Section VIII.B** for further information.

If a PSQ4 is not administered, the Research Assistant may recycle this form.

#### **11) Toddler Enrollment Form (TEN)**

The Toddler Enrollment Form (TEN) enrolls the child into Visits 5-8. The TEN should be filled out after the Project Viva Ages 1-4 consent has been reviewed or sent in the mail. If the RA reviews the consent, either in person or over the phone, but the consent is NOT signed, the TEN form should be coded as ‘5-Not Yet-D/A administered’. If the consent is sent via the mail w/o being reviewed, question 1 should be coded as ‘6- Not Yet- D/A not reviewed’.

The date on the form should reflect the date the consent was reviewed with the participant or was sent in the mail to the participant without being reviewed.

If a Project Viva Ages 1-4 Consent form is received in the mail, the form should be placed in the green hanging folder of the Research Assistant who signed the forms. The Research Assistant should check to confirm that the participant signed the forms, pull the TEN form, and code question 1 accordingly.

If the participant has missed her Visit 4 altogether, she is sent a packet with the Dietazma Consent. The TE event should reflect the date the packet was sent and the TEN form should be coded as '6- Not Yet- D/A not reviewed'.

If the Research Assistant completes a TEN form at a time other than the TE date, the TEN should be logged in the blue, Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

The TE event is identified by an orange highlighted label. The label on the TEN and the TE folder should be highlighted in orange. The event for the TEN is the visit event "04". The folder event is "TE"

## 12) Six Month Questionnaire (SMQ4)

The Research Assistant should mail the Six-Month Questionnaire (SMQ4) to the participant a week before the Visit 4 date. Most participants will bring the SMQ4 to the Visit 4. If the participant did not complete and return a SMQ4 at the time of a Visit 4 (e.g. she lost or didn't receive a copy) the Research Assistant should give her a copy at the end of the visit. The Research Assistant should request that the participant complete the form within two weeks and mail it back to the study PO Box. A Business Reply Envelope should be provided for this purpose.

If a phone visit is scheduled for a Visit 4, the SMQ4 should be mailed after the phone visit, along with two copies of the Project Viva Ages 1 through 4 consent and the appropriate Six-Month Supplement.

## 13) Additional V4 Forms

There are three types of forms that may be added to a Visit 4 that are not automatically expected by the DMS, the Child Enrollment Form (CEN), the Missed Visit Form, and the Disenrollment Form (DIS).

### a) Child Enrollment Form (CEN)

The Child Enrollment Form (CEN) enrolls the child into the study. The CEN is usually completed at Visit 3. However, if the participant was not met at the hospital, or if the participant had not yet enrolled her child at Visit 3, the Visit 4 Research Assistant should review child consent at Visit 4.

**The CEN should not be filled out until child consent has been reviewed. The child cannot be enrolled in the study unless the Informed Child Consent Form (CONC) is signed and received.**

After the CEN is completed, the Research Assistant may proceed with the measurements if the child is enrolled in the study. The Visit 4 child forms (MSC4 and VIS4) may not be completed unless the CEN is complete with "Full" or "Partial" consent status.

If the Research Assistant is not able to review child consent in person (e.g., the Visit 4 is being conducted over the phone), the Research Assistant may review the CONC by telephone. If the CONC was signed at or after Visit 2, the Research Assistant should complete the CEN after this phone call, and note the date of the call at question II. If the participant has not yet signed the CONC, the CONC should be mailed to the participant to be signed and returned. In this case, the

Research Assistant should set the CEN to missing in the DMS. The CEN should not be completed until the CONC is received. The date the CONC is received should be noted at question II.

If the CONC is received in the mail, the form should be placed in the Research Assistant's green hanging file. The Research Assistant who co-signed the Informed Child Consent Form should then complete the CEN, and log the CEN in the blue Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

If the participant enrolls the child in the study (CEN3 QA1 = Full or partial participation) but is unable to bring the child in for an in-person Visit 4, the Research Assistant should complete a Missed Visit Form and place it in the Child's Visit 4 folder.

The CEN is not an expected form at Visit 4, and therefore should be added to the DMS at the time of data entry if the form is in the Visit 4 folder.

**b) Missed Visit Form (Missed Visit)**

If the participant misses the Visit 4, the Research Assistant should complete a Missed Visit Form. The Research Assistant should code the appropriate reason as to why the visit was missed. If a participant has enrolled her child in the study but is not able to bring her child in for the visit, a Missed Visit Form must be completed for the Child ID.

When a Missed Visit Form is completed at Visit 4, it should be the only form in the Visit 4 folder. The Research Assistant should write "Missed" over the label of the Visit 4 folder.

**c) Disenrollment Form (DIS)**

As with all Project Viva visits, a participant may choose to disenroll from Project Viva at Visit 4. If the participant has not yet had a Visit 4, the participant should be disenrolled at Visit 3: the DIS form should be added to Visit 3, and the event should be "03". If the participant disenrolls at Visit 4, the DIS form should be added to Visit 4, and the event should be "04".

NOTE: If a participant and her child are both enrolled in Project Viva, they both must be disenrolled if the participant requests to disenroll herself and her child. A DIS form must be filled out for both the mother and the child ID. The Research Assistant should confirm with any participant who intends to disenroll whether she also wishes to disenroll her child.

**E. Visit 4 Follow-up**

Two weeks (14 days) after a Visit 4, all participants receive a thank you letter/reminder that is mailed centrally to a list generated by the DMS (**Appendix S: Printing and Sending Visit 4 Thank You Letters and Visit 4 Thank You Letter**). In most cases, the participant will bring the completed SMQ4 to the Visit 4 and will complete the rest of the components of the visit in the presence of the RA. In these cases, no follow-up is required on the part of individual Visit 4 Research Assistants. If the Viva materials (i.e., SMQ4, SMS4) are not returned to the study, the Visit 4 Research Assistant should follow up with the participant.

Call logs are printed within 10 days of a Visit 4 to assist Research Assistants in keeping track of Visit 4 follow-up (**Appendix R: Printing Call Logs**). At visit 4, call logs are only printed for those participants that have outstanding Six-Month Questionnaires. Each day, the Research Assistant should check her personal file (green hanging file) in the file cabinet for any new call logs.

The timeline and steps for Visit 4 follow-up are as follows:

- 10-13 days after Visit 4, the Research Assistant should call the participant to follow-up on SMQ4 (SMS4) if it has not yet been received. The Research Assistant should continue calling the participant until she speaks with her.
- 14 days after Visit 4, a Visit 4 Thank You/Reminder Letter is automatically sent to all participants who have been met for their Visit 4.
- 21-27 days after Visit 4, the Research Assistant should continue to call the participant to follow-up on the SMQ4 (SMS4) if they have not yet been received.
- 28 days after Visit4, the Research Assistant should set the form to missing.

If the participant says that she lost the forms, the Research Assistant may offer to mail her another questionnaire. If a Research Assistant needs to mail a participant another form for any reason, she should put the date that she mailed the new questionnaire on the label, not the date of the original visit.

The Research Assistant should try to get the forms back during the four weeks following Visit 4. After this time, the Research Assistant should set the forms to missing in the DMS.

### **1. Out of Window**

Any participant who is not met before her visit four window closes (8.5 months after delivery) receives an out-of-window packet (**Appendix RR- Preparing and Sending V4 out of Window Packets, V4 Out Of Window PI Letter, V4 Out Of Window RA letter**). This packet presents the participant with the opportunity to enroll in Diet-Asthma and is mailed at 8.5 months.

If a participant, who is past her V4 window, would have been approached with the genetics consent at visit four, a separate genetics out-of-window packet is also created. Though put together at the same time as the Diet-Asthma packet, it is mailed separately at about 9.5 months post delivery.

If the consents are received in the mail, the form should be placed in the Research Assistant's green hanging file. The Research Assistant who co-signed the Dietazma Consent Form should then edit the TEN form to reflect the child new enrollment status, and log the TEN in the blue Log of Forms Received binder in the top of the file cabinet (**Appendix MM: Log of Forms Received**).

## **Section VIII. PROTOCOLS**

### **A. Standardized Research Interview**

#### **1) Introduction**

Research Assistants are extremely valuable members of the research team. The quality of the data and the success of the study depend largely upon the ability of each Research Assistant to obtain consistent and comparable data. Data must be collected in a standardized manner and in a way that minimizes response bias.

This section includes a number of guidelines to assist the Research Assistants in standardizing the interview process.

#### **2) Question By Question Specifications**

Question by Question specifications (QxQs) explain the purpose of questions, clarify terminology and provide additional instructions to assist the Research Assistant with each form. They are designed to resolve questions that may arise during the data collection process and should be carefully reviewed before the Research Assistant conducts his/her first interview. If any questions arise during the interview process, the Research Assistant should feel free to check the QxQs for further instruction.

#### **3) Getting Started**

Before going to the interview, the Research Assistant should make sure that she is prepared and has all the necessary materials. In some cases, it may be advisable to leave a set of recruitment materials at a site in case an additional participant unexpectedly arrives at the site.

#### **4) The Interview Environment**

The interview should always be conducted in a private and quiet room where there will not be interruptions or distractions. The environment of the interview room sets the stage for the participant's ability to stay focused, to provide complete information, and to provide truthful responses to personal questions about her health, eating habits and marital status. If a friend accompanies the participant, the Research Assistant should ask the friend to leave the room for the course of the interview. **If the friend does not want to leave the room, the Research Assistant should allow him or her to stay.** If a partner or friend stays in the room, the Research Assistant should note on the forms "partner present" or "person present." This will not be data entered.

