# 1. Blood Pressure/Pulse

## 1.1 Background and rationale

A standard automated blood pressure measurement device and a specific protocol for the measurement of blood pressure and pulse will be utilized.

## 1.2 Definition

Seated blood pressure and pulse are measured three times at each clinic visit. The seated BP and pulse readings are the averages of the three systolic and diastolic BPs and pulse rates measured by the Omron HEM-907 automated blood pressure and pulse measurement device. The Space Labs Medical Model 90207 Ambulatory Blood Pressure (ABP) Monitor will be used to measure BPs in participants with an arm circumference between 43-50 cm.

## 1.3 Methods

This protocol is written for use with the Omron HEM-907 automated blood pressure and pulse measurement device and the Space Labs Medical Model 90207 ABP. Special attention must be placed on assessment and maintenance of the instrument's accuracy as per the manual that accompanies the instrument.

The design and operation of the Omron HEM-907 automated BP measurement device and the Space Labs Medical Model 90207 ABP are based upon the combined principles of compression of the brachial artery under an elastic, inflatable cuff and estimation of the systolic and diastolic blood pressure levels by oscillimetric methods. The observer places the correct size cuff on the participant's arm, pushes the button on the device and waits for the output.

All readings will be recorded to the nearest digit.

<u>Required Equipment</u>

- One OMRON HEM-907 automated blood pressure measurement device.
- BP cuffs in three sizes:
  - Large: 32-42 cm (13-17")
  - Medium: 22-32 cm (9-13")
  - Small: 17-22 cm (7-9")
- One Space Labs Medical Model 90207 ABPM
- 4 AA batteries
- XL adult cuff: 43-50 cm
- ABPM software
- Monitor cable
- Metric tape
- Black felt-tip pen

- Chair and table (table must provide for a comfortable resting posture of the arm with mid-cuff at heart level). Chair must have a back for participant's back to be supported during rest and BP determinations.
- Data collection form.
- stopwatch

Cuff Size Determination

BP measurements should usually be taken in the right arm. The left arm may be used in the presence of an anomaly or other circumstance prohibiting use of the right arm.

Proper cuff size must be used to avoid under or over-estimation of blood pressure. Cuff size refers to the cuffs bladder, not the cloth. A copy of the chart below should be attached to the sphygmomanometer for easy reference.

Cuff Size Indicated by Measured Arm Circumference

| Arm Circumference | Cuff |
|---|---|
| 17-22 cm (7-9") | Small |
| >22-32 cm (9-13") | Medium |
| >32-42 cm (13-17") | Large |
| >42 cm (>17") | Space Labs Medical Model 90207 |

- Have the participant remove his/her upper garment (bare arm).
- Have the participant stand, holding forearm horizontal (parallel) to the floor.
- Measure arm length from the acromium (bony protuberance at the shoulder) to the olecranon (tip of the elbow), using a metric tape.
- Mark the midpoint on the dorsal surface of the arm.
- Have participant relax arm along side of the body.
- Draw the tape snugly around the arm at the midpoint mark. NOTE: Keep the tape horizontal. Tape should not indent the skin.
- Use the criteria in the Table (above) for determining cuff size.

Wrapping the Blood Pressure Cuff Around the Arm

The participant should then be seated with back supported, legs uncrossed, in a quiet room, with the elbow and forearm resting comfortably on the table with the palm of the hand turned upward. The area to which the cuff is to be applied must be bare.
Locate the brachial artery by palpation and mark the skin with a little dot from a felt-tipped marker. (The brachial artery is usually found at the crease of the arm, under the muscle and slightly towards the body).

Cuff Placement:

a) Apply cuff around the upper right arm approximately 1" above arm crease
b) The midpoint of the length of the bladder is positioned over the brachial artery
c) The mid-height of the cuff is a heart level.

Wrapping the Cuff:

a) Wrap the cuff tightly around the arm, -i.e. tight enough that you can insert only one-two fingers between the cuff and arm.
b) The cuff should uniformly contact the circumference of the arm

Taking the Blood Pressure and Pulse Measurements

Record the OMRON device number and the Space Labs 90207 ABPM device number used for measurements.

**Settings for the function keys on the OMRON device:**
(F1) to take an average of 3 measurements
(F2) delay function to 0 seconds.

## (F3) wait time between recordings set for 30 seconds.

**Procedure for blood pressure measurement:**

**Set 'P-SET' dial to AUTO**

1) Set 'MODE' dial to 'AVE'

**Procedure for blood pressure measurement using the Space Labs ABPM:**

1) **Programming/ "Initializing" ABP Monitor**
   - **Insert fresh batteries into monitor (new batteries should be inserted after 40 readings)**
   - Log into computer and bring up windows. Double click on the ABP Report management System icon

- Turn on monitor
- Be sure the ABPM cable is attached to the appropriate port on the computer and to the monitor (arrow towards arrow)
- From the menu bar click on "Communications". From the "Communications", choose "Init monitor"
- To set the default settings choose "Setup" from the menu bar. Choose "monitor" from the pull down menu. From the settings menu choose "New" to change the settings as to the OmniHeart protocol. To accept default settings click on save, then OK
- Since you will be initializing the monitor for multiply readings, enter 99999 both in the "name" field and in the "ID number" field.
- Click on "Start Inil" to initialize the monitor. Disconnect monitor from cable, turn it off, and place monitor in its padded carrying case.

**2) Down-Loading the monitor**

- You must download the 40 readings in order to initialize again
- Access the ABP Report management Systems in windows.
- Connect the monitor via the cable (arrow to arrow)
- Turn monitor on
- Click on the "Communications" and choose "Read Monitor" from the pull down menu
- The system will ask for a unique 9-digit number
- Enter 999990000
- When "Select A Group" message appears, select OmniHeart from the scan groups.
- Click OK
- The screen will display 99999
- If you want to print out readings you can.
- To initialize the monitor for the next group of readings, repeat steps in "Programming/Initializing" the ABPM

The participant should sit quietly for a period of 5 minutes before the first blood pressure is taken.

The following should be confirmed before leaving the participant for their 5 minute rest:

1. No smoking, caffeine or vigorous exercise 30 minutes prior to blood pressure reading.
2. All beepers and cell phones must be turned off.
3. They should use restroom if necessary.
4. Room temperature should be 65-75 degrees F.
5. They should be seated comfortably, feet flat on the floor and back supported.
6. Their right arm (with cuff on), should be supported comfortably on a surface with mid-cuff at heart level.

7. The Omron device is not sharing an outlet with another unit or electric appliance.

After a 5 minute rest period, the research assistant enters the room silently and pushes the start button to begin the automated measurements.

**Record the 3 systolic and diastolic blood pressure and pulse readings, and the averages from the OMRON device in the spaces provided on the blood pressure measurement form. Be sure to shield the BP measurements from the participant. When using the Space Labs ABPM you will record the three readings and then determine the average using a calculator. All math work should be done using a calculator.**

## 1.5 Guidelines for Proper Use and Maintenance of Equipment

### Omron and Space Labs ABPM Calibration

The Omron and Space Labs ABPM units have been validated to remain in calibration for up to 100,000 measurements. The units need to be calibrated every 4 months per manufactures instructions against a mercury sphyngomanometer. Machine should be within +or- 3mmHg. Have two people available during calibration. One to read Omron and Space Labs ABPM unit and the second person to read the mercury sphyngomanometer.

Any machine that is dropped should be re-calibrated before any further use.

### Omrom and Space Labs ABPM Maintenance

Regularly check lines on BP cuff and machine for any leaks.

Clean machine with detergent per manufacturer's guidelines.

Launder BP cuffs as needed.

# 2. Eligibility

***Study Population***

The study sample consists of approximately 160 healthy, free-living adult men and women, age 30 years and older, who have a SBP of 120-159 mm Hg or DBP of 80-99 mm Hg.

***Eligibility Criteria***

Participants must meet a number of eligibility requirements for participation in OMNI (Table 2-1). These eligibility requirements were selected to exclude individuals with conditions, special dietary requirements, or taking medications, that would affect blood pressure or micronutrient metabolism. Individuals with potentially serious chronic health conditions will also be excluded.

The OMNI eligibility criteria are assessed during the course of several screening visits and during a period of run-in feeding prior to randomization. This section lists the various eligibility requirements and gives the operational criteria by which they are determined. Because of the lag between the initial screening visit and the start of run-in, the Protocol stipulates that key medical eligibility criteria, if initially determined more than one month prior to the start of run-in, must be confirmed within this timeframe.

Several of the eligibility criteria relate to laboratory tests conducted using blood or urine specimens. Any initially abnormal laboratory values that would result in exclusion may, at the discretion of the local Principal Investigator (PI), be repeated once and the participant retained if the second value falls within eligible limits (except where noted below). All laboratory assessments for eligibility are performed locally, and, unless specifically noted otherwise, eligibility is based on local normal ranges.

**Table 2.1: Inclusion and Exclusion Criteria of the Trial***

- Baseline SBP 120-159 mmHg or DBP 80-99 mmHg (mean over three screening visits) [note: stage 2 hypertension (SBP ≥ 160 or DBP ≥ 100 mmHg) based on the mean over three screening visits will be excluded, as well as a mean systolic BP > 170 or diastolic BP > 105 at any one visit]
- age 30 or older
- willing to eat at least one on-site meal/day, five days/week, and willing to eat study diets and nothing else for the 19 weeks of controlled feeding

**Medication Exclusions**

- Use of antihypertensive drugs (any in two months prior to SV1)
- Chronic use of medications that raise or lower blood pressure
- Use of a lipid lowering agent (any in 3 weeks prior to SV1)
- Unstable dose of hormone replacement therapy, psychotropic medications and thyroid hormone replacement therapy (defined as a change in dose within two months of the SV1 visit)
- Use of lithium, insulin, oral hypoglycemic agent, oral corticosteroid, anti-psychotic drugs, weight loss medications, oral breathing medication, nitrate, or digitalis

**Medical History Exclusions**

- Active or prior cardiovascular disease (stroke, MI, PTCA, CABG, congestive heart failure, symptomatic ischemic heart disease (angina), or ASCVD-related therapeutic procedure)
- Cancer diagnosis in past two years (however, persons with non-melanoma skin cancer, localized breast cancer, or localized prostate cancer can enroll if they did not require systemic chemotherapy)
- Inflammatory bowel disease, colostomy, malabsorption, or major GI resection
- Renal insufficiency as determined by a serum creatinine > 1.2 mg/dL for women or > 1.5 mg/dL for men. These participants can enroll if their estimated GFR is ≥ 60 ml/min by either the Cockcroft-Gault equation or the simplified MDRD equation.
- Emergency room visit or hospital stay for asthma or COPD in last six months
- Any serious illness not otherwise specified that would interfere with participation

**Laboratory Exclusions***

- Fasting LDL cholesterol > 220mg/dL, triglycerides > 750 mg/dl
- Fasting blood sugar ≥ 126 mg/dl
- Urine dipstick protein ≥ 2+

**Other Exclusions**

- Consumption of more than 14 alcoholic drinks per week, or consumption of 6 or more drinks on one occasion twice or more per week
- Significant food allergies, preferences, intolerances, or dietary requirements that would interfere with diet adherence
- Weight over 350 pounds
- Weight loss or gain of 10 pounds during 2 months prior to SV1
- OMNI-Heart staff
- Planning to leave the area prior to the anticipated end of participation
- Pregnant, breast feeding, or planning pregnancy prior to the end of participation
- Requirement for use of thigh cuff (arm circumference > 41 cm) or inability to obtain accurate blood pressure measurements
- Current participation in another clinical trial with an intervention that affects blood pressure or lipids
- Investigator discretion (e.g. for concerns over safety, adherence, or follow-up or for inappropriate behavior) reasons
- Vitamin, fish-oil, weight-loss, soy, mineral, or herbal supplements that cannot be stopped prior to run-in

* For any laboratory-based exclusion, one repeat laboratory test is permitted if the initial value would have excluded the individual

*Inclusion Criteria*

- SBP 120–159 mm Hg or DBP 80-99 mm Hg

Three blood pressure measurements are taken at each of the first three formal screening visits (SV1, SV2, and SV3), and the average of these nine measurements must fall within the stated limits for SBP or DBP. In order to identify participants not likely to meet these limits, somewhat wider eligibility limits are also established for the average cumulative blood pressures at each of SV1 and SV2 (see MOP Chapter 6).

Participants who are excluded from the screening process because of blood pressure may re-start the screening process for another cohort.

- Age > 30 years

Participants must be 30 years of age or older at start of run-in feeding.

Operationally, this is assessed by asking, at the prescreening visit, whether the participant is currently 30 years of age or older. Date of birth is also collected for confirmation.

- Willing to eat at least one on site meal/day, five days/week, and willing to eat study diets and nothing else for 19 weeks

The nutrition staff repeatedly stress this issue with potential participants, and the run-in feeding period is a further test of the participant's willingness to comply with the trial's strict eating requirements.

- Willing to provide written informed consent

In order to participate in the study, all subjects must provide written, informed consent using procedures that are reviewed and approved by each center's local IRB.

*Exclusion Criteria*

- Specific medication use

In addition to having any of the medical conditions listed in Table 2.1, participants are also excluded from participation if they report taking any of the following medications. Unless noted otherwise, **current medication use is defined as any use within 21 days of the SV1 visit or at any time thereafter**. All participants are expected to bring their medication bottles to the SV1 or SV2 visit for review by a clinic staff member.

<u>Medication Exclusions:</u>

—Use of blood-pressure-lowering drugs within the two months prior prior to SV1
—Use of any lipid-lowering agents within 3 weeks of SV1
—lithium
—insulin
—oral corticosteroids
—unstable dose of hormone replacement therapy, psychotropics, phenothiazines, or theyroid hormone replacement therapy (defined as a change in dose within 2 months of SV1).
—oral breathing medications, such as theophylline. Liekotriene receptor antagonists are not an exclusion because this class of 'oral breathing' medications does not affect blood pressure
—dilantin
—antacids containing magnesium or calcium, unless they can be discontinued
—digitalis
—weight-reducing medications
— OTC medications or other consumer products providing 3 or more mmol of sodium per serving, unless they can be discontinued

Medical History Exclusions

- Cardiovascular disease or congestive heart failure

Participants are excluded if they report a prior CVD event (defined as stroke, MI, heart failure, CABG, hospitalization for unstable angina, or coronary angioplasty) or if they report a clinical diagnosis of congestive heart failure. Confirmation is not necessary unless the participant is uncertain of the diagnosis and the clinical center still wishes to include him/her.