#### **5) Guidelines For Conducting The In-Person Interview**

Throughout Project Viva, participants are asked several questions that are very specific and at times quite personal. Using the general guidelines outlined below will help Research Assistants maintain control of the interview and collect meaningful data from the participants without introducing bias.

Before conducting an interview, the Research Assistant should familiarize herself with these guidelines and all the study forms to be used.

**a. Be prepared:**

Before undertaking the first interview, it is crucial that each Research Assistant be familiar with all study protocols and procedures, study instruments, skip patterns, and the entire interview process. This will help minimize the burden to the participant.

**b. Asking the questions:**

- **Always Remain Neutral**

The Research Assistant must take every precaution to avoid showing any personal feelings or judgments. Any reactions that may imply criticism, surprise, approval or disapproval of either the questions or the participant's answers will introduce bias into the interviewing situation. This may influence the participant's response. Through a relaxed, professional attitude, the Research Assistant can ease the participant's anxieties and gain her confidence.

Read everything in a natural, even-toned manner.

- **Ask All Questions (Unless Otherwise Instructed)**

If the participant provides more information than required for a particular question, the Research Assistant may feel that the participant has already answered a later question without being asked formally. DO NOT RECORD the response to a question that the participant indirectly provides out of sequence during the interview. If the participant becomes annoyed at the repetition (and says something like "I just told you that"), respond pleasantly with phrases like: "You may have already told me this, but let me ask the question to be sure that I have the correct answer."

- **Ask Each Question Exactly As It Is Worded**

Each participant in the study should hear exactly the same question. Changing even one or two words can affect the entire meaning of the question and lead to bias. Although some questions could be phrased differently or more simply, it is important that the Research Assistant stick with the standardized language. This is important for the study team to be able to combine the responses of all participants and analyze the data later.

Occasionally, the participant will ask the Research Assistant to define words in a question or further explain some part of a question. Changing words, using synonyms or providing definitions that are not specified in the question or QxQs may influence the participant's interpretation of it. If the participant does not understand the question after exhausting standard alternatives, encourage her to answer the question "to the best of her ability."

- **Discourage Conversation That Isn't Related To The Topic**

If the participant is overly chatty or discusses irrelevant topics during the interview, do not hesitate to gently interrupt her to refocus her attention. Acknowledge the answer with a professional tone and neutral comments such as "I see" or "O.K." and repeat the question if she did not respond initially. At the same time, however, take precautions to avoid offending or antagonizing her. Politely use comments such as: "That sounds very interesting, but what I need to ask is..." or "I see what you mean, but let me repeat the last question..."

This will ensure that the Research Assistant maintains control of the interview situation at all times.

The Research Assistant should bring a pad of paper to the interview and if the participant asks about something not directly related to the interview question, the Research Assistant should make a note on the pad. Explain to the participant that it can be discussed later by saying: “That’s a good question. I am going to make a note of it so that we don’t forget to talk about it after we have finished the interview.”

**c. Resolving Inconsistent Responses:**

• **Opinion or Perception Questions**

If the participant contradicts herself in her opinion and perceptions during the course of the interview, the Research Assistant should not try to reconcile the responses.

• **Factual Information**

If the participant provides factual inconsistencies, the Research Assistant should try to reconcile the differences without challenging the participant. The Research Assistant can say something like: “I must have misunderstood, I thought you said earlier that...” or “Let me repeat the last series of questions just to be sure that I have recorded your answers correctly.” This way the Research Assistant appears to be the one who has made the mistake, not the participant. The questions should be read again and recoded consistently.

Factual inconsistencies should only be corrected based on information obtained from the participant during the interview. If the participant provides information during the interview that the Research Assistant thinks contradicts his/her prior knowledge about the participant, the Research Assistant should not say anything or attempt to reconcile the inconsistency.

**d. Maintaining Rapport and Dealing with Sensitive Issues**

The rapport building process begins with the initial contact between the Research Assistant and participant. By coming across with an attitude of acceptance and understanding, and by expressing an interest in the participant, the Research Assistant can create an atmosphere in which the participant feels able to speak freely without reservation. It is important to be able to present the questions in a professional, matter-of-fact manner without being abrupt, tactless or insensitive. Avoid acting too serious or too jovial as this, too, can bias the interview.

If the participant appears nervous or uncomfortable during the interview, reassure her that she may speak freely and that the information will be kept confidential. The Research Assistant must help the participant feel safe to speak during the interview process and remind her that her participation and contribution is very important to the research at hand. Use phrases such as “I can understand that you might be concerned about the privacy of what you tell me, but let me reassure you that your answers are strictly confidential.”

If a participant refuses to answer a question after providing reassurances, indicate “REFUSED” on the instrument and go on to the next question. Although missing data is problematic, it is better to accept a refusal to one question than risk losing the entire interview.

**e. Probing**

Probing techniques are used by the Research Assistant to obtain more information from the participant when a response is incomplete or does not adequately address the question. The Research Assistant must understand the objective of each question, be able to recognize when the

participant's reply does not answer the question, and use unbiased, neutral probes while maintaining rapport with the participant.

The Research Assistant can offer probes: 1) when the participant misunderstands the question or its intent; 2) when the participant has trouble remembering events that took place several years ago; or 3) when the participant answers "I don't know". Often the best probe is simply to pause expectantly or to repeat the question or the participant's reply.

Sometimes a participant will provide an irrelevant response to a question, but assume that she has answered it sufficiently because she misunderstood the purpose or intent of the question. Usually the participant didn't hear or missed a key word or phrase in the question. In these cases, it may be most appropriate to simply say something like: "I see, let me reread the question...." If the interviewer emphasizes the key words the second time, the participant will then recognize the question's objective and answer appropriately. When a participant answers "I don't know", it doesn't necessarily mean that she doesn't have a response to the question. Instead it may mean:

- 1) That the participant didn't understand the question and doesn't want to admit that she didn't understand it.
- 2) That she needs more time to think about the question and says "Don't know" to break the silence and give herself time to think more about it.
- 3) That she feels uninformed, or is afraid of giving a wrong answer, or because the question seems too personal.
- 4) That she may not know or may have no opinion on the question.

The Research Assistant should not be in too big of a rush to settle for a "Don't know" response. If you sit quietly and expectantly, the participant will usually think of something to say. An expectant pause is usually your best probe for a "Don't know" response.

### **Keep in mind:**

The probe should never change the frame of reference of the question.

The probe should never indicate that one answer is expected over another.

The probe should never indicate that one answer is more socially acceptable than another.

The probe should motivate the participant to meet the question objective.

Appropriate probe categories and examples include:

- **Clarifying:** "What do you mean exactly/by...?" "I don't think I quite understand."
- **Specifying:** "Could you be more specific about that?" "What in particular do you have in mind?"
- **Generalizing:** "Generally.... (REPEAT EXACT QUESTION)" "What is your best estimate?"
- **Fine-tuning:** "I see. Well, let me ask you again...(REPEAT EXACT QUESTION)"
- **Gathering more information:** "Anything else?" "What else can you think of?"



## 6) **Scripts and Q&As**

Scripts are provided to Research Assistants to assist them in administering many of the forms. There are two types of scripts, those that are written directly on forms, and those that are separate documents. Scripts that are written on forms (i.e. the script at the beginning of SCR1, or those interspersed in EPI1) should be read exactly as they are written on the form. Scripts that are separate documents (i.e. Script for Visit 3 Child Consent) should be followed very closely, but it is not imperative that they be read verbatim.

In addition, canned responses to questions that may come up during visits have been developed to aid Research Assistants in responding to participants' (and recruits') questions as accurately and directly as possible (**Appendix Z: Questions and Answers**). Research Assistants should be familiar with these responses before going to a visit, in case questions should arise.

## 7) **Interviewer Points To Remember**

- Read the question as written and follow the skip patterns carefully.
- Use non-directive probes to elicit accurate and complete information.
- Read the questions at a pace that is easy to follow. Enunciate clearly.
- Focus the participant's response to address the actual intent of the question.
- Establish a good, professional rapport with the participant. Maintain control of the interview.
- Keep the respondent focused and interested in completing the interview.

## **B. Personal Safety Questionnaire**

### 1) **Background**

Violence is a prevalent part of many women's lives both within and outside of the home. Abuse of women by their partners knows no socioeconomic, racial, ethnic, religious, or age barriers. Estimates of lifetime physical and sexual abuse include the following: at least one quarter of girls are sexually abused; more than a third of women report ever having been physically or sexually abused; and three per cent of women suffer severe physical abuse from their husbands in any given year.

Pregnant women are not exempt from this treatment. Many studies have estimated that 4 to 8 per cent of pregnant women are physically or sexually abused. Abuse during pregnancy puts both the mother and the child at risk. Three of the seven studies published to date on violence during pregnancy and pregnancy outcomes have found that battered women had large and statistically significant increases in the risk of low birthweight or preterm birth. To our knowledge, no published study to date examines lifetime experience of violence prior to pregnancy and pregnancy outcomes.\*

The purpose of the Personal Safety Questionnaire (PSQ) is to enable Project Viva to gather information from participants about their experiences of violence and fear throughout their lifetimes. This information will be used to evaluate the associations between racism, violence, corticotropin-releasing hormone (CRH) levels, and preterm outcomes in the context of sociodemographic factors, health habits, reproductive and medical history, and medical conditions during pregnancy.

## 2) Research Assistant Protocol For Administering The PSS and PSQ

The PSQ was designed as a self-administered questionnaire to be filled out by a participant in the presence of a Project Viva Research Assistant. Because some participants may feel more comfortable answering the questions in an interview format, this questionnaire may also be administered by the Research Assistant.

While the nature of the questions asked in the PSQ may be more personal and sensitive than that of other Project Viva questionnaires, the role of a Research Assistant/Interviewer does not change. The Research Assistant is there to obtain information about violence in participants' lives in the most sensitive way possible, and to provide information at the end of the visit. As with the other interviews, the Research Assistants interactions with the participants while administering the PSQ should be sensitive, professional, and non-judgmental.

The PSQ is administered at Visit 2, Visit 3 and Visit 4.

At Visit 2, after completing Infant Consent, the Research Assistant should introduce the PSQ2 to the participant by administering the PSS2. At Visit 3, the Research Assistant should introduce the PSQ3 to the participant by administering the PSS3 after the Delivery Supplement. At Visit 4, the Research Assistant should introduce the PSQ4 to the participant by administering the PSS4 after the break.

Because of the sensitivity of the questions in the PSQ, the Research Assistant should only administer the questionnaire to a patient who is alone (or with a child). If a spouse or partner (or other adult) refuses to leave the participant alone, the Research Assistant should not administer the PSS (and therefore the PSQ), and should circle NO-PERA on question IV. If the participant is with a child older than 1 year (verbal), the PSS should be still be administered, but with the alternate scenario for "IF WOMAN IS WITH A CHILD." In this instance, the Research Assistant should automatically have the questionnaire be self-administered.

If a participant is not interested in completing the PSQ (interrupts the PSS2 before Question A2), the Research Assistant should thank her for her time, and hand her the Resource Card (**Appendix W: Scripts for Personal Safety Questionnaire**). People may be at various stages of healing from violent experiences, and it is important that they be in control of when and if they want to talk to someone about their abuse.

The PSQ should be administered in a private, closed room. The Research Assistant should give the participant a hard surface to write on, and hand her the PSQ to be filled out.

**If the participant chooses to self-administer the questionnaire**, the Research Assistant should review the form with the participant, highlighting the following:

### PSQ2

- Research Assistants should point to the paragraph on page 2 about Massachusetts law and say "Please be sure to read this instruction."
- For questions 1-4 and 6-9, if she responds "Yes," she should continue to question "i"

- If the participant is less than 18 years old, that Q2 is “When you were a teenager (age 12-17) *until this pregnancy...*” and Q3 is deleted. Similarly, Q7 is “When you were a teenager (age 12-17) *until this pregnancy...*” and Q8 is deleted.

### PSQ3

- Research Assistants should fill in the appropriate time referent (since your last Viva visit or since your 26<sup>th</sup> week of pregnancy) and cross out the other time referent.
- If she responds “Yes,” she should continue to question “i”

### PSQ4

- Research Assistants should point to the paragraph on page 2 about Massachusetts law and say “Please be sure to read this instruction.”
- For questions A5 and A6, if she responds “Yes,” she should continue to question “i”

The Research Assistant should also hand each participant a Viva envelope so that the participant can place her questionnaire in it and seal it when she is finished.

**If the participant chooses to have the questionnaire interviewer-administered**, the Research Assistant should remember to:

### PSQ2

- Read the “Disclosure Statement” (“According to Massachusetts’s law...”) on the top of page 2.
- Read each instruction and each question to the participant. The Research Assistant does not need to read the skip instruction on page 5, and can simply follow the skip pattern.
- Change the “I” to “you” for questions 12 and 13 (i.e. Keeping it to *yourself*. Like *you* deserved better...)

### PSQ3

- Read each instruction and each question to the participant.

### PSQ4

- Read the “Disclosure Statement” (“According to Massachusetts’s law...”) on the top of page 2.
- Read each instruction and each question to the participant.

If a participant becomes uncomfortable while filling out the PSQ and wants to stop, the Research Assistant should leave the PSQ incomplete, and offer her the Resource Card (**Appendix W**:

**Scripts for Personal Safety Questionnaire 2, 4).** If a participant becomes uncomfortable while filling out the PSQ (for example, she begins to cry, or looks upset) but does not stop the PSQ, the Research Assistant should offer that the participant takes a break (**Appendix W: Scripts for Personal Safety Questionnaire 1**). If the participant is still upset after a break, the Research Assistant should check with the participant to see if she is able to continue (**Appendix W: Scripts for Personal Safety Questionnaire 1**).

### 3) **Disclosure Of Experiences Of Violence Or Fear**

Most of the participants will self-administer the PSQ, and therefore, the Research Assistant will not see participants' recorded responses to the questions. A sticker with the name and number of the HVMA site social worker should be affixed to Resource Card at Visits 2 and 4 should participants feel the need to talk with a clinician about safety issues (**Appendix W: Scripts for Personal Safety Questionnaire 2** and **Appendix AA: Medical Social Worker's Schedule**).

If a participant answers "Yes" to any question on an interviewer-administered PSQ3, OR verbally discloses to the Research Assistant while self administering the PSQ3 that she has recently experienced violence, the Research Assistant should offer to have a nurse at the hospital contact a social worker. (**Appendix W: Scripts for Personal Safety Questionnaire 3**.)

For the participant's safety, the Research Assistant should not mark the Resource Card in any way (e.g. highlighting numbers, putting stars next to certain agencies).

The Research Assistant may be the first person that a participant tells about her experiences of violence, and it is important for Research Assistants to understand that this could be very difficult for a woman. The Research Assistant is not expected or trained to provide in-depth crisis counseling to a participant, but she can give the participant the Resource Card, which has important information about where a woman can find help. If a Viva participant is interested in speaking with someone, the Research Assistant should point out the sticker with the name and number of the social worker on call at the appropriate site (**Appendix AA: Medical Social Worker's Schedule**), and encourage her to speak with her clinician.

The Research Assistant should give every participant a Resource Card whether or not she has disclosed past experiences of violence. The Research Assistant should let the participants know that we are distributing these numbers to all women.

### 4) **Disclosure Of Someone Else In Danger**

Massachusetts law mandates that a care provider who has reason to believe that a child (under age 18), disabled person, or elder (person over the age of 65) is enduring ongoing physical or sexual abuse or neglect, must call the appropriate hotline to file a report. Research Assistants are not mandated reporters. However, the Principal Investigator, Matthew Gillman, is a mandated reporter, and should be notified, according to the procedures listed below, if abuse of a child, elder or disabled person, is disclosed.

Because they are pregnant, all Project Viva participants, including women under age 18, are considered adults under Massachusetts's law, and are therefore not covered under mandated reporting laws. The PSQ was designed to ask participants about *their* experiences of violence and fear. Questions that ask about the participant's knowledge of abuse of other people in her home (Q5 and Q10 on PSQ2) are too vague to draw conclusions about the abuse of a specific person in

the participant's home. Therefore, any answers a participant provides to the PSQ do not need to be reported.

However, if a participant mentions, throughout the course of Visit 2 or a Visit 4, that a child, disabled person or elder is currently in danger, the Research Assistant should follow the procedure below:

Explain to the participant that, as you pointed out at the beginning of the interview, you are required to consult with your supervisor about what she's told you about the ongoing abuse of a child, elder or disabled person (**Appendix W: Scripts for Personal Safety Questionnaire 4**). Let the woman know that everything else she has shared with you will be kept confidential.

Write down what she told you about the ongoing abuse of a child, elder or disabled person. Do not include the patient's name or identifying information on any notes you take – record the participant's ID# in a separate place.

Discuss the situation with Matthew Gillman, Principal Investigator, who will make the decision whether or not the abuse needs to be reported.

#### **5) Confidentiality**

As with all Project Viva data, it is important that the information gathered on the PSQ be kept strictly confidential. The Research Assistant should not discuss what a participant discloses with the HVMA office staff. The Research Assistant may, and should, discuss the situations she has heard about with the other study staff, including the Project Coordinator. As always, conversations should not include participant's names or other identifying information.

### **C. Blood Protocol**

#### **1) Blood Specimen Collection**

At the end of Visit 1 and Visit 2, the Research Assistant accompanies the participant to the HVMA laboratory for the blood draw. The blood draw is not mandatory for participation in Viva but it is requested of all participants. Twenty milliliters is collected from each participant, with half of the collection in a purple-top tube and half the collection in a green-top tube.

The Research Assistant gives the two blood tubes to the lab receptionist or directly to the phlebotomist. If this is not possible, the Research Assistant may give the tubes to the participant. Each tube must each have a Viva ID label on it. Before putting the label on the tube, the Research Assistant must write "Viva", the participant's date of birth, date of the blood draw, the Viva visit number, and RA initials on the label. The Research Assistant completes questions 1, 2 and 3 of the Blood Collection Form at this time and then completes questions 1a and 4 after the blood has been collected.

Viva visits are scheduled to coincide with OB appointments that include a blood draw. If a visit occurs at a time when a participant is not having her blood drawn, the Research Assistant should ask the participant to have it drawn for Viva. If the participant consents, the Research Assistant gives a "DO NOT LOG" form to the receptionist at the time of check in (**Appendix BB: Do Not Log Form**).

All HVMA labs have been notified about the Project Viva protocol. The phlebotomists are instructed to place the blood tubes in a ziplock bag and to place the bag into the HVMA

refrigerator immediately after the blood is drawn. If the Research Assistant is leaving the HVMA office immediately following the blood draw, the blood tubes are placed directly in the cooler with an ice pack. An item (styrofoam, gray foam) should be put between the blood tubes and the ice packs to prevent the blood from freezing.