- Cancer diagnosis in past two years (however, persons with non-melanoma skin cancer, localized breast cancer, or localized prostate cancer can enroll if they did not require systemic chemotherapy)

The diagnosis of cancer and the status of therapy are based on the participant's self-report and do not need to be confirmed with the participant's physician unless a question exists about whether the cancer is currently active.

- Inflammatory bowel disease, colostomy, malabsorption, or any prior GI resections other than localized colonic resections

Defined based on self-report. Confirmation is not necessary unless the participant is unsure of the diagnosis and the clinical center still wishes to include him/her.

- Renal insufficiency

If the serum creatinine level is >1.5 mg/dL (men) or > 1.2 mg/dL (women) AND the calculated GFR is < 60 ml/min, the participant is ineligible. The GFR can be calculated using the Cockroft-Gault formula or the simplified MDRD formula:

Cockroft-Gault Formula:
Men: GFR = [(Wt in Kg)*(140-Age in years)] / [72* serum creatinine in mg/dl]

Women: GFR = 0.85 * [(Wt in Kg) * (140-Age in yrs)] / [72* serum creatinine in mg/dl]

Simplified MDRD Formula:

GFR = 186.3*(sCr)-1.154 * age-0.203 * (0.742 if female)* (1.21 if African-American)

- Unstable asthma or COPD

Defined as an emergency department visit or hospital stay for asthma or COPD in last six months, or other evidence of recent instability in asthma or COPD. Health care utilization is based on participant self-report and need not be confirmed. The local PI must determine "Other evidence of recent instability" based on information provided by the participant.

- Any serious illness not otherwise specified that would interfere with participation

Based on self-report. Final determination of whether an illness would preclude participation is left to the local clinical center.

- Hyperlipidemia

Defined as a serum LDL cholesterol level > 220 mg/dL or a fasting triglycerides > 750 mg/dl.

- Non insulin-dependent diabetes
  Defined as fasting glucose $\geq$ 126 mg/dl.

- Urinary protein

Defined as a urine dipstick protein level of 2+ or more.

- Consumption of more than 14 alcoholic drinks per week, or consumption of 6 or more drinks at an occasion twice or more per week.

This is determined at the prescreening visit and confirmed subsequently as part of the Eligibility Review that takes place between SV1 and SV2. In both cases the information is based on self-report. One drink of alcohol is defined as one can or bottle of beer, one glass of wine, or one shot of liquor.

- Unwilling or unable to modify current diet

A necessary prerequisite for participation in the study is a willingness and ability to comply with the study's strict eating guidelines. In particular, participants with significant food allergies, preferences, or dietary requirements that would interfere with dietary adherence are excluded from participating.

Since this criterion, along with the blood pressure limits, is likely to account for the majority of study exclusions, it is imperative that participants understand the nature and demands of the study as early into the screening process as possible. The Protocol therefore builds in several levels of review with the participant during screening as well as a run-in feeding period prior to randomization.

- Weight over 350 pounds

  This weight precludes accurate measurements by available scales at the clinical centers.

- Weight loss or gain of 10 pounds or more during the 2 months prior to SV1.

This is based on self-report.

- Planning to leave the area prior to the anticipated end of the intervention period

- Pregnant or planning to conceive prior to the anticipated end of intervention (women only)

Operationally, any woman who is pregnant or trying to conceive a child at the time of the prescreening visit is excluded from the study.

- Breast feeding

Women who are actively breast feeding at the time of the prescreening visit are excluded from the study.

- OMNI Heart staff

- Inability to provide reliable blood pressure measurements

As detailed in MOP Chapter 6, individuals for whom valid and reliable measurements of blood pressure cannot be obtained are excluded from participation in the trial.

- Poor compliance during screening and/or run-in

At any time prior to randomization, each clinical center has the option of excluding participants for noncompliance with the study protocol. Noncompliance may include, for example, repeated no-shows or reschedules for clinic visits, poor attitude, or any other aspect of the participant's behavior that would suggest he/she is a poor candidate for the trial.

In addition, each participant's eating record is reviewed by the clinic staff just prior to randomization in order to assess compliance with the feeding protocol. Participants who do not comply with the demands of the feeding protocol are excluded at this time. A more detailed discussion of dietary compliance is given in the Diet MOP.

- Investigator discretion for reasons of safety

In addition to the trial's mandatory blood pressure escape levels, individual centers always have the option of excluding participants for reasons of safety as determined locally.

- Current use of food supplements that cannot or will not be stopped

### *Overview of Recruitment*

Each OMNI clinical center recruits its participants in multiple feeding waves. Feeding for each wave lasts 19 weeks (1 week of run-in plus three 6 week periods) with at least 2 weeks separating each period. Specific recruitment approaches include 1) targeted mailings to specific groups (e.g., employees of local industries, previous screenees), 2) mass mailings (e.g., vis-à-vis inserts in coupon packs and brochures to registered voters or licensed drivers), 3) community and worksite screenings, 4) and mass media advertising (e.g., radio and television advertisements and public service announcements).

Recruitment efforts at each site are broad-based. Although previous DASH participants are not excluded from participation in OMNI, recruitment is not focused on these individuals, and the number who do enroll in OMNI are monitored.

Each clinical center has a recruitment coordinator who oversees recruitment efforts and who serves on the recruitment subcommittee. The recruitment coordinator is the primary liaison with the coordinating center for issues related to recruitment.

The coordinating center monitors recruitment activities and facilitates recruitment efforts by providing regular recruitment reports, organizing meetings and conference calls, and distributing meeting/call minutes. In addition to these regular trial monitoring reports, the coordinating center will develop additional reports (either on a regular or ad hoc basis) as requested by the recruitment committee or by the Data and Safety Monitoring Board. The coordinating center also facilitates, where appropriate, the preparation of recruitment materials for common use at the clinical sites.

### *Record Keeping*

Other than for basic demographic information (e.g., gender and race), data collected at PSV are not considered study data and are not incorporated into the study database. The demographic data are entered only for participants who are eligible to continue on to SV1. Individual clinical centers wishing to enter demographic data on all participants can do so, and the data management system will permit site-specific reports of this data for recruitment tracking purposes.

Beginning with SV1, all data collected on prospective participants must be entered into the data management system, and all subjects who drop out of screening, become ineligible, or who are otherwise lost to follow-up must be formally closed out.

## *Appendix 2.3 Exclusionary Weight-Loss Drugs*

| Generic name | Brand name |
|---|---|
| benzphetamine | Didrex |
| dexfenfluramine | Redux |
| diethylpropion | Tenuate<br>Tepanil |
| fenfluramine | Pondimin |
| phentermine | Adipex<br>Fastin<br>Ionamin<br>Obenix<br>Oby-Cap<br>Oby-Trim<br>Pro-Fast<br>Zantril |
| mazindol | Sanorex<br>Mazanor |
| phendimetrazine | Plegine<br>X-trozine<br>Bontril<br>Prelu-2 |
| phenmetrazine | Preludin |
| phenylpropanolamine | Dexatrim<br>Accutrim |
| d-amphetamine | Dexadrine<br>Dextrostat |
| methamphetamine | Desoxyn |
| orlistat | Xenical |
| sibutramine | Meridia |
| Adderall | dextroamphetamine & racemic amphetamine |
| Methylphenidate | Ritalin, Methylin, methadate ER |
| Modafinil | Provigil, Alertec |

| | |
|---|---|
| Pemoline | Cylert |
| Ephedra-containing supplements | Metabolife (e.g.) |

***Appendix 2.4 Lipid-Lowering Drugs Are Exclusionary Including***

| **Generic name** | **Brand name** |
|---|---|
| lovostatin | Mevacor |
| pravastatin | Pravachol |
| simvastatin | Zocor |
| fluvastatin | Lescol |
| atorvastatin | Lipitor |
| nicotinic acid | Advicor<br>Niacin<br>Slo-Niacin<br>Niacor<br>Nicobid<br>Niacinamide<br>Nicotinamide<br>Niaspan |
| gemfibrozil | Lopid |
| fenofibrate | Tricor |
| probucol | Lorelco |
| cholestyramine | Questran, LoCHOLEST |
| colesevelam | Welchol |
| cholestipol | Cholestid |
| Omega-3fatty acids | Promega, Super EPA, etc |

## *Appendix 2.5 Medications ALLOWED during OMNI*

| **Medical condition or symptom** | |
|---|---|
| Aches and pains | Tylenol<br>Aspirin<br>Ibuprofen (but not within 48 hours before BP measurement) |
| Indigestion | Amphogel<br>Nephrox |
| Cold/flu/allergy | Tylenol, Extra Strength Tylenol<br>Chlortrimeton<br>Benadryl<br>Hismanal<br>Allegra (Fexoferadine)<br>Tavist<br>Afrin, Otrivin or Ayr nasal spray<br>Robitussin (NOT Robitussin DM)<br>Claritin<br>Beconase nasal spray |
| Constipation | Correctol<br>Senokot |
| Infections | Antibiotics |
| Hormones | Estrogen and progesterone (but don't start these meds or change dose during the study) |

If you want to take any other medication, you must first discuss it with OMNI study personnel. Many medications can interfere with the OMNI study, so please ask first!

# 3. SCREENING VISITS

# Summary of Edits

## Prescreening Visit (PSV)

***Overview***

In order to be randomized, participants must complete a series of screening visits and a run-in period. Each screening visit includes questions and procedures designed to determine eligibility for the trial.

The PSV is intended as a fast, efficient way to identify ineligible participants. The visit includes questionnaire data for exclusion and a single, optional, blood pressure measurement. Individuals who complete the PSV are either excluded from further participation or scheduled for screening visit #1 (SV1), which may occur concurrently with the PSV.

If more than 120 days elapse between the PSV and SV1, the PSV must be repeated.

***Setting***

The PSV may take place at the clinical center (e.g., coincident with the initial screening visit), via telephone, or at a location in the community convenient to the population being recruited. If the PSV is being conducted at an off-site location, the clinic staff need to make sure that adequate space and facilities (e.g., tables and chairs) are available to accommodate the participant flow and to assure privacy for the participants when answering questions.

***Preparations for Prescreening Visit***

The following materials are needed to conduct the prescreening visit:

- OMRON unit or other blood pressure device (optional). Note: After PSV, an Omron or SpaceLabs device must be used.
- Informed consent form for PSV (if required by local IRB)
- Prescreen Eligibility Form (Form #01)

If SV1 is to be held in conjunction with the PSV, additional forms and equipment are also needed.

***Core Information about OMNI-Heart***

Please use the following "script" to describe the key features of the study as a part of PSV screening. This will help ensure that all participants have a common knowledge base about the study.

- Purpose of the OMNI Heart Study is to find out if eating foods rich in certain nutrients will reduce BP and risk for cardiovascular disease.
- Provide all meals for 19 weeks.
- Must be available to come to (name of facility) every M-F for a meal (lunch or dinner).
- Food for the other two meals/day plus snacks and weekend meals will be provided to "Take-Home."
- Must eat only study food for the 1 week (1 week sample of 3 diets, then six weeks on each of the 3 diets).
- A break of 2 or more weeks separates each diet period [Note: the interviewer should have a feeding schedule for the next group].
- NOT a weight-loss study; weight is monitored and amount of food provided is adjusted to make sure that weight does not change during study.
- BP monitoring - one set during each of weeks 1-4 and five set during the final 10 days of feeding.
- seven or eight blood tests required (once during screening and six times during feeding).
- Four 24-hour urine collections required (once or twice during screening and three times during feeding period).
- There will be a process of three screening visits (each visit at least one week apart) in which the prospective participant must qualify (all three visits) before eligible to participate in study.
- At the completion of participation in the study, participant will receive $xxx.

## *Conducting the Prescreening Visit*

The procedures for conducting the PSV vary depending on whether it is being done over the phone or in person. This section provides procedures to cover each of these situations.

In general, however, the following sequence of activities will occur:

- Greet the participant
- Describe the study and answer the participant's questions
- Administer informed consent form (if appropriate)
- Administer the Prescreen Eligibility Form
- If face-to-face, conduct a single, blood pressure measurement (optional)
- Schedule or conduct SV1

### *Procedures for Conducting the Visit by Phone*

At most sites, the initial direct contact between participants and clinic staff will most often be by telephone. Potential participants will usually be responding either to a direct mailing, radio advertisement, or some other recruitment effort. The level of knowledge about the study will vary greatly among respondents depending on the manner in which the participant heard about the study. For example, if the participant has received a copy of the OMNI brochure, she may already be aware of some of the study's feeding requirements and is likely to satisfy many of the PSV eligibility requirements.

#### *Greet the Participant*

Telephone staff should identify themselves by name and should indicate the name of the institution where they work. For example,

> "Hello, <u>name of institution</u>, this is <u>first name of staffer</u> speaking. May I help you?"

The participant will then identify herself and ask to speak with someone about the study. Participants may either identify the study by name or they may refer to it as the "eating study" or use other similar language. Be sure that whoever answers the phones, if the line is used for more than one study, is familiar enough with the study and the recruitment materials to be able to properly refer the participant to an OMNI staff member.

#### *Describe the Study and Administer Prescreen Eligibility Form*

The OMNI staff member should quickly confirm that the participant is calling about participating in the study, provide a brief overview, and begin to administer the Prescreen Eligibility Form. For example,

"That's right, the name of the study is the 'Optimal Macronutrient Intake to reduce heart disease', or OMNI Heart Study for short. Let me tell you a little bit about the study, and then if you are still interested I have a few quick questions to ask you to see if you might be eligible to participate."