The Research Assistant transports the cooler to Kenmore and places the blood tubes in the Kenmore lab refrigerator in the red bucket. The tubes should be kept in the ziplock bags. The Research Assistant may also bring the cooler directly to the Channing lab.

## 2) **Blood Specimen Delivery**

Every day of the week, a courier picks up the Viva blood specimens from the Teaching Center and delivers them to the Channing Lab. The pick-up is between 1:00 and 1:30. If there are no bloods to be delivered, the pick-up must be cancelled by 12:00. If the courier is late, a Research Assistant may need to transport the bloods to the Channing Lab. This is done in order to avoid having the bloods sit too long before being spun, aliquoted and frozen.

When the courier arrives, a Research Assistant picks up the Blood Delivery Logs from the file cabinet and gets the blood specimens from the Kenmore lab (**Appendix CC: Blood Pick-up Protocol**). The Blood Delivery Log is completed at the time of pick up. If there are several Blood Delivery Logs, the forms are stapled together and the delivery time information is completed for the form on top.

## 3) **Blood Specimen Processing**

At the Channing laboratory, the blood specimens will be centrifuged and separated into **three 2 ml plasma, two buffy coat, and two red cell specimens**. The specimens will then be split, and specimens from each subject will be frozen in two separate dedicated liquid nitrogen freezers ( $\leq -130$  degrees Celsius) for the duration of the study. Only aliquots necessary for specified assays will be unfrozen at the time they are required.

## D. **Placental Weight**

We will measure placental weight for participants delivering at the Brigham and Women's Hospital. Data on placental weight in a subsample will allow us to examine its intermediate or confounding effects on the relationship of prenatal diet with infant blood pressure.

## E. **Cord Blood Collection**

We will collect cord blood from participants delivering at the BWH. We will use a standard technique of keeping the umbilical cord clamped through the third stage of delivery and allowing free flowing umbilical arterial and venous blood to enter the tubes by gravity. (**Appendix DD: Cord Blood Collection Protocol**).

## F. **Newborn Blood Pressure**

At Visit 3, the hospital Research Assistant should obtain one set of 5 blood pressure measurements, each one minute apart, from the newborn participants using the Dinamap 8100 automated blood pressure recorder. The Research Assistant should note the time of day, pulse, and activity state of the newborn at the time of measurements.

Blood pressure is measured as systolic pressure/diastolic pressure. Systolic pressure indicates the pressure of the blood as it is pumped out of the heart and is the higher number displayed on the

Dinamap monitor. Diastolic pressure indicates the pressure of the blood when the heart is relaxed, and is the lower number displayed on the monitor. The average blood pressure of a newborn is about 70/40. The average newborn pulse is about 120 beats per minute.

Blood pressure varies from minute to minute, so it is necessary to take multiple readings. The Research Assistant should take five readings each one minute apart. The readings will be averaged for data analysis.

Blood pressure measurements should be taken with the newborn lying face-up in the bassinet. If necessary, the newborn may be held in an assistant's (i.e. father, another Research Assistant) arms during the measurements. However, if held, the newborn must be in a reclined position with arms alongside the body. The newborn's hand should be held gently, to keep the arm straight and prevent it from moving.

If possible, the newborn should be quiet or asleep during the blood pressure measurements. If the newborn begins to move during the process of taking the blood pressure measurements, the Research Assistant should not hold the newborn down. The Research Assistant should disconnect the cuff (so that the cuff will deflate), press **silence** or **cancel** and wait for the newborn to calm down before resuming measurements

#### **1) Choosing the correct cord**

The Dinamap comes with 2 sets of cords, a dark blue cord and a light blue cord. The light blue cord is used with the white, 'push-in' cuffs (labeled 'disposable'). The light blue cord is used for most of the newborn measurements. The dark blue cord is used with the rust-colored, nylon cuffs with 'threaded' connectors. For the six month olds (at Visit 4), the dark blue cord with the threaded cord connectors will most often be used.

The Research Assistant determines which cord is appropriate for the measurement and connects it to the Dinamap.

#### **2) Selecting and placing the cuff**

Most often, the white, push-in cuffs, will be used with the newborns. The rust colored cuffs will most often be used with the 6-month-olds. The white cuffs come in 5 neonatal sizes – sizes 1-5 – and are decorated with animals. Each cuff has a range indicated on the cuff. The most common sizes for newborns are sizes 3 and 4.

The Research Assistant should locate the brachial artery on the inside of the right arm using two or three extended fingers. The thumb should not be used to locate the artery. The brachial artery is located on the inside of the elbow, just above the elbow crease between elbow and shoulder and slightly medial to the center of the arm (towards the body when arm is held palm up). The cuff should be put on a bare arm. The Research Assistant should hold the arm steady with one hand and wrap the cuff snugly around the arm with the other.

The Research Assistant should line up the artery arrow on the cuff with the brachial artery on the inside of the biceps. The cuff should cover 80% of the upper arm, and should be placed above the elbow.

If the cuff is too small, a larger cuff should be used, even if it covers the elbow. The most important factor that the Research Assistant should keep in mind when selecting a cuff is that the cuff not be too small, as this will raise the blood pressure artificially.

### 3) **Preparing the Newborn for the Measurement**

The Research Assistant should put the cuff on the newborn, and then should be sure to make the newborn comfortable before beginning the blood pressure measurements. The Research Assistant may want to put the newborn's shirt on, swaddle the newborn in blankets, and/or put something soft between the cuff and the newborn's body. It is important that the newborn be calm and comfortable for the blood pressure measurements, because the Dinamap often reads an error code if a newborn is crying. If the newborn is crying or upset when the Research Assistant puts the blood pressure cuff on, the Research Assistant should wait until the newborn has relaxed completely before connecting the cuff to the Dinamap machine. After the child has calmed down, the Research Assistant should plug the cuff into the cord to connect the cuff to the Dinamap machine.

### 4) **Setting the machine**

After the machine is turned on, the Research Assistant should press the auto/manual button to switch the machine to "auto." The auto function in the Dinamap machine defaults to taking blood pressure measurements every 3 minutes. The cycle should be set to 1 minute by pressing the SET button once (the number 1 should be displayed in the box). Readings will then be taken approximately every minute until the machine is set to manual or turned off. After each measurement, the Dinamap will beep. At the time of the beep, the Research Assistant should record the state of the newborn, systolic pressure, diastolic pressure and pulse. After five readings have been taken, the Research Assistant should press the auto/manual button (to change to manual) to stop the machine from taking any more readings.

If the newborn is crying, the Dinamap will inflate the cuff excessively, causing more and more discomfort to the newborn, and will not take a blood pressure reading. If a child becomes upset during the measurements the Research Assistant should disconnect the cuff (so that the cuff will deflate), press **silence** or **cancel**, and wait for the newborn to calm down before resuming measurements.

Five accurate blood pressure and pulse measurements are needed for each newborn. If the tubes are not connected properly, the cuff is in the wrong position, or the newborn is moving or very upset, the blood pressure machine will beep, read 00/00 or display a pulse measurement that is unusual. If the machine does not resume normal function, the Research Assistant should disconnect the cuff and hit **silence** or **cancel**. This should stop the beeping. Check that all connections are connected properly – tubes screwed in, etc – before resuming measurements.

If the beeping stops and the machine appears to be functioning properly, the Research Assistant should resume measurements. If the beeping does not stop, the Research Assistant should remove the cuff and turn the machine off.

To confirm the accurate recording of data, the Research Assistant should press the PRIOR DATA button to see the blood pressure measurements before turning the machine off. The number shown next to the prior data button shows the number of minutes before the last reading. For example, the number 1 shows the reading from one minute ago. The prior data will go back as far as 4 previous measurements. The most recent reading (the 5<sup>th</sup>) will have no number showing in the prior data window. The Research Assistant should turn off the machine only after the stored data is recorded or no longer needed.



## **5) Problems**

Any problems with the Dinamap 8100 should be directed to Product Quality Service (1-800-237-2033-X3).

## **G. Newborn Abdominal, Head and Chest Circumferences and Length**

At Visit 3, the hospital Research Assistant should measure head, chest and abdominal circumferences of newborn Viva participants (children for whom an Informed Consent Form was signed) using the Ross Insertion tape (head) and the Hoechstmass tape (chest and abdominal). In addition, the Research Assistant should measure the newborn's length using a Shorr length board.

If the participant has decided to enroll her child in Project Viva, the Research Assistant should ask the participant (after completing the Child Enrollment Form (CEN)) if it would be a good time to measure her newborn. If it is, the Research Assistant should proceed with the measurements. The measurements can be done in the mother's room or in the nursery. If the measurements are done in the nursery, the Research Assistant should approach a nurse and ask permission to move the newborn into a semi-private space so as not to disturb the other newborns. Possible rooms are the room adjacent to the nursery, or empty patient rooms. The newborn should never be moved from the nursery without informing the nurse on duty, and should never be left unattended.

If the newborn is in the Neonatal Intensive Care Unit no measurements should be taken. If two research assistants are not available to take the length measurement, the research assistant may ask the mother or father to assist. At the Beth Israel Deaconess Medical Center the measurement cart is located in the 6<sup>th</sup> floor nursery. At the Brigham and Women's Hospital the measurement cart is located in the room next to the 9<sup>th</sup> floor nursery.

### **1) Preparing for the Measurements**

Before handling the newborn, the Research Assistant should remove all jewelry, including rings, watches, and bracelets. The Research Assistant should be aware of pens, pencils, and long nails, and should always move slowly and carefully around the newborn, paying particular attention to the newborn's head and neck. Before handling all newborns check in with the nurse in the nursery to confirm that the newborn has been bathed. If a newborn has not been bathed, the Research Assistant must wear gloves to handle the newborn. Before measuring the newborn, the Research Assistant should explain the measurement procedures to the mother. Hands should be washed thoroughly with soap and warm water before touching the newborn. During all measurements, the Research Assistant should make sure the measuring instruments do not harm the newborn—measuring tapes have sharp edges that could cut the newborn and the long ends of the measuring tape can be a strangulation hazard.

For the head, chest and abdominal measurements to be as accurate as possible, the measuring tape should be against the newborn's skin. It may be necessary, therefore, for the Research Assistant to remove or adjust clothing on the newborn before taking any measurements.

### **2) Taking the Measurements**

The ideal sequence for measuring the newborn is head circumference, chest circumference, abdominal circumference, and recumbent length. The Research Assistant may do the

measurements in a different sequence if necessary. Newborns should lie in the bassinet for the anthropometry measurements, and should be placed on the height board on top of the measurement cart for the length measurement.

The newborns may cry or become agitated when the Research Assistant sets up the measurements (puts the measuring tape under the torso, lies the newborn on the height board). The Research Assistant should wait until the newborn calms down before taking any measurements.

The Research Assistant should follow the protocol outlined below for each measurement.

**a. Head Circumference**

If the newborn is wearing a hat or headband, the Research Assistant should remove it before measurements are taken. The head circumference is taken with the Ross Insertion tape, which is hard, flexible plastic. To measure head circumference, the Research Assistant should:

- Place the Ross Insertion tape on the newborn's head so that the zero end of the tape is on the lateral aspect of the head (the side of the head, above ears). Make sure to place the tape under long hair.
- Position the tape just above the eyebrows and gently lift the newborn's head to place the tape around the widest part of the back of the head.
- If the newborn is crying or agitated, wait until the newborn calms down before taking the measurement.
- Pull the tape tightly to get rid of crimps.
- Read the measurement to the nearest tenth of a centimeter (31.4, etc.). (**See Section VIII.A, 3) Reading the Measurements**)
- Call out the measurement repeatedly until it is recorded.
- Check the measurement for accuracy and legibility.

**b. Chest Circumference**

The chest circumference should be taken using the Hoechstmass measuring tape, which is a blue, retractable tape. To measure the newborn's chest circumference, the Research Assistant should:

- Lift the newborn, making sure to support the head and neck, and place the Hoechstmass tape under the newborn's back, directly behind the nipples. It is necessary to lift the newborn to place the measuring tape underneath, because sliding the measuring tape from behind the shoulders can cut the newborn.
- Align the tape with the nipple line. The measuring tape should be kept parallel front and back. The measuring tape should not be kinked or wrapped around clothing or a diaper.
- If the newborn is crying or agitated, wait until the newborn calms down before taking the measurement.
- Take the measurement at the end of a normal expiration— usually this is when the chest is at its smallest diameter. The measuring tape should just lay against the newborn's skin.

- Read the measurement to the nearest one tenth of a centimeter. (**See Section VIII.A, 3) Reading the Measurements**)
- Call out the measurement repeatedly until recorded.
- Check the measurement for accuracy and legibility.

#### **c. Abdominal Circumference**

The abdominal circumference should be taken using the Hoechstmass measuring tape, which is a blue, retractable tape. To measure the newborn's abdominal circumference, the Research Assistant should:

- Lift the newborn's torso and place the Hoechstmass tape under the newborn's back, directly behind the umbilicus. It is necessary to lift the newborn to place the measuring tape underneath, because sliding the measuring tape from behind can cut the newborn.
- Place the tape just above the umbilicus. The measuring tape should be kept parallel front and back. The measuring tape should not be kinked or around clothing or the diaper.
- If newborn is crying or agitated, wait until the newborn calms down before taking the measurement.
- Take the measurement at the end of a normal expiration — usually this is when the abdomen is at its smallest diameter. The measuring tape should just lay against the newborn's skin.
- Read the measurement to the nearest tenth of a centimeter. (**See Section VIII.A, 3) Reading the Measurements**)
- Call out the measurement repeatedly until recorded.
- Check the measurement for accuracy and legibility.

#### **d. Recumbent Length**

If the newborn is wearing a hat or headband, the Research Assistant should remove it before the length measurement is taken. The length measurement is taken using the Shorr Length Board, which is on top of the measuring cart. The length board should be cleaned with a baby wipe before placing a newborn on it. To minimize the discomfort that the newborn might experience during this measurement and to ensure cleanliness, the length board should be covered with a blue, cushioned sheet. The Research Assistant should keep the sheet flat beneath the newborn during the measurement. The newborn should never be left unattended on the length board.

Because the use of this instrument requires two people, the Research Assistant should have someone (mother, father, other Research Assistant) assist by holding the newborn's head during the measurement. The person assisting should cup their hands over the newborn's ears with the thumbs tucked in. This assistant should also make sure that there is no gap between the newborn's head and the top of the length board when the measurement is called out.

To measure recumbent length, the Research Assistant should:

- Gently place the newborn on the length board. Ask an assistant to support the head and neck.
- Place the newborn's knees and feet in any of the following three positions:
  - 1) Knees together and feet together
  - 2) Knees together and feet apart
  - 3) Knees apart and feet together
- If the newborn is crying or agitated, wait until the newborn calms down before taking the measurement.
- Press down firmly on the newborn's knees with an open hand (flat, palm down) to straighten the newborn's legs. The Research Assistant should be sure not to put her fingers between the newborn's knees.
- Bring the footpiece firmly against the newborn's heels. Both feet should be flat against the length board and the knees should be straight. Confirm with the assistant that the newborn's head is against the board.
- Call out the measurement repeatedly until it is recorded. (**See Section VIII.A, 3) Reading the Measurements**)
- Remove the newborn from the height board as soon as the measurement is taken, so that the newborn can be held and calmed down.
- Check the measurement for accuracy and legibility.

### 3) Reading the Measurements

The Research Assistant should read all measurements at eye level. To take the measurements, the Research Assistant should count visible lines on the tape measure or length board ruler. The Research Assistant should call out the measurement while the newborn is still on the length board or tape. The Research Assistant should call out the number only i.e. 42.4 cm as “forty-two point four” not “four two point four centimeters”. The Research Assistant should call out the measurement repeatedly until recorded.

If a measurement falls between two lines, the Research Assistant should call out the nearest number. If a measurement falls “exactly” in the middle of two lines, the Research Assistant should call out the higher number.

## H. Infant Cognitive Development

We will measure development using the visual recognition memory (VRM) paradigm. It consists of 9 sets of trials and usually takes between 10 and 15 minutes to complete. Each set includes 1 familiarization trial and 2 test trials. In the familiarization trial, 2 identical, 5 by 7-inch pictures are presented on stage at a distance of 18 inches in front of the infant while he or she is seated on the primary caretaker's lap. The pictures are either of a face (adult or child with representatives from different ethnic/racial groups) or a geometric design. The familiarization trial lasts until the infant has accumulated either 10 or 20 seconds of visual fixation time, depending on the type of picture. Test trials present 1 familiar and 1 novel stimulus in the same format and last a total of 5

seconds beginning with the first fixation. The infant may use a bottle or pacifier during the procedure. The developmental assessments will be completed before the visit with the clinician and, thus, any invasive or uncomfortable procedures.

## **I. Lab Analyses**

### **1) Fatty Acid and Carotenoid Assays (Frank Sacks)**

These will be performed by standard methods employed by the laboratory of the Department of Nutrition. Erythrocytes are hemolyzed, and total lipids are extracted with chloroform-methanol and washed to remove proteins. The fatty acids are methylated via methanolic hydrochloride, dried under nitrogen, and analyzed in iso-octane. Analysis of fatty acid methyl esters is achieved by automated gas-liquid chromatograph equipped with a 100-m capillary cyanosilicone column and flame ionization detector. The procedure for carotenoids has been adapted from the procedure of Hess et al. The analytes are removed by ethanol precipitation and extraction with hexane. Data acquisition is achieved by a computer automated HPLC system on reverse phase silica column (C18), using both ultra-violet and visible wavelength automated detection. The system can be readily set up to focus exclusively on carotenoids.

The fatty acid analyses will be performed by standard methods employed by the laboratory of the Department of Nutrition: Erythrocytes are hemolyzed, and total lipids are extracted with chloroform-methanol and washed to remove proteins. The fatty acids are methylated via methanolic hydrochloride, dried under nitrogen, and analyzed in iso-octane. Analysis of fatty acid methyl esters is achieved by automated gas-liquid chromatography equipped with a 11-m capillary cyanosilicone column and flame ionization detector. Carotenoids and tocopherols will be assayed as by an HPLC method that simultaneously measures retinol, a gamma, and total tocopherol,  $\alpha$ - and  $\beta$ -carotene, lycopene, lutein, and cryptoxanthin. Folate will be measured by competitive protein binding using the Immuno-1 analyzer (Bayer, Tarrytown, NY) according to the manufacturer's recommendations. The assay for folate has a CV% of 12%, 6.3%, and 1.5% for concentrations of 169, 263, and 1275 pg/mL, respectively.