[Review OMNI Fact Sheet with participant. A copy is included at the end of this chapter.]

"Does the study sound like something you might be interested in?"

If No,

"Well, thanks for your interest anyway."

If Yes,

"Great. What I'd like to do then is to ask you a few questions and, if you are still eligible, schedule you for a clinic visit. Are you ready?"

Begin administering the Prescreen Eligibility Form, the instructions for which may be found in the Forms Manual. At any point that it becomes evident that the participant is not eligible, you can terminate the visit.

***Ending the Prescreening Visit***

If, after completing the Prescreen Eligibility Form, the participant is ineligible, thank her for her time and interest and conclude the conversation. The Prescreen Eligibility Form does not need to be entered into the data entry/management system unless the site chooses to do that for their own tracking purposes.

If the participant is eligible, complete fields 20 - 21 on the form. Schedule a date for the SV1 visit, thank the participant for his interest in the study, and terminate the conversation.

The Prescreen Eligibility forms will be collected and entered for those participants who are deemed eligible for the screening process, i.e. eligible for SV1 visit (data entry will occur locally at JHU; BWH data will be entered by the DCC). For those SV1 eligible participants, a study ID# (lists provided to each site by the DCC) will be recorded on the Prescreen Eligibility Form.

Participant IDs are assigned using a check digit algorithm: It is a 5 digit number, with the first 4 following a numerical sequence and the last digit representing the check digit. The algorithm is as follows:

Participant ID: S1 P1P2P3 D1

Where:
S1 = the site identifier 1 or 2 = BWH; 3 or 4= Johns Hopkins
P1-3 = the patient sequence number within the organization

D1 = the check digit code:
Defined as:

D1 = Mod (S1*2+P1*3+P2*4+P3*5, 11)

If D1=10, then use D1= "A", otherwise use the digit D1.

Example of List of Participant ID's to be used at BWH

| Participant ID |
|---|
| 10009 |
| 10014 |
| 10020 |
| 10035 |
| 10041 |
| 10056 |
| 10061 |
| 10077 |
| 10082 |
| 10098 |
| 10105 |
| 10111 |
| 10126 |
| 10131 |
| 10147 |

***Procedures for Conducting the Visit in Person***

In some cases, such as health fairs, the initial contact with the participant will be in person. Depending on the format of these screenings, the participants may or may not have heard about the study when they meet the study staff person. For example, they may simply think they are waiting for a free blood pressure screening, or they may have been given a copy of the OMNI brochure to read while they are waiting in line. If blood pressure is measured as the first part of the visit and the participant is ineligible (see guidelines below), the Prescreen Eligibility Form need not be completed.

*Describe the Study and Administer Prescreen Eligibility Form*

Whenever it makes sense to do so in the context of the screening, the OMNI staff member should introduce herself as part of the study, provide a brief overview of the study, and begin to administer the Prescreen Eligibility Form. For example,

> "Your blood pressure is xxx over xxx, which is in the high end of the normal range, and as a result you might be eligible to participate in a study we are doing to help people reduce their blood pressure by changing what they eat. The name of the study is the

'Optimal Macronutrient Intake to reduce heart disease', or OMNI Heart Study for short. Let me tell you a little bit about the study, and then, if you are still interested, I have a few quick questions to ask you to see if you might still be eligible to participate."

[Review OMNI Fact Sheet with participant. A copy is included at the back of the chapter.]

"Does the study sound like something you might be interested in?"

If No,

"Well, thanks for your interest anyway."

If Yes,

"Great. What I'd like to do then is to ask you a few questions and, if you are still eligible, schedule you for a clinic visit. Are you ready?"

Begin administering the Prescreen Eligibility Form, the instructions for which may be found in the Forms Manual. At any point that it becomes evident that the participant is not eligible, you can terminate the visit.

Most likely the blood pressure assessment will occur as the first stage of these visits, though in some cases it may occur after the Prescreen Eligibility Form has been administered. The PSV blood pressure assessment consists of a single blood pressure measurement conducted in the seated position. No eligibility limits are established for the PSV blood pressure measurement. For just this visit, you can use any BP device. It is recommended, however, that individuals with both a DBP less than 76 mm Hg and a SBP less than 116 be excluded. Individual clinics should establish their own upper eligibility limits, and participants whose blood pressure exceeds these limits should be excluded and referred to a physician for further follow-up.

***Ending the Prescreening Visit***

If, after concluding the visit, the participant is ineligible, thank him for his time and interest and conclude the conversation. The Prescreen Eligibility Form does not need to be entered into the data entry/management system unless the site chooses to do that for their own tracking purposes.

If the participant is eligible, schedule an SV1 visit. Thank the participant for his interest in the study and terminate the conversation.

The Prescreen Eligibility forms will be collected and entered by the data entry person on site.

## Screening Visit 1 (SV1)

***Purpose***

The purpose of SV1 is to continue screening prospective participants for eligibility based on blood pressure and their responses to the General Dietary Questionnaire (Form #100). Participants will also be instructed on how to fill out the Health (Eligibility) Questionnaire (Form #6). The initial SV1 may occur at any time, including the day of the PSV. However, if the SV1 occurs more than 120 days after the PSV, the PSV data are invalid and must be recollected prior to obtaining SV1 data. If a participant is excluded on or after SV1, that individual cannot be re-screened for the same cohort. The participant may, however, be re-screened for later cohorts.

***Setting***

The SV1 visit may take place at the clinical center or at a location in the community convenient to the population being recruited. If conducted offsite, the SV1 will usually be conducted in conjunction with the PSV visit. Persons who are eligible at PSV may immediately receive an SV1 visit or they may be scheduled for an SV1 visit at a later time. In order to conduct the SV1 visit in an off-site location, it is essential that appropriate space and facilities are available. This requires a quiet, private or semi-private setting where the required relaxed waiting time can occur before a blood pressure is taken, and an interviewing setting that permits privacy of response to the questions that are asked.

If the SV1 visit is conducted at the same time as the PSV visit, the OMNI staff person should leave the room at the end of the PSV visit and ask the participant to sit quietly for five minutes with his legs uncrossed. The SV1 visit is then conducted.

***Preparations for SV1 Visit***

The following materials are needed to conduct the SV1.

- OMRON 907 BP monitor or SpaceLabs ABPM 90207 (thigh cuff use only)
- Scale
- Consent materials
- SV1 Blood Pressure Form (Form #02)
- Health Questionnaire (Form #06)
- General Dietary Questionnaire (Form #100)
- SV1 Visit Form (Form #03)
- Study charts for scheduled participants (if available)
- Participant Information Sheet (Form #29)

The following forms may also be needed and should therefore be on hand.

- Participant Closeout/Termination Form (Form #18)

- Prescreen Eligibility Form (Form # 01), in case the PSV needs to be redone

The number of forms and pieces of equipment are determined by local staffing configurations and the anticipated participant flow. If available, a spare OMRON device should be available as back-up.

***Conducting the SV1 Visit***

SV1 activities are listed below. Briefly re-describe OMNI, obtain consent, and obtain the participant's assurance that they are interested in participating. In general, blood pressure should be done before the other procedures because the forms need not be administered if the individual is not blood pressure eligible.

- Confirm participant ID
- Briefly re-describe the study; ask participant if they think they are interested in participating
- Obtain consent
- Take 3 blood pressure readings, complete the SV1 Blood Pressure Form, and note eligibility on SV1 Visit Form
- Have participant fill out the General Dietary Questionnaire and note eligibility on SV1 Visit Form
- Instruct participant in how to complete the Health Questionnaire
- Record events and final eligibility status on the SV1 Visit Form
- Weigh participant and measure height (Form #3)

*Confirm participant ID and check for completed PSV*

If a participant has completed a PSV on an earlier day, they will have already been issued a study ID. If the PSV and SV1 visits are completed at the same time, then the ID# should be noted on each page of each form completed.

If the person has been screened before but no study ID exists and a hard copy of the Prescreen Eligibility Form is not available, a new one must be done before the visit can proceed. In this case any old versions of the Prescreen Eligibility Form, if subsequently found, should be discarded.

The SV1 visit must occur within 120 days of the PSV visit. If this is not the case, then the PSV must be repeated.

*Review the study, confirm participant interest, and obtain consent.*

Briefly describe OMNI again, emphasizing the commitment required of participants. Ask if the individual thinks he would like to participate if eligible. Tell the participant that it is very important that those who participate follow through and complete the study. Of course, anyone has the

right to drop out whenever they wish, but they should not enroll unless they plan, as this time, to complete the whole study.

*Assess blood pressure*

After expressing continued interest (and obtaining consent), take the participant's blood pressure using the OMRON (or SpaceLabs) device and the procedures described in Chapter 6 of the MOP (Blood Pressure and other physical measurements). If the average of 3 systolic blood pressures is between 118 and 170 mm Hg (inclusive) or the average of the 3 diastolic pressures is between 78 and 104 mm Hg (inclusive), the participant is eligible to continue to SV2. Note: An SBP >170 or DBP > 104 makes a person ineligible.

OMRON cuff size must be appropriate. If it is impossible to get an accurate measurement (e.g., if large cuff covers the antecubital fossa or arm circumference is >42 cm., (i.e. requires a thigh cuff), the SpaceLabs ABPM device with a thigh cuff can be used.

Participants who are excluded based on blood pressure readings above the allowable limits may need to be referred to a physician for further evaluation. If the average of the SBP measurements is >170 mmHg or the average of the DBP measurements is > 104 mmHg, the participant must be referred to a physician. The participant may also be referred to a physician if deemed appropriate based on symptoms and clinical judgment even if the BP is lower than the above limits. If escape levels are reached or the participant is referred for BP management for some other reason, a BP escape tracking from should be filled out and one copy put in the participant chart at the site and one copy sent to the CC.

*Measure participant's weight and height*

The participant's weight and height measurement must be collected at SV1. Measure the participant's weight and height per the protocol outlined in MOP. Note the eligibility status on the SV1 Visit Form (Form #3).

*General Dietary Information Questionnaire (Form #100)*

The General Dietary Questionnaire is a short form designed to identify people who have food allergies or medical conditions that limit the types of foods they can consume and thus could interfere with their participation in OMNI Heart. Have the participant complete this form. If there are questions about specific items, discuss them with the participant. Persons who cannot consume the food items listed on the form are not eligible to participate.

*Health Questionnaire (Form #06)*

The Health Questionnaire is designed to identify persons who are ineligible for medical or other reasons. Remove the last page ("office use only" section) from the form, store it in the participant's study chart, and give the rest of the form to the participant to be administered as a

part of the SV1 visit. If the participant is not eligible for SV2, he should not receive this form. Be sure to place a label with the participant's study ID on each page of the form. If an ID has not yet been assigned, write the participant's name on each page of the form. Later the written name must be written over and replaced with the participant's ID number. No study form should have both ID number and name.

The instructions for completing the questionnaire should be discussed with the participant at this time. Ask participants that when they have questions or are unsure about an item to check. For each item marked "unsure", write a comment or question in the comment section for that item and ask about it at the SV2 visit. Staff should discuss these items with participants at SV2. Eventually, all 'unsure' responses on this form must be resolved to either yes or no.

The questionnaire asks participants to indicate whether or not they are taking various medicines or over-the-counter products, including vitamins and other supplements. Ask participants to check their medication bottles for the names of their medications. In addition, instruct participants to bring to the SV2 visit all medications and over-the-counter products (including vitamins, supplements, and other non-prescription drugs) that they regularly take. An OMNI staff person will list these medications in the "office use only" section of the Eligibility Questionnaire at the SV2 visit.

*Participant Information Sheet*

Fill out a Participant Information Sheet (Form #29) on each participant to file in the participant chart.

*SV1 Visit Form (Form #3)*

After each portion of the visit is completed, an OMNI staff person should check the appropriate "Done?" box on the SV1 Visit Form and (if applicable) indicate whether the participant is eligible or not eligible to continue based on that portion of the visit. At the end of the visit a staff person should review this form to make sure that the participant has completed all of the necessary components. This person should also make sure that a single outcome status is coded at the bottom of the form and should enter their ID in the "Reviewed by staff ID" field.

If a participant is excluded at the investigator's discretion (i.e., not as part of the regular screening activities for that visit), check "ineligible" under the Visit Outcome section of the SV1 Visit Form and in addition complete the Participant Closeout/Termination Form (Form #18) to record the reason for the exclusion.

### *Ending SV1*

To complete the SV1 visit, do the following:

- Inform the participant of eligibility status. You may inform the participant of eligibility status and terminate the visit whenever it is clear that the individual is not

eligible for OMNI. Explain the reasons for ineligibility to participant. Enter the visit outcome status onto the SV1 Visit Form.

- If participant is eligible, schedule an appointment for SV2 at least seven days and no more than 60 days from SV1. Enter the SV1 Visit Form and SV1 Blood Pressure form into the data entry/management system. This should be done within one week of the visit.

## Screening Visit 2 (SV2)

***Purpose***

The purpose of SV2 is to continue to identify ineligible participants as accurately and efficiently as possible. The activities of SV2 are listed below and include a review of the Health Questionnaire (Form #6, if not done already); measurement of blood pressure, collection of urine and blood samples; and distribution of the instructions and supplies for the Food Frequency Questionnaire and the 24-hour urine collection. The Food Frequency Questionnaire will be completed at SV2 and the 24-hour urine collection will be completed before SV3.

***Setting***

The SV2 visit takes place at the clinical center. It requires a quiet, private or semi-private setting where the participant can wait prior to the blood pressure measurement. Questionnaires also need to be administered/reviewed in a setting that permits privacy for the participant.

***Preparations for SV2***

The following materials are needed to conduct the SV2.

- OMRON 907 BP device or SpaceLabs ABPM 90207 (thigh cuff use only)
- Local laboratory chemistry panel blood supplies
- Urine sample containers
- Local Lab Worksheet (Form #14)
- Participant instructions and materials for 24-hour urine collection (Form # )
- Food Frequency Questionnaire and instructions (Form #09)
- SV2 Visit Form (Form #05)
- SV2 Blood Pressure Form (Form #04)
- Study charts for scheduled participants

The following forms may also be needed and should therefore be on hand.

- Blank Eligibility Questionnaire (Form #06)
- Participant Closeout/Terminiation Form (Form #18)

The number of forms and pieces of equipment are determined by local staffing configurations and the anticipated participant flow. If available, a spare OMRON device should be available as back-up.

***Conducting SV2***

In general, performing the SV2 activities in the order listed below should provide the most efficient identification of ineligible subjects. SV2 may be politely concluded at any point after an exclusionary condition or situation has been identified.

- Attach pre-printed participant labels for all forms
- Confirm participant ID and check visit window
- Briefly review the Health Questionnaire for obvious exclusions
- Distribute and administer Food Frequency Questionnaire
- Take 3 blood pressure readings and complete SV2 Blood Pressure Form
- Collect urine sample for dipstick measures of protein
- Collect blood samples for local exclusionary labs
- Distribute instructions and urine container for the 24-hour urine sample - instruct women to make the 24-hour urine collection when they are not menstruating
- Record events and eligibility status on the SV2 Visit Form

*Confirm ID, check visit window, and obtain informed consent*

Check to make sure that at least seven days have transpired since the blood pressure was taken during the SV1 visit. SV2 can occur no later than 60 days after SV1. Otherwise, the participant restarts screening.

*Review/complete Health (Eligibility) Questionnaire*

The participant may have already completed the Health Questionnaire at SV1 (except perhaps the medication and over the counter products review). If so, then it does not need to be completed again. Check to see if it is in the participant's study chart and, if so, mark the "Done?" and eligibility status on the SV2 Visit Form.

If a completed Health Questionnaire is not in the participant's study chart, he/she should bring the completed form with him to the SV2 visit along with all of his/her medication bottles, vitamin bottles, and any other supplements he/she is taking. The "office use only" section of the questionnaire should be in the chart.

Before proceeding with the remainder of the visit, a staff person should briefly review the questionnaire for obvious exclusions and, if any are found, apologize and excuse the subject.

Clarification of items and a review of the medications can be deferred to later in the visit. Detailed instructions for reviewing the form and determining eligibility may be found in the OMNI Forms Manual.

Once the questionnaire review is complete, check the "Done?" box on the SV2 Visit Form and record the appropriate eligibility status.

If the participant fails to bring the form with him to the visit, have him/her complete a new form. It will be necessary to call the participant at home to review his medications.

*Distribute and instruct on the Food Frequency Questionnaire (Form #09)*

Distribute both the Food Frequency Questionnaire and the "How to Fill Out FFQ Respondent Guide" (Form 103) to the participant and review the instructions in the OMNI Forms Manual for filling it out. Administer the Food Frequency Questionnaire. Make sure that the participant's ID# is noted (in pencil) on each page the form. Even SV2 ineligible participants should complete this form.

*Review Participant's Food Frequency Questionnaire*

Review the Food Frequency Questionnaire for completeness, resolve any unanswered questions or invalid responses, and check the appropriate "Done?" box on the SV2 Visit Form. The FFQ will be sent to the coordinating center for batch entry and will become part of the central database (see further instructions for mailing procedures on page 5, Form #09). The FFQ Shipping Log (Form #36) is used to process the FFQs.

*Assess blood pressure*

Take the participant's blood pressure using the OMRON device or the SpaceLabs ABPM 90207 for participants requiring a thigh cuff. Follow procedures described in MOP Chapter 6 (Blood Pressure Assessment and other physical measurements). **Be sure to use the same cuff size as was used in SV1.** If the average of the SV1 and SV2 systolic blood pressure measurements is between 119 and 165 mm Hg (inclusive) or the average of the SV1 and SV2 diastolic blood pressure measurements is between 79 and 102 mm Hg (inclusive), the participant is eligible to continue to SV3.

If the cumulative average of the SV1 and SV2 SBP measurements is >165 mm Hg or the cumulative average of the SV1 and SV2 DBP measurements is >102 mm Hg, the participant is not only excluded from further participation but must be referred to a physician. The participant may also be referred to a physician if deemed appropriate based on symptoms and clinical judgment even if the BP is lower than the above limits. The BP escape tracking form must be filled out and a copy filed in the participant chart at the site and a copy sent to the CC.

If the cuff size is found to differ from that used during SV1 and the participant has not left the clinic, a replacement blood pressure should be taken using the proper cuff. Otherwise, the original measurement will stand.

*Collect urine sample for dipstick measure of protein*

Collect a spot urine sample from the participant, measure protein and record on the SV2 Visit Form. The dipstick urine test can be done at either SV2 or SV3. The participant is ineligible if

either the urine dipstick protein is ≥2 +, although each site has the option of conducting a confirmatory test at a later time.

If the results are not acceptable and the participant will not be retested, check the "ineligible" box under Visit Outcome on the SV2 Visit Form. If the results are acceptable or the participant will be retested, initiate the Local Lab Worksheet, enter the results and details of retesting (if appropriate). The participant is considered eligible for purposes of the SV2 Visit Form.

*Complete the review of the Health Questionnaire*

Complete the review of the Health Questionnaire, clarifying the participant's questions or comments. Record results on SV2 Flow Form. Confirm list of medications with medication bottles. An OMNI clinician must review and sign the form assuring that the participant is eligible. Note: a physician review is only required for participants that are eligible and interested in the study. For participants who are ineligible or become ineligible, physician review of this form is not required.

*Collect blood samples for local exclusionary labs*

Draw the necessary blood samples for the local exclusionary labs. This can be done at either SV2 or SV3 visits. Follow the procedures outlined in MOP Chapter 7 for collection and processing. Remind participant that you may recall him for additional blood draws if any questions arise on these tests. The Local Lab Worksheet (Form # 14) is used to track whether the specimens are collected, if a repeat test is ordered, and the eligibility status of the participant based on the results of each test. The Local Lab Worksheet should be initiated at this point if it has not been done previously.

*Distribute instructions and urine container for the 24-hour urine sample*

Distribute the 24-hour urine container and instructions to the participant and review the instructions with the participant. Inform the participant that she needs to bring the container back within 24 hours of collection, and that it must be returned at or before the SV3 visit. Make sure that a label is affixed to the collection jug and that it is filled out with the appropriate identifying information. Refer to Chapter 7 of the MOP for detailed instructions.

Instruct women to make the 24-hour urine collection when they are not menstruating.

***SV2 Visit Form***

After each portion of the visit is completed, an OMNI staff person should check the appropriate "Done?" box on the SV2 Visit Form and (if applicable) indicate whether the participant is eligible or not eligible to continue based on that portion of the visit. At the end of the visit a staff person should review this form to make sure that the participant has completed all of the neces-

sary components. This person should also make sure that a single outcome status is coded at the bottom of the form and should enter his ID in the "Reviewed by staff ID" field.

If a participant is excluded at the investigator's discretion (i.e., not as part of the regular screening activities for this visit), check "ineligible" on the SV2 Visit Form and in addition complete the Participant Closeout/Termination Form (Form #18) to record the reason for the exclusion. This includes participants who are excluded because of high levels of urinary protein.

***Ending SV2***

To complete the SV2 visit, do the following:

- Inform the participant of eligibility status. You may inform the participant of eligibility status and terminate the visit wherever it is clear that the individual is not eligible for OMNI. Explain the reasons for ineligibility to participant. Enter the visit outcome status on the SV2 Visit Form.
- If eligible, schedule an appointment for SV3 at least seven days and no more than 60 days from SV2.
- Enter the outcome status on the SV2 Visit Form.
- Send Food Frequency Questionnaires to the Coordinating Center
- Prepare and ship lab samples according to MOP procedures (Chapter 7).
- When all data on the SV2 Visit Form have been collected, enter the SV2 Visit Form, the SV2 BP Form and the Health Form into the data entry/management system.

## Screening Visit 3 (SV3)

***Purpose***

The purpose of SV3 is to continue screening prospective participants for eligibility based on blood pressure and to collect data on physical activity and weight. The visit is also used to collect and process a 24-hour urine specimen, collect a fasting blood sample to be analyzed centrally (if it wasn't done at SV2), collect additional blood samples as needed for eligibility, and review in detail the study foods and menus with the participant.

***Setting***

The SV3 visit takes place at the clinical center. It requires a quiet, private setting where the participants can wait prior to the blood pressure measurement. Questionnaires also need to be administered/reviewed in a setting that permits privacy for the participant.

***Preparing for SV3***

The following materials are needed to conduct the SV3.

- OMRON 907 BP monitor or the SpaceLabs ABPM 90207 device (thigh cuff use only).
- Consent materials (if needed)
- SV3 Visit Form (Form #08)
- Study Foods Checklist (Form #101)
- SV3 Blood Pressure Form (Form #07)
- Central Lab Collection Form - 24-hour urine (Form # 30)
- 24-hour urine collection materials
- OMNI Study Menus (Form #102)
- Study charts for scheduled participants
- Symptoms Form (#11)
- Local laboratory chemistry panel blood supplies
- Urine dipsticks and urine sample containers
- Local Lab Worksheet (Form #14)

The number of forms and pieces of equipment is determined by local staffing configurations and the anticipated participant flow. If available, a spare OMRON device should be available as backup.

In general, performing the SV3 activities in the order listed below should provide the most efficient identification of ineligible subjects. The visit may be politely concluded at any point after an exclusionary condition or situation has been identified.

- Confirm participant ID and check visit window
- Process 24-hour urine sample
- Take participant's blood pressure readings and note eligibility on SV3 Visit Form
- Review Study Food Checklist (Form #101) with participant to identify possible problems and record eligibility on SV3 Visit Form
- Review OMNI Study Menus (Form #102) with participant to identify possible problems
- Review Local Lab Worksheet and collect additional laboratory specimens if needed
- Collect fasting blood sample to be analyzed centrally
- Administer Symptoms Questionnaire (Form #11)

*Confirm ID, Check Visit Window, and Obtain Informed Consent*

Confirm that at least seven days an no more than 60 days have elapsed since the SV2 visit. If necessary, obtain informed consent for the visit.

*Process 24-hour Urine Sample*

The participant may have completed the 24-hour urine collection at any time between SV2 and SV3. Since the specimen should be returned within 24 hours of collection, the participant may or may not be bringing a specimen container with her to the SV3 visit. If she does not bring a container, check her study chart to confirm that she returned it previously and that it was an acceptable specimen.

Complete details on the processing of 24-hour urine specimens are contained in Clinic MOP Chapter 7 (Central Lab). The instructions for processing the specimen should be followed no matter when the specimen is returned. The Central Lab Collection Form – 24-hour urine (Form #30) is used for processing the sample.

**If the specimen is inadequate (collection < 22 hrs or >26 hr s or <500 cc), or if the participant failed to bring it in, another (acceptable) specimen must be obtained prior to the start of run-in.** Give the participant a new set of collection materials, attach and fill out the labels correctly, and write in "missing" next to "24-hour urine collection" on the SV3 Visit Form. If the participant is otherwise eligible to continue at the end of the visit, code "eligible" under Visit Outcome on the SV3 Visit Form.

*Assess Blood Pressure*

Take the participant's blood pressure using the OMRON (or SpaceLabs) procedures described in Clinic MOP Chapter 6 (Blood Pressure and other physical measurements). **Be sure to use the same cuff size as was used at SV1.** Record the measurements on the SV3 Blood Pressure Form. If the average of the SV1, SV2, and SV3 systolic blood pressure measurements is between 120 and 159 or the average of the SV1, SV2, and SV3 diastolic blood pressure measurements is between 80 and 99 mm Hg (inclusive), the participant is (blood pressure) eligible to continue to run-in.

If the sum of the SV1, SV2 and SV3 SBP measurements is $\geq$160 mm Hg or the sum of the SV1, SV2, and SV3 DBP measurements is $\geq$100 mm Hg, the participant is not only excluded from further participation, but must be referred to a physician for follow-up. The participant may also be referred to a physician if deemed appropriate based on symptoms and clinical judgment even if the BP is lower than the above limits.

If the participant cuff size is found to differ from that used during SV1 and the participant has not left the clinic, a replacement blood pressure should be taken using the proper cuff. Otherwise the original measurement stands.

*Review Study Food Checklist and OMNI Study Menus with Participant*

The SV1 visit included a brief review of common food items in the OMNI diets to make sure the participant could eat them. During the SV3 visit a member of the clinic's nutrition staff should carefully review with the participant the Study Foods Checklist (Form #101) and the OMNI Study Menus (Form #102). (See the OMNI Diet MOP for details on this process.) The purpose of this review is to make sure that the participant is fully aware of the foods/menus that he may be fed and is willing to eat these foods. It is important that the participant be willing to comply with all dietary patterns. It is much better, from the study's perspective, to exclude participants prior to randomization than to have them drop out of the study or be very noncompliant post-randomization. This is particularly true for cross-over trials.

This review should take approximately 10 minutes. At the end of the review, the OMNI staff person reviewing the foods should classify the participant as eligible or ineligible to continue based on the review. This should then be noted on the SV3 Visit Form.

*Collect Additional Laboratory Specimens if Needed for Eligibility*

For participants whose SV2 exclusionary labs came back as ineligible, clinics have the option of repeating the analyses once. Note that men with a creatinine > 1.5 and women with a creatinine > 1.2 may still be eligible if their estimated GFR from either the Cockroft-Gault of simplified MDRD formula is $\geq$ 60 ml/min.

If the participant needs additional blood drawn, this can be done at this point. Note that some of the repeat tests require a fasting sample. In this case, the participant should have been instructed ahead of time to fast prior to the visit, and this should be confirmed at the time of the visit. If a repeat blood is drawn, record that on the Local Lab Worksheet (Form # 14). Check the appropriate "Done?" box on the SV3 Visit Form to indicate that the laboratory review was conducted.

Similarly the urine protein may be repeated at this visit. The participant is ineligible if the urine dipstick protein is $\geq$ 2+. Record the result and check the appropriate box to indicate if he is ineligible on the SV2 Visit Form.