### **2) CRH Peptide Measurement (Joe Mazjoub)**

CRH peptide in plasma will be measured by radioimmunoassay following C<sub>18</sub> SepPak extraction, using I-labelled CRH (New England Nuclear, Boston, MA), synthetic CRH peptide (Peninsula Labs) and anti-CRH polyclonal antiserum R-12 (provided by T. Suda, Hirosaki University, Japan), as we have described. Synthetic CRH recovery is 96%, and intra-assay coefficient of variation is 2.1%. This extraction method dissociates CRH from its binding protein, such that total CRH is measured in plasma. Sensitivity is 2 pg/tube (20 pg/mL 0.1 mL plasma). We will not measure CRH-binding protein or unbound levels of CRH. However, CRH-binding protein levels do not vary during the first or second trimester,<sup>155</sup> and thus should not be relevant to our study.

### **3) Estriol measurement**

Maternal plasma estriol will be measured by commercial radioimmunoassay (Endocrine Sciences).

#### **4) Cortisol and Cortisol-sulfate measurement**

Our method is modified from those of Fencl et al. and Hall and Giroud. After the addition of <sup>3</sup>H-cortisol (1000 cpm) as a recovery marker, 0.1 mL plasma is precipitated with 64% ethanol, and the aqueous phase (containing cortisol and cortisol-sulfate) is digested with glucuronidase (2000 U, Sigma) in 0.1 M Na Acetate, pH 5 at 37C for 16 h. After neutralization with 0.2N NaOH (which inactivates glucuronidase), total (sulfated + nonsulfated) is measured in a traditional cortisol I-cortisol radioimmunoassay which does not detect cortisol-sulfate. Duplicate samples are measured with the addition of glucuronidase only after NaOH neutralization, under which conditions glucuronidase is inactive. This yields nonsulfated cortisol, since the anti-cortisol antibody does not react with cortisol-sulfate. All values are corrected for the recovery of <sup>3</sup>H-cortisol. Cortisol-sulfate is calculated by subtracting nonsulfated from total cortisol.

#### **5) Cord Serum Osteocalcin (Endocrine sciences in CA)**

At the Division of Preventive Medicine, BWH, and a technician will separate each specimen into 3 aliquots of serum, 2 of red blood cells, 2 of white blood cells. These all will be stored in liquid nitrogen freezers until ready for analysis.

## **Section IX. FORMS MANAGEMENT**

### **A. Confidentiality of Forms**

In order to assure confidentiality, all Viva participants are assigned a study ID number. This ID number will be the only identifier stored with participant questionnaires, blood samples or data. The participant's name and ID number will only be linked on Locator Forms and in a password-protected computer file. The Locator Forms will be stored in a separate locked file cabinet, with limited access by the Principal Investigator and his designee.

Participant ID numbers range from 10000 to 79999. HVMA patients who are not enrolled in the study will be assigned an ID number ranging from 80000 to 99999. Each child enrolled in the study will be given the same ID number as his/her mother. There will be an "M" or a "C" before the ID number to indicate if the number is for the Mother or the Child.

All data forms, excluding the Locator Forms, should be kept intact, filed in order by visit number, with each visit in a separate folder, within a locked cabinet. This will ensure that there is an official, easily accessible, permanent Viva file, to be reviewed and edited for quality control purposes. Completed Viva folders and forms must always be kept in the Viva file cabinet unless they are being used by a Research Assistant at that time. Completed folders and/or forms should never be kept at a Research Assistant's desk when a Research Assistant is not actively using them.

If Research Assistants are data entering forms and need to leave their desk, they should place the folder in the Viva file cabinet or in a locked desk drawer. If a form needs to be taken from the folder to be completed (i.e. EPI, MPI, LOC, etc.), the Research Assistant should put a dated post-it note in the folder indicating that it was taken. The form should be returned to the folder immediately after it is completed.

The participant's name and ID number should NOT be linked in any place other than on the Locator Forms. Because the Locator Forms contain both pieces of information, they are stored in a separate locked file cabinet in a locked office. If other forms contain the participant's name and ID number are stored in the main file cabinet, the Research Assistant should black out the participant's name.

### **B. Form Preparation**

Research Assistants are responsible for maintaining the supply of and processing data collection forms. On a regular basis, the Research Assistants are expected to photocopy forms, collate forms, and data enter forms.

Visit materials are kept in the Viva conference room bookshelves. All shelves are clearly labeled with a sticker indicating the form/material name. Materials are ordered and/or copied by the study staff, as needed (**Appendix EE: Supplies and Ordering**). The supplies are collated into Decliner Study Folders, Acceptor Study Folders, Participant Folders and Visit 2 Folders on a regular basis (**Appendix T: Compiling Visit Materials**).

### **C. Form Completion**

All Viva forms include the following fields:

- Study Number. Letter – 5 study digits – 1 check digit. M#####-#.
- Event. This refers to the visit number. Screening Form and Locator Form are identified as “00”. All other forms correspond to the actual visit number: 01, 02, etc.
- Date. This refers to the date when the data were collected or the take-home questionnaire was given to the participant.
- Research Assistant (RA) Initials. These appear as: first, middle, last or first, last, blank. Each form should be initialed consistently and legibly. This will allow edits and questions to be directed to the appropriate individual.
- Form version dates. All forms include the version date in the footer. If a MAJOR change is made to a form (one that requires new programming), the form version date is changed to reflect the date the new form is fielded. If a MINOR change is made to a form (typos, formatting), the date is not changed but a letter is added to the footer and version date name. This letter does not need to be data entered. Staff will receive emails introducing all new forms; all forms should immediately be replaced in packets. A form-tracking sheet that shows all fielded form versions is kept near the Viva bookshelf.

All of these fields must be completed for the form to be able to be entered into the Data Management System.

The data collector should write legibly and carefully. If it is necessary to change a response after something has already been written, draw a single line through the erroneous response, recode the question, and initial and date the change. Do not erase or use white out.

### **D. Form Review**

Forms collected at a Viva visit should be reviewed immediately following the visit. Each Research Assistant who initially completes the form is responsible for its review, checking for completeness, missing pages, legibility, internal consistency, skip pattern use, and overall clarity. After the forms have been reviewed, the participant folder is put in the Viva file cabinet according to the day of the visit.

During this post-visit review, certain edits can be made by the Research Assistant:

- Information that was not obtained from the participant can be coded as missing. Code “-9”, “RA error”, initials, and date. Information that is missing from a form completed by the participant can be coded “-9”, “Blank”, with the initials.
- To avoid an edit, information that seems out of range can be marked “Valid” and initialed.
- Information can be cleaned. Change partner’s height from “5’11” to “05’11”. Change dates from “3/3/99” to “03/03/99”. Change abbreviations to full words.
- Check legibility.

The Research Assistant may not change information that was provided by the participant during the interview.



## **E. Form Receipt and Form Cleaning**

Participants are expected to complete and return Viva forms within two weeks. Participants mail the Viva forms to the Project Viva PO Box 15710 at the Kenmore Square post office. Viva study staff retrieve mail from the Project Viva PO Box every day after 10:00 am.

When the study staff returns from the Post Office, he/she sends an email of ITEMS RECEIVED to the rest of the Viva group. These emails are printed and saved in a single log by the Data Manager. Immediately after the email is sent, the forms are logged into the DMS and then cleaned (**Appendix FF: Form Receipt & Form Cleaning**). For most forms, this involves stamping the form with the date received, and coding “-9” and the Research Assistant’s initials by missing values. For an FFQ, this entails stamping the form with the date received, calculating a Date Completed if this field is empty, and drawing a red circle on the tab of the folder to indicate that an FFQ has been received.

At a later date, the FFQ must be further cleaned and coded in preparation for scanning (**Appendix FF: Cleaning FFQs**).

## **F. Data Flow**

Once logged, the forms are placed in sequential order according to ID in the main section of the file cabinet. All forms should be data entered within 48 hours of receipt.

After being entered, the Locator Form should be removed from the Participant Folder and placed in the “LOCATOR” section of the file cabinet. These are removed from the cabinet on a daily basis and put in a separate, locked file cabinet. If there are multiple Locators Forms for a participant, they are stapled together with the most recent LOC on top (LOC1 is stapled to LOC2, with LOC2 on top). The Consent Forms are also removed from the participant folder and placed in a separate locked file cabinet on a daily basis. These forms are also sorted alphabetically by the participant’s last name.

If the interview has not been completed by the time of data entry, the Locator form remains in the participant folder to alert the Research Assistant that the information still needs to be collected. Once the interview is conducted, the Research Assistant places the Locator Form into the “LOCATOR” section of the file cabinet. If an interview is never obtained, the Research Assistant should set the EPI1 to “MISSING”. The Research Assistant should then remove the Locator form from the folder and put it into the “LOCATOR” section of the file cabinet.

## **Section X. DATA MANAGEMENT**

To perform data entry, a Research Assistant should open the DMS by entering a valid name and password at the prompt.

### **A. Orientation**

Every study ID number has a screen in the DMS (see the example below).