*Collect Fasting Blood Sample to be Analyzed Centrally and Locally (optional)*

A fasting blood sample must be collected at SV3 or prior to the beginning of run-in. Record the information on the Central Lab Collection Form - Fasting Blood (Form #31). The participant must have fasted for a period of 8-14 hours prior to drawing the sample. It is to be sent to the central lab (see Clinic MOP Chapter 7) for processing. If not done at SV2, the specimen should also be sent locally to determine if lipid levels, glucose and creatinine are within range.

*Administer Symptoms Form*

Complete the Symptoms Form (#11) with the participant. Check the appropriate "Done?" box on the SV3 Visit Form.

***Ending SV3***

To complete the SV3 visit, do the following:

- Review SV3 Visit Form to make sure visit is complete.
- Inform the participant of eligibility status. You may inform the participant of eligibility status and terminate the visit at any point that it is clear that the individual is not eligible for OMNI. Explain the reasons for ineligibility to the participant. Enter the visit outcome status on the SV3 Visit Form. Enter the SV3 Visit Form and the

Symptoms Form into the data entry/management application. These forms need to be entered within one week of the SV3 visit.

- If the participant is eligible for run-in, remind her of the start date and provide other instructions as appropriate so that she is ready to begin. Remind participant, if needed, that final eligibility for run-in will depend on results of pending laboratory tests and the completion of pending questionnaires. In addition, remind the participant of the requirement to maintain her current weight between this visit and the start of run-in for continued eligibility. Give information on the individual weight limits for eligibility and tips on maintaining weight.
- If the participant was excluded due to escape-level blood pressure criteria, refer him to his physician.
- Prepare and ship lab samples to be analyzed centrally according to Clinic MOP (Chapter 7) procedures.

## Summary of Edits

# 4. Run-In and Randomization

***Overview and Definitions***

All participants who are eligible based on the three screening visits will undergo a run-in period on a varied diet (consisting of menus from all three intervention diets) prior to randomization. The run-in phase has two main objectives: 1) to identify and exclude individuals who will not comply with the trial's eating and measurement requirements, and 2) to determine, for each participant, the appropriate energy level needed to maintain weight. (The Harris Benedict Equation, which are based on age, gender, and weight, are used to estimate resting energy expenditure. Total energy requirement is estimated by multiplying the resting energy expenditure by a factor indicating overall physical activity level).

During the run-in period, participants receive all of their food from the clinic and are required to attend the clinic for at least one meal per weekday, either lunch or dinner. Feeding for each participant lasts 19 weeks (1 week of run-in plus three 6 week periods) with at least 2 weeks separating each intervention period. In contrast, the first feeding period can start immediately after run-in. Recruitment for the initial cohort of participants commences during the first study year, in anticipation of initial feeding in the 4$^{th}$ quarter. Recruitment and feeding occurs in study years 2 – 4. In order to allow for dropouts and exclusions during the run-in phase, the number of persons enrolled in run-in should exceed the randomized goal by 10-20%.

***Materials Needed During Run-In***

- Consent form (if needed)
- Run-in Flow Form (# 16)
- Scale
- Daily Diary (Form # 24)
- Health Questionnaire (Form #6)
- Patient History Questionnaire (Form #19)
- OMRON 907 BP device
- Initial Run-In Blood Pressure Form (#37)
- Brief Physical Activity Questionnaire (#21)
- BP Escape Tracking Record (Form #23)
- Adverse Events Form (#12)
- Medication Questionnaire (# 17)
- Case Conference Form (# 33)
- Study charts for scheduled participants
- Participant Closeout Form (#18)

*Run-In Logistics*

Run-in feedings are scheduled to start on the same day for all participants in a given feeding cohort in a given clinic. However, participants may be allowed to start run-in feeding up to one day late if the clinic determines that the delay is due to exceptional circumstances not likely to affect future compliance. In this latter case, the length of run-in feeding for those participants is shortened by one day so that all subjects are scheduled to finish run-in feeding on the same day.

The duration of run-in feeding may vary between 6 and 7 days, is determined locally, and may vary from cohort to cohort. **To provide consistent terminology, we shall refer to these as run-in days 0 through 7, and shall use the notation RI-0...RI-7.** Thus a participant who starts run-in feeding two days late is said to start on run-in day 2 (RI-2).

Because feeding does not begin with the breakfast meal, the first and last days of run-in feeding represent partial feeding days. For example, if feeding begins with dinner, then only dinner is fed on run-in day 0 and only breakfast and lunch are fed on run-in day 7. All data gathered on run-in day 7 will be assigned to that day, even if this coincides with the initial day of intervention feeding. In order for study measurements to reflect the effect of the diets, no study measurements are taken on run-in day 0 or, if a participant starts late, on the initial day of feeding.

Neither the participants nor the staff conducting the measurements are told the randomization assignment. Only staff involved in meal preparation are allowed to be unblinded to treatment allocation. There is an optional break of up to seven days between the end of run-in and the beginning of the initial intervention feeding period. Subsequent intervention feeding periods must be separated by a break of at least 2 weeks in duration. The duration of these breaks may vary from period-to-period and from site-to-site, within a cohort, and from cohort-to-cohort. During the breaks between feeding periods, subjects are not provided any food and are allowed to return to their original diets.

### *Preparing for Run-In*

Prior to the start of run-in, all eligibility information needs to be completed. Run-in feeding must begin within 60 days of SV3; all eligibility criteria must be met prior to the start of run-in. If the Health Questionnaire (Form #6) was completed more than one month prior to the start of run-in, it must be re-administered (current within one month). In addition, a fasting blood sample must be **collected prior** to the start of run-in.

Run-in consists of a series of visits, the preparations for which may vary from day-to-day. Certain aspects, such as those related to the preparation and distribution of food, are nearly identical from day to day. Other activities, such as blood draws and blood pressure assessment, happen much less frequently. Table 4.1 lists the various activities that take place during run-in.

Food preparation, feeding, and compliance assessment are comprehensively discussed in the Omni-Heart Diet MOP.

**Table 4.1**
**OMNI-Heart Activity Sequence: Run-in Feeding Period**

| | ------- Day of Run-in -------- | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ***Run-in Event*** | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** |
| **Blood Pressure (3 readings)** | | **<======== One set ========>** | | | | | | |
| **Weight** | | **X** | **X** | **X** | **X** | **X** | **X** | **X** |
| **Run-in Feeding Activities** | **X** | **X** | **X** | **X** | **X** | **X** | **X** | **X** |
| **Health Questionnaire** | | **<==== Any time during RI ===>** | | | | | | |
| **Patient History Questionnaire** | | **<==== Any time during RI ===>** | | | | | | |
| **Brief Physical Activity Q'aire** | | **<==== Any time during RI ===>** | | | | | | |
| **Medication Questionnaire** | | **<==== Any time during RI ===>** | | | | | | |
| **Case Conference** | | | | | **<==========>** | | | |
| **Randomization** | | **Any time after Day 3 of RI ====>** | | | | | | |
| **Compliance Monitoring** | | **X** | **X** | **X** | **X** | **X** | **X** | **X** |

***Run-In Activities***

*Obtain Informed Consent If Needed*

If necessary, obtain informed consent for the run-in phase prior to the start of run-in feeding. Check the appropriate box on the Run-In Flow Form (#16) when it is completed.

*Measure Weight at Each Clinic Visit*

All participants are weighed at each clinic visit during the run-in and intervention phases of the trial. Use the procedures outlined in Clinic MOP Chapter 6. **All participants whose weight changes by 10 pounds or more between SV1 and the first full day of run-in (RI-1) are excluded from the trial at that point.** After taking the RI-1 weight, record the eligibility status on the Run-In Flow Form (#16).

The the first two run-in weights (those taken on RI-1 and RI-2) defines the participant's **target weight** and is used as the baseline against which to measure weight change during run-in

feeding. As noted in Diet MOP chapter 41 (Participant Management and Compliance), weight must remain stable during the study. These daily weight measurements are used to monitor weight changes, and the overall caloric content of the participant's meals is adjusted as needed in order to assure that the participant's weight remains stable throughout the study. The weight is recorded on the Daily Diary (Form #24). The weight data should be entered daily so that the weight tracking reports generated from the data entry/management application can be reviewed daily.

*Collect Remaining Baseline Blood Pressure Measurement*

As part of each participant's baseline blood pressure measurements, the Protocol requires that one set of blood pressure measurements be taken during the week of run-in feeding. Clinic staff should measure blood pressure using an OMRON 907 device and follow the procedures described in Clinic MOP Chapter 6 (Blood Pressure Assessment). The appropriate cuff size, as captured at SV1, is also recorded on the Initial Run-In Blood Pressure Form (#37).

Other than for escape level exclusions, the run-in blood pressure measurement is not used to determine eligibility. The Protocol defines two blood pressure escape levels during run-in. Escape level 1 is defined as a single day's average SBP measurement in excess of 180 mmHg or a single day's average DBP in excess of 110 mmHg. Escape level 2 is defined as a single day's average SBP measurement in excess of 170 mmHg or a single day's average DBP measurement in excess of 105 mmHg. In each case, the appropriate follow-up actions are discussed in Clinic MOP Chapter 10, Safety Monitoring. If a participant hits an escape level, complete the BP Escape Tracking Record (Form #23).

Persistently elevated blood pressure during run-in results in exclusion from further participation in the trial and referral to a physician, regardless of whether the participant has already been randomized. **Participants reaching blood pressure escape limits may not begin intervention feeding unless a subsequent blood pressure measurement, taken within the appropriate time frame, falls within acceptable limits** (as defined in Chapter 10, Safety Monitoring.)

The blood pressure measurement taken during the week of run-in is recorded on the Initial Run-In Blood Pressure Form (#37) and are entered into the data entry system (MS Access program) at the DCC (for BWH participants) or directly at the Hopkins clinical site. The entry of the blood pressure readings taken during run-in are not required before randomization occurs. They do, however, need to be entered within seven days after the end of run-in. Check the appropriate boxes on the Run-In Flow Form (#16) as they are collected.

*Complete Health Questionnaire*

The Health Questionnaire should be re-administered during Run-in if it has been more than sixty days since it was first completed during the screening process. Remove the last page ("office use only" section) from the form before giving it to the participant. Ask participants that when they have questions or are unsure about an item to check "unsure" and write a comment or

question in the comment section. Any unsure items/comments will need to be reviewed by clinical staff.

*Complete Patient History and Brief Physical Activity Questionnaires*

Sometime during run-in, and preferably before randomization, the participants complete the Patient History Questionnaire (Form #19) and the Brief Physical Activity Questionnaire (Form 21). These are self-administered questionnaires that can be completed at home. Clinic staff should review returned questionnaires for completeness and should resolve any unanswered or vague responses. Check the appropriate box on the Run-In Flow Form (#16) when the forms are collected.

*Complete Medication Questionnaire*

All participants complete the Medication Questionnaire (Form #17) during the week of run-in. The questionnaire, which is repeated towards the end of each intervention feeding period, is designed to identify those individuals who start taking medications during the course of the study.

The questionnaire should be administered in an interview format, and all positive responses can be reviewed by a staff clinician, if deemed necessary. Individuals taking exclusionary medications (see Clinic MOP Chapter 2) must be advised to stop taking these medications if they are not prescription medications. If the medication is prescribed for reducing blood pressure or controlling cholesterol, an investigator must be notified. Such individuals may be excluded from the trial. Completed questionnaires will be entered on-site within 7 days, or passed onto the DCC for data entry. Check the appropriate box on the Run-In Flow Form (#16) when the form is collected.

*Prepare And Distribute Daily Meals*

Kitchen staff must prepare and distribute food for participants on an ongoing basis throughout run-in. Details of food preparation are given in the Diet MOP Chapter 40.

*Review Daily Food Diaries*

Dietary staff must assess compliance with the study's eating requirements on an ongoing basis. Details on compliance monitoring are given in the Diet MOP Chapter 41. In addition, diet staff through the reviewing of these completed forms, may become aware of a serious adverse event (e.g. hospitalization) which will require reporting. Staff should complete a Serious Adverse Events Form (#12) and contact an investigator. See MOP Chapter 10 (Safety Monitoring) for further details.

*Conduct Overall Compliance Assessment/Case Conference*

In addition to the exclusionary criteria applied during the screening visits, participants may be excluded during run-in for unusually large weight swings or for noncompliance with the protocol**.** Participants may also be excluded prior to randomization for missed meals, poor clinic attendance, and over- or-under consumption of food. Finally, clinics subjectively evaluate each participant's overall compliance and attitude just prior to randomization and may exclude participants on the basis of this assessment as well. This is referred to as a case conference and the Case Conference Form (#33) is completed. Completed forms will be entered on-site and must be done so prior to randomization. Check the appropriate box on the Run-In Flow Form (#16) when the case conference is completed. A more detailed discussion of compliance assessment is provided in the Diet MOP Chapter 41. If the participant is excluded by the case conference, the Participant Closeout Form (#18) must be completed.

*Randomize Participant*

Randomization will occur at any point beginning at day 3 of the run-in feeding period, and extend to as late as 4 days after the completion of run-in. The timing of randomization may vary from cohort to cohort, provided that it occurs at least three days after the start of run-in feeding and at least three working days prior to the start of intervention feeding. The former criterion permits adequate assessment of dietary compliance, while the latter assures that the kitchen staff have adequate time to assemble and prepare the foods that are needed for the start of intervention feeding (they need to know each participant's dietary assignment).

Following randomization, participants remain on their assigned diet schedule until the run-in period ends. Participants are not told the order of their diet assignment, and except for staff involved in meal preparation, clinic personnel are also blinded to diet order.

The timing of events to complete randomization within the three-day window demands tight coordination between the Coordinating Center and the intervention sites. The following timeline is recommended to ensure adequate time to resolve all pre-randomization issues and to give kitchen staff adequate time to prepare for intervention. However, as long as all the appropriate data are entered and the data issues resolved, the randomization can be done as early as RI-3. If the site has a break between run-in and intervention period 1, the randomization date can also be pushed back if need be. There needs to be a three-working-day preparation time between randomization and the start of intervention feeding, however.

*Randomization*

Randomization is stratified by clinic and, within each clinic, structured to assure comparable treatment group sizes over time with respect to diet order. The sequences of diet assignment will be randomly computed in advance of any enrollments. At selected intervals, groups of 20 envelopes will be delivered to each site with an external sequence number on each envelope. At each site, inside the Kth envelope is the diet sequence for the Kth participant enrolling at that site. To cater for the possibility that some patients will drop very early post-randomization, the assignments and envelopes for the next 20 may be re-computed to dynamically establish balance

that dropouts may disturb. [We need to address the longest period post randomization at which dropout can be assigned by enrolling a replacement subject?]

*End Run-In*

Remind subjects of dates and procedures for starting Intervention Feeding Period 1, and dismiss them for the break period (if applicable).

## CHAPTER 5: INTERVENTION 2

# Chapter 5: Intervention

***Overview***

The intervention feeding period begins 0 - 7 days after the end of run-in. During this period participants receive all of their food from the clinic and eat on-site at least one meal per day, five days per week. As with the run-in feeding, the on-site meal should be a lunch or dinner if possible. Intervention feeding is divided into three separate 6-week (42 day) feeding periods. Feeding periods 1&2 and 2&3 are separated by a washout period (break) of at least 2 weeks during which subjects return to their usual diets.

To provide consistent terminology, we shall refer to the three intervention feeding periods as ***intervention feeding periods I, II, and III***. Within each intervention feeding period, days are numbered 0-42. Thus, intervention feeding period I, day 10 can be written as PI-10, and intervention feeding period III, day 30 can be written as PIII-30.

Because feeding does not begin with the breakfast meal, the first and last days of each feeding period represent partial feeding days. For example, if feeding begins with dinner, then only dinner is fed on day 0 and only breakfast and lunch are fed on day 42. Thus the feeding periods cover 43 calendar days but only 42 metabolic days. In order for study measurements to reflect the effect of the diets, no study measurements are taken on feeding day zeros.

Weight is recorded at each clinic visit and blood pressure is assessed weekly during the first four weeks of each intervention feeding period. A blood pressure assessment consists of a single day's set of 3 measurements. During the last 10 days of each intervention period, BP is measured on 5 days; 2 days of these 5 measurement days occur during the last 5 days of the intervention period (i.e., days 38-42). The requirement for 5 measurements during the last 10 days (2 measurements during the last 5 days) of each period ensures that participants will have been exposed to the diet for the full 6 weeks of feeding.

During the **Week 3** of each intervention period the following procedures are performed
Satiety questionnaire (2x, before and after the clinic meal)
Diet Acceptability questionnaire

A fasting blood sample is obtained during **Weeks 4 and 6** of each intervention period.

During **Weeks 5 to 6** of each intervention feeding period, a 24-hour urine is collected.

During the **final 10 days** of each intervention feeding period, five sets of daily blood pressure measurements are recorded, including at least two sets during the final 5 days.

During the **final 7 days** of each intervention period the following procedures are also performed
Fasting blood sample
Symptoms questionnaire
Brief Physical Activity questionnaire
Medication questionnaire

A sample from the 24-hour urine specimen is sent to a central laboratory for assessment of Na, K, Ca, urea nitrogen, phosphorus, and creatinine for group analyses. Samples of urine, serum, and plasma are also frozen and stored for future analyses.

After participants complete the study (i.e., at the end of PIII), they receive a summary of their study blood pressures and dietary counseling for heart disease prevention.

Preparing for Intervention

Intervention consists of a series of visits, the preparations for which vary from day-to-day. Certain aspects, such as those related to the preparation and distribution of food, are nearly identical from day-to-day. Other activities, such as blood draws and blood pressure assessment, happen much less frequently. Table 6.1 lists the various activities that take place during the intervention feeding phase.

***Materials Needed During Intervention***

- OMRON 907 automatic BP machine
- Generic Blood Pressure Form (#15)
- BP Escape Tracking Record (Form #23)
- Central Laboratory supplies (see Chapter 7)
- Central Lab Collection Form - Fasting Blood (Form #31)
- Participant instructions and materials for 24-hour urine collection (see Chapter 7)
- Central Lab Collection Form - 24-hour urine (Form #30)
- Scale
- Daily Diary (Form #24)
- Intervention Flow Form (#20)
- Symptoms Form (#11)
- Medication Questionnaire (Form #17)
- Serious Adverse Events Form (#12)
- Diet Acceptability Questionnaire (Form #35)
- Brief Physical Activity Questionnaire (Form #21)
- Satiety Questionnaire (Form #135)
- Study charts for scheduled participants
- Participant Closeout Form (#18)

***Table 6.1: Schedule of activities by visit***

| | | Screening Visits | | | Run In (RI) | Each of 3 Intervention (INT) Periods | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | PSV | SV1 | SV2 | SV3 | | INT Wk 1 | INT Wk 2 | INT Wk 3 | INT Wk 4 | INT Wk 5 | INT Wk 6 |
| Informed consent | | T | | | T | | | | | | |
| Blood pressure | Opt | T | T | T | T | once per week ---------- > | | | | 5 times in last 10 days; 2 in last 5 days | |
| Health questionnaire | | T | | | T | | | | | | |
| General dietary information questionnaire | | T | | | | | | | | | |
| Weight | | T | | T | each weekday of feeding ---------- > | | | | | | |
| Height | | T | | | | | | | | | |
| Urine dipstick | | | T | | | | | | | | |
| 24 hour urine collection* | | | T | | | | | | | T | |
| Food Frequency Questionnaire | | | T | | | | | | | | |
| Fasting Blood** | | | T | | | | | | T | | T |
| Symptoms questionnaire | | | | T | | | | | | | T |
| Feeding activities | | | | | daily ---------- > | | | | | | |
| Randomization | | | | | T | | | | | | |
| Patient history questionnaire | | | | | T | | | | | | |
| Brief physical activity questionnaire | | | | | T | | | | | | T |
| Medication questionnaire | | | | | T | | | | | | T |
| Diet Acceptability q'aire | | | | | | | | T | | | |
| Satiety questionnaire | | | | | | | | T | | | |

- Sodium, potassium, phosphorus, urea nitrogen, creatinine**
- Total cholesterol, HDL-C, triglycerides, LDL-C, glucose, insulin, and storage specimen at each phlebotomy; VLDL-apoB, VLDL-apoCIII, total plasma apolipoprotein B, and lipoprotein(a) at week 6 of each period; whole blood for subsequent DNA extraction (just once).

Blood pressure and weight measurements are always taken prior to eating, with the exception that no measurements are made on intervention feeding days zero. Collection of the fasting blood samples must also be done prior to eating and after a 10 hour (minimum) fast. The timing of other one-time activities (i.e., before or after eating) is left to clinic discretion.

### *Intervention Activities Occurring During Each Intervention Feeding Period*

*Measure Weight at Each Clinic Visit*

All participants are weighed at each clinic visit (except days zero) during the intervention phase of the trial using the protocol outlined in Clinic MOP Chapter 6. The average of all weight measurements recorded during run-in feeding defines the participant's **baseline weight** and is used as the baseline against which to measure weight change during intervention feeding. The daily weight measurements recorded during intervention are used to monitor for weight changes, and the overall caloric content of each participant's meals is adjusted as needed to assure that weight remains stable throughout the study. The daily weight is recorded on the Daily Diary (Form #24).

*Collect Blood Pressure Measurements*

As part of each participant's final blood pressure measurements, the protocol requires that five sets of blood pressure measurements be taken during the final 10 days of each intervention feeding period, and that at least two of these five should be taken during the last 5 days of intervention feeding (i.e., days 38-42). In addition, blood pressure is assessed once (set of 3 measurements) during each of weeks one through 4 (days 1-28) of each intervention feeding period. These latter blood pressures, under no circumstances, should be taken on the first day of an intervention feeding period (i.e., day 0).

Clinic staff measure blood pressure using the automatic device, OMRON, and follow the procedures described in Clinic MOP Chapter 6 (Blood Pressure and other physical measurements). In order to minimize the potential for subjective biases, **the clinic staff who participate in blood pressure measurement must be blinded to each participant's intervention assignment. Also, please be sure that all blood pressure measurements are made using the same cuff size as was used at the beginning of SV1**.

In order to ensure participant safety, blood pressure thresholds are established that trigger repeat measurements and medical referral. These limits are discussed in Chapter 10, Safety Monitoring. Participants who are started on blood pressure medication are excluded from further participation in the trial. Clinic staff should therefore attempt to obtain as many daily blood pressure measurements as possible (up to a maximum of five days) from the time a participant is referred to her provider until such time as she starts on medication.

If the participant's provider decides that she does not need to go on medications, then the participant should continue to be followed in the study as usual. However, the clinic staff should still have attempted to collect the five blood pressure measurements as a precaution. Complete the BP Escape Tracking Record (Form # 23).

**For reasons of safety, participants should not be asked to defer the start of therapy in order that the clinic be able to obtain a complete set of five measurements.**

The intervention blood pressure measurements are recorded on the Generic Blood Pressure Form (#15). Data should be entered within seven days of collection.

*Collect a 24-Hour Urine Sample at End of Each Feeding Period*

**NOTE: 24-hour urine collection should not be done during menstruation. Schedule urine collection to avoid collections during this time.**

A 24-hour urine specimen needs to be collected during Weeks 5 to 6 (days 29 – 42) of each intervention feeding period. A sample from this specimen is sent to the central laboratory for processing for subsequent group analyses. Details on the processing of 24-hour urine specimens are contained in Clinic MOP Chapter 7. The Central Lab Collection Form - 24-hour urine (Form #30) is used for tracking the 24-hour urine sample. Check the appropriate box on the Intervention Flow Form (#20) when the sample has been collected and the form is completed.

*Collect Fasting Blood Sample*

During days 22-28, and days 36-42 of intervention feeding subjects must provide a fasting blood sample. To be valid, the participant must have been fasting for a minimum of 10 hours and must have been in an upright position (defined as seated or standing) for at least 1½ hours prior to the blood draw. The requirement to have been in an upright position for 1½ hours is a target. Details on drawing and processing this specimen are given in Clinic MOP Chapter 7 (Central Lab). The Central Lab Collection Form-Fasting Blood (#31) is used for tracking the specimen. Check the appropriate box on the Intervention Flow Form (#20) when the sample is collected and the form is completed.

*Complete Diet Acceptability Questionnaire*

All participants complete the Diet Acceptability Questionnaire (Form #35) during each feeding period, once during Week 3 (days 14 – 21). Dietary staff administer the questionnaire and review returned questionnaires for completeness. Check the appropriate box on the Intervention Flow Form (#20) when the form has been completed.

*Complete Satiety Questionnaire*

All participants complete the Satiety Questionnaire (Form #135) twice a day during week 3 (days 14-21) for each feeding period. The questionnaire should be completed by the participant and reviewed by clinic/dietary staff for completeness. Check the appropriate box on the Intervention Flow Form (#20) when the form has been completed.

*Complete Symptoms Form*

All participants complete the Symptoms Form (# 11) between days 36-42 of each intervention feeding period. The questionnaire is primarily designed to document gastrointestinal symptoms associated with the diets. Check the appropriate box on the Intervention Flow Form (#20) when this is completed.

The questionnaire should be completed by the participant and reviewed by clinic staff for completeness. Any positive responses may be reviewed by a study clinician, who determines if further follow-up is needed.

*Complete Medication Questionnaire*

During the last week of each intervention feeding period (week 6), the medication questionnaire (Form # 17) will be given to participants for completion. This questionnaire is designed to identify individuals who have taken medications that would exclude them from being part of the study analysis.

*Complete Brief Physical Activity Questionnaire*

All participants complete the Brief Physical Activity Questionnaire (Form #21) once during each feeding period, between the days 36 and 42 (week 6). The questionnaire should be completed by the participant and reviewed by clinic staff for completeness. Check the appropriate box on the Intervention Flow Form (#20) when the form has been completed.

*Storage and Transmission of Lab Specimens*

Urine and blood specimens collected during intervention feeding are stored locally until the end of the third intervention feeding period, at which time they are shipped to either the central lab or to long-term storage. Shipment must occur within two weeks of the end of the final intervention feeding period. Details for storage and shipment of specimens is found in Clinic MOP Chapter 7.

***Activities Occurring Only Once During Intervention***

*Exit Interview and Counseling*
After all intervention feeding is concluded, participants receive a personalized Health Risk Assessment and nutritional counseling. This activity can happen in a group or individually. It does not need to coincide with the final day of feeding but may be incorporated into a celebration event. The associated activities are conducted primarily by the dietary staff. See MOP Chapter 11 for more details.

### *Early Termination of Feeding*

Inevitably, some participants will complete all required data collection, except for daily compliance monitoring, prior to the scheduled end of intervention feeding. Such subjects may be excused from further intervention feeding. This does not affect the timeline for data collection, however. Since final blood pressures must be taken on two of the final five days, intervention feeding cannot terminate prior to day 41. Participants who have not completed all required data collection cannot be excused early from feeding. Missed meals in such subjects count as noncompliance with the dietary requirements of the trial.

### *Premature Termination from Study*

If for any reason a participant chooses to terminate from participation in OMNI-Heart prior to the end of the cohort, complete the Participant Closeout Form (#18). Collect as much of the study data as possible prior to the termination. See Clinic MOP Chapter 11 for details of closeout activities.

## 7. Central Laboratory Procedures

### *Introduction*

The Core Laboratory for Clinical Studies (CLCS) of Washington University Medical School will serve as the central laboratory for OMNI Heart. The NHLBI will serve as the repository for the storage specimens. Specimens will also be sent to the Sacks Lab and to local labs from each site. This manual contains the information needed to collect, process, and ship specimens to the laboratories for analysis and the repository for storage. Please review the manual before the beginning of the study and contact the central laboratory or the repository if you have any questions or require additional information.