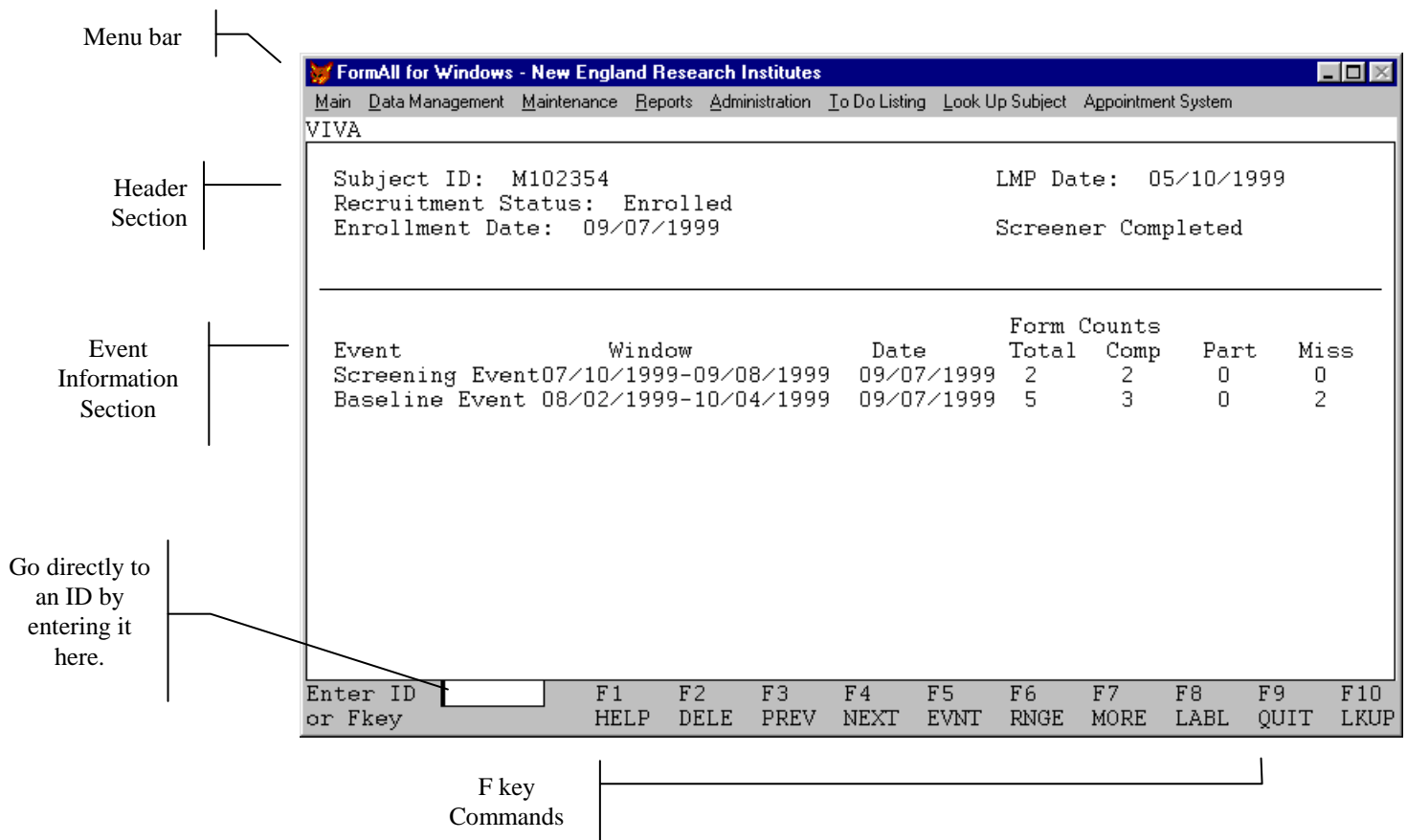
#### **1) The Header Section**

The Header Section shows some basic information about the ID number, such as the recruitment status (Enrolled, Declined, Disenrolled, Ineligible), Enrollment Date, LMP Date and the status of the Screening Form.

#### **2) The Event Information Section**

The Event Information Section provides information regarding the events for the ID # shown in the header.

1. On the left is a list of possible events for that ID.
2. The Window column shows the date range of when a visit is expected to take place and is calculated automatically based on the LMP.
3. The Date column shows the date the visit was initiated. If the Date column is blank, the visit has not been initialized.
4. Form Counts show the number of forms. The Total column is the number of forms expected for each visit. Comp is the number of forms completed. Part is the number of partial forms. Miss is the number of missing forms.



### 3) F Key Commands

The *F Key Commands* allow shortcuts to certain menu items:

- F1 HELP provides a help screen
- F2 DELE deletes the ID # displayed in the screen (only works for Decliner IDs).
- F3 PREV moves screen to previous ID (IDs are in numerical order)
- F4 NEXT moves screen to the next ID
- F5 EVNT displays the Event Screen for that ID
- F6 RNGE prints a range of labels specified by the user
- F7 MORE shows additional function keys (currently not in use)
- F8 LABL prints a full sheet of labels for the ID # displayed in the screen (Acceptor IDs only).
- F9 QUIT Quits the DMS
- F10 LKUP will identify the name of an ID#, or the ID# for a last name.

## B. Event and Form Status Screens

As forms are data entered, the DMS simultaneously checks for data entry errors, missing data, and invalid or out-of-range values. The DMS tracks the status of every form using the following codes: ?, P, C, M, N and L. Pressing F5 allows access to the Events for the ID shown in the header. The Research Assistant should select an event by using the arrow keys and then pressing enter. This Form Status screen (below) provides more detailed information about the forms for this event. Each form is listed on the left with its data entry status on the right.

FormAll for Windows - New England Research Institutes

Main Data Management Maintenance Reports Administration To Do Listing Look Up Subject Appointment System

VIVA

Subject ID: M101422 LMP Date: 05/15/1999

Baseline Event Date: 07/19/1999

| FORMS STATUS                       |             |          |       |
|------------------------------------|-------------|----------|-------|
| FORMS                              | Explanation | Statuses | Entry |
| BLD - Blood Collection - Visit 1 a |             |          | C     |
| EPI - Early Pregnancy Intervie     |             |          | P     |
| EPQ - Early Pregnancy Questionair  |             |          | M     |
| EPS - Early Pregnancy Supplement   |             |          | C     |
| FFQ - Food Frequency Questionna    |             |          | ?     |

Commands

|             |               |            |                  |
|-------------|---------------|------------|------------------|
| Delete Form | Form History  | Add Data   | Change Date      |
| Browse Data | Edit Report   | Log Form   | Delete Event     |
| Edit Data   | Set Overrides | Specimen   | Add Form         |
| Missing     | QC Data Entry | In Transit | Add Special Note |
| NA          |               |            | Exit             |

Each form is assigned a status as follows:

- ? outstanding These are forms which the protocol requires, but have not yet been data entered.
- P partial When any value entered into the DMS requires an edit, the DMS flags the variable and includes an explanation of the problem in an edit report, which is printed out after all data entry is complete. Edit reports are generated when values entered into the DMS do not fall within the limits permitted by validation checks. The DMS then changes the status of the form to a partial status (status of “P”) – i.e. the form has been entered, but it requires edit resolution.
- C complete If the form does not required any edits, the status of the form is complete (status of “C”). Once the edits for a partial form are resolved and entered, the DMS will change its status to complete.
- M missing Missing indicates a form that should be entered into the DMS, yet cannot for any number of reasons. When a form is set to missing, the D/E operator should enter a reason that the form is no longer expected.
- N not applicable Not applicable indicates that while a particular form is usually collected at a particular visit, it does not apply to this particular participant.
- L logged This form has been received. Logging a form allows us to quickly indicate that the form is received without entering the form. Ideally, all forms should be entered after they are received. When this is not possible due to limited time, the forms should be logged. No form should be filed without having at least an L status in the DMS. It is not necessary to log a form that can be entered immediately.

Commands are listed in the bottom half of the Form Status screen. The most common data entry commands are listed below. Press the key of the highlighted letter to select that command.

- A Add Data Add data to a form that was either expected or logged. (No data already exists for that form)
- E Edit Data Edit data that has already been entered. Usually used when a form is partial but can also be used to edit a completed form.
- B Browse Data Browse the form without modifying the data.
- L Log Form Log a form as received without data entry.
- M Missing Set a form to missing when a form is no longer expected.
- F Add Form The D/E operator is given options to add a form appropriate to that event.
- Q QC Data Entry QC (quality control) a form by repeating data entry.
- X Exit Exits to the main screen.

## C. Entering Data

### 1) Codes recognized by the DMS

| Code | Data Status    | Notes  |
|------|----------------|--|
| -9   | Missing        | This also applies to data that are invalid, illegible or ambiguous.  |
| -1   | Not Applicable | This should be entered for questions that are left blank because they are not required. For example, a participant's weight may be provided in pounds or kilograms, if kilograms are provided, -1 should be entered for the pounds variable. Another example would be if several lines of space for text are given; if all text can be entered into the first line then -1 should be entered into the second line. |
| -8   | Partial Date   | A -8 should be entered for the MM and/or DD portion of the date fields if they are missing. This is still considered a valid answer during data entry. NOTE: this is not true for all date fields, i.e., this would not be allowed for key dates such as the date of the Screener or Last Menstrual Period (LMP) since these dates are used to trigger other activities.   |
| -4   | < 1 / week     | This is only used in Section E of the Early Pregnancy Interview (EPI) to indicate that a woman is taking a vitamin with a frequency of less than once per week.  |
| -5   |                | This is never data entered. It exists as a default for fields where zero is a valid answer.  |

### 2) Errors

When the DMS encounters an error, an unexpected missing value or value that does not meet a validation, an error screen will appear. This screen will identify the error and the validations and ask "Proceed Anyway?" The data enterer should:

Press N to return to the form to change the value.

Press Y to proceed despite the error.

Press O to override the validation and then proceed.

Errors on RA-administered forms: An error can only be overridden if the Research Assistant has initialed and dated the error. If the Research Assistant has made a notation by the error (RA error, Part DK, Sticker, Valid, Refused), the data enterer should use that as the override reason. If the Research Assistant has not recorded a notation, Blank should be used as the override reason.

Errors on Self-administered forms: If a participant has left a question blank, illegible or ambiguous, the data enterer should write -9 on the form in red ink and initial and date it. The error should then be overridden. Generally, forms completed by the participant should never have

unresolved errors.