### *Contacts at CLCS*

Customer Service (314) 362-3522
Email: CLCS@im.wustl.edu

Laboratory Fax Number (314) 362-4782
Website: http:/clcs.wustl.edu

Laboratory Director
Thomas Cole, Ph.D.

Laboratory Manager
Connie Ferguson, MBA, M.T. (ASCP)

Clinical Studies Coordinator
Judi Jones BS, MT

Information Systems Supervisor
Dave Gibson

Technical Supervisor
Caswalyn Landry MS, C-MT (ASCP)

U.S. Mail Address:

Core Laboratory for Clinical Studies
Washington University School of Medicine
660 S. Euclid Ave., Box 8046
St. Louis, MO 63110

Shipping Address: (Federal Express)

Core Laboratory for Clinical Studies
Washington University School of Medicine
4940 Parkview Place
St. Louis, MO 63110

### *Contacts at NHLBI*

Shipments to the NHLBI central storage facility will be coordinated through:

Misti Dowell
BBI Biotech Research Laboratories
NHLBI Repository
217 Perry Parkway
Gaithersburg, MD 20877
Voice (301)208-8100 ext 107
Fax (301)208-8829
e-mail nhlbi@bbii.com

Shipping address: (UPS & FedEx): Contact Misti Dowell before shipping.

### *Study Supplies*

**The following will be provided before screening begins:**

- Blood collection tubes
- Labels and vials for specimen aliquots
- Shipping and storage boxes for specimens
- Urine collection hats and jugs
- Disposable transfer pipettes

**The following will be provided as requested for specimen shipments**

- Shipping containers and supplies
- Pre-addressed Federal Express Airbills

The CLCS will distribute specimen collection kits, supplies and shipping containers directly to each center as requested. Request supplies by submitting a Supply Request From to the CLCS. See Appendix B for a copy of the Supply Request Form.
**Contact the CLCS at least 2 weeks before your Lab Supplies are needed.**
The provided supplies must be used only for this study. If a large number of redraws or abnormal situations occur, inform the CLCS of the need for replacement supplies. Each center will be responsible for maintaining an adequate inventory of supplies.

**The following are found on the OMNI Heart website:**

- Central Laboratory Operations Manual (Lab Procedures, Chapter 7)

- Central Lab Collection Form- 24-Hour Urine (Form #30)
- Central Lab Collection Form - Fasting Blood (Form #31)
- Central Lab Shipping Log - Urine (Form #38)
- Central Lab Shipping Log - Blood (Form #39)

**The following must be available at each clinical center:**

- Standard refrigerated clinical centrifuge
- Ultra-low temperature freezer -70°C or colder, (i.e., ultra low REVCO or equivalent). All blood specimens must be stored at -70°C. If necessary, urine specimens may be stored in a non-cycling -20°C freezer, for up to 30 days before shipping.
- Dry Ice for shipping
- Federal Express pick-up or drop-off service
- Racks for tubes
- Phlebotomy supplies
- Indelible markers for labels
- Biological waste bags
- 2 L graduated cylinder for measuring urine volume
- Deionized/Distilled Water for rinsing the cylinder

***Preparing for the Visit:***

*Materials Needed*

- Visit-specific kits (see description below)
- Visit and participant specific labels

**Note:** Request preprinted labels for each participant by e-mailing the ID to the CLCS at least one week prior to the SV3 visit. The format for the participant ID is ID# (space) Accrostic. Use this format to request labels and to complete Forms 38 and 39.
Labels will be printed and sent to the site via Federal Express. A complete set of labels to be used throughout the study will be provided.

Description of Visit Kits used for Blood Draws

A single kit of blood collection supplies will be used for all visits including:
SV3, PI-4, PI-6, PII-4, PII-6, PIII-4, and PIII-6.

**Plasma Kit contains:**

3 x 10 mL EDTA Vacutainer tubes (purple top)
1 x 30 mL plastic pooling vial (purple cap)
10 x 2 mL plastic freezing vials (purple caps)

Note: 1 x 2 mL plastic freezing vials (plain top for buffy coat) required at Visit PI-4 only.

**Serum Kit contains:**

3 x 10 mL SST Vacutainer tubes (red/black top)
1 x 30 mL pooling vial (red cap)
10 x 2 mL plastic freezing vials (red caps)

Description of Visit Kits used for Urine Collection

Urine collection hats and jugs will be provided in bulk for distribution prior to visits SV3, PI-6, PII-6, and PIII-6. Labels are included in preprinted label set.

**Urine Supplies**

24-hour urine collection jug
Labels for jugs
6 x 8 mL plastic freezing vials (yellow caps)

**Additional Supplies**

Transfer pipettes (bulk supplies)
Shipping supplies (airbills, coolers, boxes, Dry Ice stickers, etc.)

***Prepare the Labels***

1. E-mail the CLSC with the participant ID# and acrostic as soon as the participant is eligible. A set of labels will be generated for each participant. Allow 1 week for labels to be printed and shipped. Labels are provided for all tubes and vials.

2. Affix the completed labels to the appropriate tubes found in the kits before the draw. Position the labels on the 2 mL freezing vials over the white patch allowing the volume markings to remain visible.

**Note: It is imperative that all tubes are labeled correctly and completely.**

***Prepare Forms 30 and 31***

1. Use one copy of each form and its worksheet per subject per visit. Fill out the top of each form (ID and Visit) and the top of each worksheet (ID) prior to the visit.
2. The remainder of each form will be completed at the visit.

***Prepare the Storage/Shipping Supplies***

1. A -70°C freezer must be available for storing samples after collection and processing. Specimens will be shipped by Federal Express to the laboratories and the storage facility in batches at mutually agreeable intervals. Contact each laboratory to arrange the shipping schedule. Contact the CLCS for shipping supplies.

2. Store specimens in boxes in the freezer until each batch is ready for shipment to CLCS, Sack's lab, or the NHLBI. Complete the Central Lab Shipping log forms (form #38 and #39) when processing and freezing the samples in order to record which sample is going into the slots in the freezer boxes. These forms will accompany the specimens when shipped.

***At the Visit:***

*General Instructions*

- Treat all materials that have been in contact with blood or urine as potentially infectious. Dispose of these materials, including needles, by approved procedures for the individual site. Wear gloves to minimize the transmission of infection.

*Collection of Blood Samples*

- A fasting blood must be collected at SV3 and twice during each intervention period. Participants must have fasted at least 10 hours prior to blood collection, with only water allowed. If the participant has not been fasting, the visit must be rescheduled.

- Due to the sensitivity involved in specific testing, standardization of specimen collection is imperative. The subject must be seated for at least 10 minutes prior to specimen collection. A tourniquet may be used for no longer than 2 minutes. Deviation from this standardization sample collection protocol will cause significant variability in assay results. **Be consistent from visit to visit**.

- Clean arm with an alcohol pad, then draw blood from the crook of the arm, generally from the antecubital vein. Fully fill all tubes.

- Draw the three SST serum tubes before the three EDTA plasma tubes. Non-additive tubes are drawn before additive tubes to avoid additive contamination of the non-additive tube. Cross-contamination between different additive tubes can also occur, making test results erroneous.

- Thoroughly mix all tubes immediately after collection by gently inverting the tubes at least five times. **Do Not Shake**.

- Remove the needle and apply pressure to the venipuncture site. Cover with an adhesive strip when the blood has stopped flowing.

- The Central Lab Collection Form - Bloods (form #31) is used for processing the fasting blood samples.

*Collection of Urine Sample*

- At SV2 and before each subsequent collection period during intervention, instruct the participant to collect a 24-hour urine specimen (See appendix A for sample instructions for participants).

- 24-hour urine collection should not be done during menstruation. Schedule urine collection to avoid collections during this time.

- 24-hour urine collection should start on a Tuesday, Wednesday or Thursday. If this is not possible, start on a Friday. Starting on the weekend days should be used as a last resort. Incentives might be useful to encourage collection during the week.

- Distribute the 24-hour container and instructions to the participant and review the instructions with the participant. Attach the four labels provided to the collection jug. Complete the labels with the appropriate identifying information. If the specimen is to be returned the next day, have the participant start the collection before leaving the clinic (i.e., void the bladder into the toilet). Inform the participant to bring the container back within 24 hours of collection. Specimens should be refrigerated or kept in a cool place during collection.

- The instructions for processing the specimen should be followed no matter when the specimen is returned.

- Take the 24-hour urine container from the participant. Check to make sure that the labels on the tab attached to the jug are filled out correctly and completely, and verify that the ID listed on the label matches that of the participant.

- Confirm that the participant:
  1) voided her bladder at the start of collection and did not save the specimen
  2) collected all voids during the collection period
  3) collected a final voiding at the end of the collection period
  4) returned the specimen within 24 hours of the final voiding

- The specimen is considered to be inadequate if any of the following are true.
  - The total duration of the collection is less than 22 hours or greater than 26 hours
  - The collection period did not start with an initial, discarded voiding
  - More than one voiding (including the final voiding) was missed
  - The total volume of the sample is less than 500 cc
  - The urine is collected during menstruation

- **If the specimen is inadequate, or if the participant failed to bring it in, a second specimen must be obtained.** Give the participant a new set of collection materials, attach and fill out the labels correctly. Save an aliquot from the original sample as a backup in case the participant is not able to provide an adequate sample, and note on the label that the

sample was inadequate. If the participant does not bring a repeat specimen, analyze the aliquot from the original (inadequate) sample in its stead, and note on the shipping label that the sample was inadequate and why. If both the samples are inadequate, send the better of the two samples.

- Assuming that the participant does bring in a specimen, either immediately take it to the clinic's lab area for processing or place it in a refrigerator until it can be processed. Avoid leaving the specimen at room temperature for any longer than is necessary.

- The Central Lab Collection Form - 24-hour urine (form #30) is used for processing the 24-hour urine sample.

***After the Visit:***

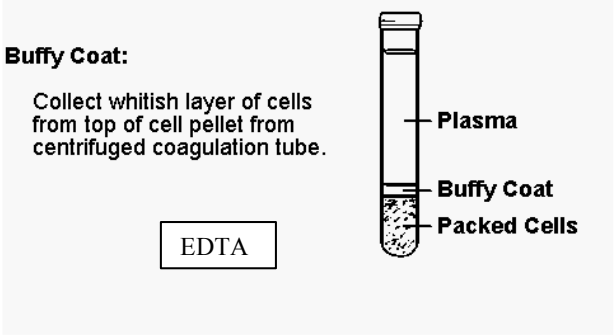
*Process and Store Specimens*

EDTA Plasma

1. Centrifuge the 3 x 10 mL (purple top) EDTA tubes without delay at room temperature. Centrifuge at >1,500 x g for 15 minutes to remove blood cells. No red cells should be present in the plasma or along the sides of the tubes.
2. Using a transfer pipette, transfer the plasma into the 30 mL plastic pooling vial. Cap the pooling vial and invert several times to obtain a homogeneous specimen.
3. Using transfer pipettes, transfer the plasma from the pooling vial into the 10 X 2 mL appropriately labeled freezing vials with purple caps.
4. Fasten the caps tightly and immediately place the vials in freezer boxes at -70$^{o}$C.
5. Fill out the Central Lab Shipping Log - Blood (Form #39) as you fill the slots in the box. Enter the participants ID# (space) Accrostic to match the preprinted label.

Note: Collect the Buffy Coat at the PI-4 visit.

- Save the EDTA tubes that contain the packed cells for the buffy coat. The buffy coat is the whitish layer of cells overlaying the packed red cells remaining in the EDTA tubes after the plasma is removed.




- Collect the buffy coats all three EDTA tubes and transfer into the 2 mL freezing vial with a clear cap labeled for "Buffy Coat."

Serum

1. Allow the 3 x 10 mL SST tubes (red/gray top) to clot for 30-60 minutes at room temperature in an upright position. Verify that the specimen is fully clotted.

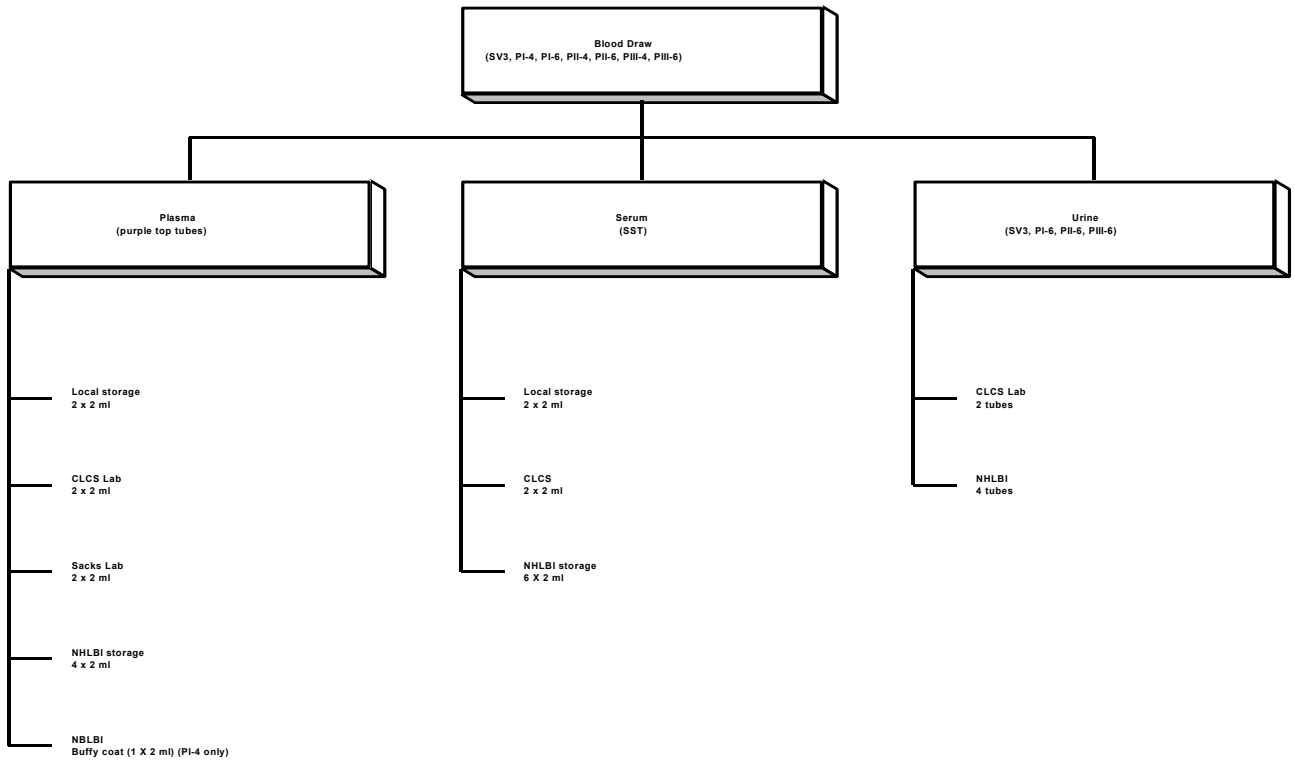
2. Centrifuge the clotted tubes for 15 minutes at 1,500 x g. After centrifugation, check the SST tubes for a complete gel barrier between the serum and the cells. Re-centrifuge if the barrier is incomplete or if red cells are seen above the barrier.
3. Pour the serum from the SST tubes into the 30 mL pooling vial. Cap the pooling vial and invert several times to obtain a homogeneous specimen.
4. Using a transfer pipette, transfer the serum from the 30 mL pooling vial into the 10 x 2 mL appropriately labeled freezing vials with red caps.
5. Fasten the caps tightly and immediately place the vials in freezer boxes at -70$^{o}$C.
6. Fill out the Central Lab Shipping Log - Blood (Form #39) as you fill the slots in the box. Enter the participants ID# (space) Accrostic to match the preprinted label.
7. Fill out the worksheet for the Central Lab Collection Form- Fasting Blood (Form #31)
8. Repeat draw if blood is hemolyzed or if there if tubes are destroyed during centrifugation.
9. After any repeat draws for this participant are complete, use the worksheet to complete Form #31