### 3) **General guidelines**

- The data should always be entered **exactly** as it appears on the form. If text will not fit in the space allowed, the data enterer should type as much as possible then proceed to the next question.
- A -9 should be entered when an answer is missing, illegible or ambiguous.
- After a form has been entered, the data enterer should:

Date and initial top, right-hand corner of the form with an “E” indicating that the form has been entered (e.g. “E-AB 10/31/99).

Place printouts of edits in Research Assistant’s mailbox.

### **D. Troubleshooting**

If the data enterer has questions while entering forms, s/he should forward the question to the Data Manager (**Appendix GG: Data Entry Questions**). If the data enterer is unable to enter a form or question due to a system error, s/he should forward the problem to the Data Manager (**Appendix GG: DMS Bug Sheet**) and return the participant folder to the “UNABLE TO ENTER” section of the file cabinet.

The data on the hard copy form is identical to the data that is entered into the Data Management System (DMS). The data entry operator can only enter what is written on the form. No assumptions can be made about missing, incomplete, contradictory or unclear data that have been collected and recorded on study forms. If a question is left blank or the response is invalid or ambiguous, the question should be coded as missing. More guidelines about data entry are included in **Appendix HH: Data Entry Guidelines**.

### **E. Validations and Edit Reports**

There are two types of validations to identify edits: hard and soft. All variables are verified by a hard validation. Some variables are also tested with soft validations.

A hard validation flags values in the DMS data that are unacceptable, illogical and/or impossible. Pre-coded questions have hard validations, which ensure that the data entry person does not mistakenly enter a value, which is not within the range of possible response choices. In the case of clinical variables, hard validations flag data, which are highly unlikely or clinically impossible. Ranges for clinical variables have been individually programmed.

### **F. Edit Resolution**

After data entry, all edits are placed in the Research Assistant’s mailbox. The Research Assistant responsible for initially completing the form must complete the edit report. Research Assistants are responsible for clearing their edits. If a Research Assistant does not have edit reports for all of the forms that have a status of partial in the DMS, she should check the DMS on a regular basis for partial forms, and clear the edits.

## 1) Resolving Edits

Edit reports reference the form number, the form name, the ID number, the visit number and the initials of the person who completed the form. The Research Assistant who completed the form must be the person to resolve an edit report.

The edit report indicates whether the value in question failed a validation or was missing. If the value failed a validation, the Research Assistant should complete the edit report by indicating that the value is correct or by correcting the value. One of two fields must be completed:

- **Value OK:** This field is checked if the Research Assistant would like to confirm that the value is indeed correct. The “Reason” must then be indicated on the adjacent line (for example, “valid”). To avoid these edit reports, the Research Assistant may confirm that the data is accurate at the time of data collection by simply initialing and writing “Valid” in the margin.
- **Correct Value:** This field is coded if the Research Assistant would like to change the answer noted. For example, if the Research Assistant coded a Delivery Date of “11/11/99” instead of “11/11/00”, they would note “11/11/00” in the Correct Value space.

If the value was missing, the Research Assistant should complete the edit report by indicating that the value is indeed missing or by adding the correct value. One of two fields must be completed:

- **Value Missing:** This field is checked if the Research Assistant forgot to code the answer and does not know the answer now. The “Reason” must then be indicated on the adjacent line (for example, “RA error”). To avoid these edit reports, the Research Assistant may code the field as missing during form cleaning by initialing and writing “-9” “RA error” in the margin.
- **Correct Value:** This field is coded if the Research Assistant is able to add a correct value. If the missing value is data obtained from the participant, the Research Assistant can not add the value at this point. If the missing value is data coded by the Research Assistant, it may in some cases be added at this point. For example, if the Research Assistant forgot to check that the form was administered on the SCR, it could be added at the time of the edit report since this is not information obtained from the participant.

If the question involves collecting factual information, it is acceptable to re-contact the participant to obtain the data and complete the edit report. The Research Assistant should record the participant’s answer in the “Correct Value” space on the edit report, with the Research Assistant’s initials in the space provided. The original form (and all copies of the data form, if applicable) must also be corrected to reflect the corrected data.

If the edit report question is not factual information but about the participant’s opinion or feeling about something, the Research Assistant should not re-contact the participant to obtain an answer. The Research Assistant should simply make note on the edit report that the data is missing due to RA error. If re-contacting the participant for factual information is not feasible, then the person completing the edit report should check the “Value Missing” space, and record a reason in the space provided (e.g., “RA error”), and her/his initials.



When completing an edit report, do not use data from any source other than the participant's direct answer to the question. Information from other sources (such as clinic records) should not be transferred under any circumstances.

## **2) Avoiding Edit Reports**

Research Assistants should watch for circumstances that will generate an edit report. If she notices a situation that may generate an edit report, record the clarifying information in the margin of the data form. The data entry person will then be able to respond to the DMS prompt for explanation immediately by entering the reason the data collector wrote in the margin. Taking the time to process and check the forms before they go to data entry can prevent the generation of an edit report. Ultimately, this will save time involved in reading the edit report, reviewing the form in question, remembering the reason for the problem, completing the edit report and sending it back for data entry.

## **Section XI. COMMUNICATIONS**

### **A. Study Inquiries**

Any questions about the study procedures (clinical issues, administrative issues, data form completion and data processing) should be directed to the Project Coordinator in the form of a Study Inquiry (**Appendix II: Study Inquiry**). The Project Coordinator will resolve the inquiry and send the Question and Answer to the entire Viva team via email. If necessary, the inquiry will be discussed at the weekly Viva meeting.

### **B. Site Communication**

The Research Assistant is the primary contact with the clinicians and staff at each HVMA office. The Research Assistant provides information to new clinicians or staff at the site and updates site staff about the study in general. If new staff join the HVMA office, the Research Assistant gives the person's contact information to the Viva Data Manager. This contact information is used to mail updates to HVMA clinicians and staff about the study.

Each month, the Project Coordinator contacts the Clinical Supervisor at each HVMA office and requests feedback about the study operations.

Viva provides periodic updates to the HVMA staff. These updates include Viva Summary Statistics and are accompanied by a food tray.

### **C. Participant Communication**

A Viva Hotline has been developed to receive calls from participants and potential participants. The line is answered by the Project Coordinator and/or other study staff prepared to answer questions about Project Viva.

A Viva newsletter (**Appendix JJ: Viva Views**) is sent to each participant at her 21-22 week of pregnancy, just before the second Viva visit. After women deliver, they become eligible to receive Viva Views II, which is sent on a quarterly basis to **all** post-partum participants. (**Appendix JJ: Identifying Recipients and Sending Viva Views**).

### **D. Disenrollment**

The Research Assistant completes a Disenrollment Form if there is a change in the status of a participant or there is a request to disenroll. The Research Assistant should complete the Disenrollment Form, enter it into the DMS and place the form in the participant folder. After the Research Assistant enters the Disenrollment Form (DIS) into the DMS, she should set all other Expected forms to Missing in the DMS.

Follow-up status changes include:

- No longer pregnant (including ectopic pregnancy)
- Moving
- Informed consent withdrawn
- Twins, triplets, etc.
- Other, specify

The Research Assistant should speak to the Project Coordinator about other disenrollment circumstances that arise.

If the participant has had a miscarriage, the Research Assistant should also send the participant a Viva card. The text for such a card might say: “We are sorry to learn that you recently had a pregnancy loss. I want to let you know that I will not be sending you any more questionnaires for Project Viva. Thank you very much for your willingness to participate in this study. Take care, ...”

## **Section XII. QUALITY CONTROL**

### **A. Initial Training of Research Interviews**

All Research Assistants will be trained in standardized methods for conducting research interviews. This training will entail:

- Observing and discussing a video on standardized interview techniques and a video on confidentiality.
- Reviewing the “Guidelines for Conducting a Research Interview”, the protocol, study forms and the Question by Question Specifications.
- Conducting several mock interviews until the Research Assistant is comfortable with the protocol and forms.
- Being observed and evaluated while conducting a mock recruitment.
- Being observed and evaluated while conducting a real Viva visit.

After the Research Assistants are comfortable with the recruitment procedures, they are also trained on conducting the Visit 2. This training will focus on the administration of the Personal Safety Questionnaire but will also review the entire Visit 2 protocol and flow.

To train the Research Assistants for Visit 3, a consultant was hired to provide detailed instruction about the anthropometric measurements. The consultant observed each Research Assistant perform the measurements on a newborn and provided immediate feedback to them.

### **B. Future QC of Research Interviews**

Every six months, the Project Coordinator will observe the Research Assistants conduct a Viva visit and will complete an evaluation form. Immediately after the visit, the Project Coordinator will review the visit with the Research Assistant and submit an evaluation to the Principal Investigator and the Project Director. If multiple issues arise during the observed visit, the Project Coordinator will observe a second visit to ensure that problem areas are resolved.

### **C. Quality Control of Data Entry**

Initially, all study forms are being re-entered for verification purposes. Ideally, two different data entry operators conduct double entry. This process is designed to correct any keystroke errors that were made during initial data entry and to verify that the data entered into the computer is identical to the data written on the form.

### **D. Quality Control of Blood Delivery**

Every week, the Channing Lab faxes the received Blood Delivery Logs to Viva. These logs are checked against the Blood Collection Forms to verify that all blood collected was received by the Channing Lab (**Appendix KK: Blood Delivery QC**). If there is a discrepant number of blood tubes sent and blood tubes received, the Project Coordinator calls the lab to check the reason.