Note: The blood specimens are stored in 2" boxes which hold 100 x 2 mL vials (10 X 10 grid). Place samples sequentially in the box starting with the front, left corner of the box, moving to the right, then to the back as each row fills. Note sample locations on Form #39 as you fill each box.

Urine

1. Record the sample identification, dates and times on the Central Lab Collection Form- 24-hour Urine (Form #30).
2. Invert the sample container at least eight times to ensure a uniform sample.
3. Measure the total urine volume by using a (use a graduated cylinder). Note the volume on Form #30.
4. Label the 6 x 8 mL freezing vials yellow capped vials using the preprinted labels for each participant.
5. Add 5 mL of well-mixed urine to tubes 1-6, using a transfer pipette. Cap securely. Invert to mix.
6. Fasten the yellow caps tightly and immediately place the vials in freezer boxes (in an upright position) at -70°C.
7. The remaining urine may be discarded. Be sure to use distilled/de-ionized water to rinse the graduated cylinders between samples to avoid cross-contaminating the specimen.
8. Fill out Central Lab Shipping Log - Urine (Form #38) as you fill the slots in the box. Enter the participants ID# (space) Accrostic to match the preprinted label.
9. Fill out the worksheet for the Central Lab Collection Form- 24-hour Urine (Form #30).
10. If a repeat collection is necessary, repeat the steps above.
11. After any repeat collections for this participant are complete, use the worksheet to complete Form #30.

Note: The urine specimens are stored in 3" boxes (7 X 7 grid). Due to the space required by caps, the 3" urine boxes will hold 36 instead of 49 vials. The fourth position in each row and the entire fourth row must be left empty for the vials to fit. As with the 2" boxes, the starting location for filling these boxes is the front, left corner of the box, moving to the right, then to the back as each row fills. Note sample locations on Form #38 as you fill each box.


Blood Draw
(SV3, PI-4, PI-6, PII-4, PII-6, PIII-4, PIII-6)
Plasma
(purple top tubes)
Serum
(SST)
Urine
(SV3, PI-6, PII-6, PIII-6)
Local storage
2 x 2 ml
CLCS Lab
2 x 2 ml
Sacks Lab
2 x 2 ml
NHLBI storage
4 x 2 ml
NBLBI
Buffy coat (1 X 2 ml) (PI-4 only)
Local storage
2 x 2 ml
CLCS
2 x 2 ml
NHLBI storage
6 X 2 ml
CLCS Lab
2 tubes
NHLBI
4 tubes

### *Shipping to CLCS and NHLBI*

1. Two sizes of cardboard freezer storage boxes are provided: 2" boxes for serum, plasma, and buffy coat specimens in 2 mL vials (10 x 10 grid) and 3" boxes for urine specimens in 8 mL vials (7 x 7 grid). Boxes of each size are provided for CLCS and NHLBI while Sacks' lab and local storage will only need the 2" box (10 x 10 grid). Specimens are processed and placed in the freezer boxes as previously outlined.

2. Forms 30 and 31 contain the detailed participant information for the blood and urine samples should be filled out and entered at the collection period.

3. Forms 38 (urine) and 39 (bloods) are shipping forms that are used when putting the samples into the boxes before freezing. As the samples are put into the box, note the box slot number, the participant ID# and Accrostic, the visit the sample is collected at, the collection date, the sample type (e.g., plasma, serum) and any comments about the particular sample. These forms will accompany the samples when shipped to each lab.

4. Contact the CLCS for shipping supplies at least 2 weeks prior to the scheduled ship date.

5. Instructions for packing and shipping samples will be included with the shipping supplies.

6. Contact each laboratory prior to shipping samples to arrange a shipping schedule.

## Appendix A

***Instructions for 24-Hour Urine Collection (Weekend collection)***

To collect a 24-hour urine specimen, you will need a plastic sample container (women may also want to use a collection device referred to as a hat). The container should be labeled with your study identification number, the date and time you begin the urine collection and the date and time you complete the collection. It is important to collect all of the urine you pass during the 24-hour collection. However, if you do forget and miss a collection, it is equally important that you indicate how many voidings were missed on the tag at the end of the collection.

Women should use the hat to help collect the sample. This is done by placing the hat under the toilet seat, urinating into the hat, then carefully empty the contents of the hat into the jug. Otherwise, urinate directly into the jug. In the event of a spill, please estimate the amount spilled; write the amount on the recording tag (e.g., "1 cup spilled"). If you miss a sample, record this on the tag in the place provided.

***How to collect the 24-hour urine.***

Do not collect the first urine of the day, but note the time of this first morning urination on the tag of the urine container. This is the start of your collection period. Beginning with the second urination of the day, collect all urine for the next 24 hours from the time of the discarded urine. Every time you have to urinate, collect the entire sample in the container. For example, the last sample collected should be voided 24 hours after the first morning urination (the times on the recording tag might be 7:30 a.m. start time and 7:30 a.m. stop time, for example) and should also go into the container. Write the date and time of your final urination on the tag of your container. Store the container in a refrigerator or a cooler between voids if possible. Bring your sample into the center as soon as possible after collection is complete.

***Instructions for 24-Hour Urine Collection (Weekday collection)***

To collect a 24-hour urine specimen, you will need a plastic sample container (women may also want to use a collection device referred to as a hat). The container should be labeled with your study identification number, the date and time you begin the urine collection and the date and time you complete the collection. It is important to collect all of the urine you pass during the 24-hour collection. However, if you do forget and miss a collection, it is equally important that you indicate how many voids were missed on the tag at the end of the collection.

Women should use the hat to help collect the sample. This is done by placing the hat under the toilet seat, urinating into the hat, then carefully empty the contents of the hat into the jug. Otherwise, urinate directly into the jug. In the event of a spill, please estimate the amount spilled; write the amount on the recording tag (e.g., "1 cup spilled"). If you miss a sample, record this on the tag in the place provided.

***How to collect the 24-hour urine.***

You will begin your urine collection at the clinic. When you arrive at the clinic, you should void but do not collect this urine. This is the start of your collection period. Beginning with the second urination of the day, collect all urine for the next 24 hours from the time of the discarded urine. Every time you have to urinate, collect the entire sample in the container. For example, the last sample collected should be voided 24 hours after the clinic urination (the times on the recording tag might be 4:00 p.m. start time and 4:00 p.m. stop time, for example) and should also go into the container. Record the date and time of your final urination on the tag of your container. Store the container in a refrigerator or a cooler between voids if possible. Bring your sample into the center as soon as possible after collection is complete.

CORE LABORATORY FOR CLINICAL STUDIES
Washington University in St. Louis ▪ School of Medicine

# Appendix B
## OMNI Heart Study
## Supply Request Form

**Fax this form to the CLCS at (314) 362-4782.**
**Request Supplies 2 weeks prior to date needed.**

Date Requested: _____ Requested by: _____

Site: _____ Contact #: _____

**Date Supplies needed by: _____**

| # needed | Lab Supplies | # needed | Lab Supplies |
|---|---|---|---|
| _____ | Plasma Kits | _____ | Urine Kits |
| _____ | Serum Kits | _____ | Urine Jugs with Labels |
| _____ | Buffy Coat Vials (20 vials/pkg) | _____ | Urine Collection Hats |

2" Freezer Box for Blood Storage Labeled:
_____ Local Lab _____ CLCS
_____ Sacks _____ NHLBI
(Indicate # needed for each)

3" Freezer Box for Urine Storage Labeled
_____ CLCS _____ NHLBI
(Indicate # needed for each)

_____Transfer Pipets (25 pipets/pkg)

**Participant Labels**: E-mail ID# and Acrostic to clcs@im.wustl.edu at least 1 week prior to the date needed. Label set to be used for the entire study will be sent via Federal Express. Indicate date labels are needed in e-mail request.

**Shipping supplies**

_____ Shipping Coolers - Indicate # of boxes to be shipped. Appropriate size cooler will be provided.
_____ # 2" Freezer Boxes to Ship _____ # 3" Freezer Boxes to Ship

Note: Shipping instructions and all needed shipping supplies will be included in the cooler.

OTHER SUPPLIES_____

**Questions? Call Customer Service at (314) 362-3522**

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**For CLCS Use**
Date Request Received: _____ Initials: _____
Date Assembled: _____ Initials: _____
Date Shipped: _____ Initials: _____
Tracking #: _____

# Summary Edits

# 8. Data Entry and Management

***Staff ID's***

All OMNI-Heart staff must have an OMNI-Heart staff ID number. To obtain a staff ID number, the clinic coordinator should e-mail the Data Manager at the Data Coordinating Center (DCC) with the following information:

- First and last name
- Project job title
- Address (work)
- Phone number (work)
- Fax number (work)
- E-mail address (work)

The Coordinating Center will assign a new number within 48 hours of receipt of this information.

***Quality Control Methods Prior to Data Entry***

The clinic coordinator will need to manually employ the quality control methods outlined below in real-time before the participant leaves the intervention site for both the batch-entered and centrally entered data. These methods include:

<u>Patient identification and record linkages.</u>

The DCC will generate the participant ID numbers. We will use a check digit mechanism to defend against digit transposition. Its construct is as follows:

Participant ID: S1 P1P2P3 D1

Where:

S1 = the site identifier 1 or 2 = BWH, 3 or 4 = Johns Hopkins

P1-3 = the patient sequence number within the organization

D1 = the check digit code:

Defined as:

D1 = Mod (S1*2+P1*3+P2*4+P3*5, 11)

If D1=10, then use D1= "A", otherwise use the digit D1.

The DCC will generate a list of individual participant identification numbers, a sequential number starting with 001. Then a check digit will be calculated and a list of up to 2000 unique participant ID's will be generated for each site (see Table 1 below). Each of the potentially eligible patients will be assigned a participant ID from the list provided by the DCC. To establish the record linkage, the lists will be formatted as logs, with space next to each participant ID to record participant initials (or name), and the participant's date of birth. The clinic coordinator's will put the patient name and date of birth on the participant ID List and then use that participant ID on all pages of all study data forms beginning with the PSV or SV1 BP form.

Table 1. Example of List of Participant ID's to be used at BWH

| Participant ID | Participant Name/Initials | DOB |
|---|---|---|
| 10009 | | |
| 10014 | | |
| 10020 | | |
| 10035 | | |
| 10041 | | |
| 10056 | | |
| 10061 | | |
| 10077 | | |
| 10082 | | |
| 10098 | | |
| 10105 | | |
| 10111 | | |
| 10126 | | |
| 10131 | | |
| 10147 | | |

Legibility. All data must be checked for illegible handwritten replies, spelling errors, etc. All checked response boxes must have checks within designated spaces. Check to be sure that the forms are filled out in pen. With the exception of the Food Frequency Questionnaire (FFQ), forms filled out in pencil are not acceptable.

Form admissibility. All forms must be checked to determine if the form was completed within the specified time window. All forms must be checked to assure that the completed form is the correct one for the indicated visit or activity.

Missing information. All forms must be checked for unanswered items or sections of an otherwise completed form. The clinic coordinator must assure that all necessary forms have been completed for the indicated visit or activity before entry of the individuals visit data can begin.

Consistency. All data must be checked to assure that information supplied in one section is consistent with data in another section of the same form. All forms for the same participant for a given visit must be checked to assure consistency. Skip patterns on forms should be checked for the correct data flow.

Range and inadmissible codes. All data must be checked to assure they do not contain values either outside specified ranges or undefined alphabetic or numeric codes.

The individual coding instructions that are attached to the relevant forms provide detailed instructions for coding and review procedures for each study form. Be sure to review the coding instructions for the form before completing the review process. See the section below for details on how to correct errors on the forms.

### *Data Edits on Forms*

It is important to use the following process when making corrections to study forms to assure the accuracy and validity of the data.

- Participant responses should never be obliterated.
- In red ink, a slash should be made through the incorrect response and the correct response written next to it.
- The reviewer's initials, date of correction and an explanation of the edit should be written next to the data field that is being edited.

For example:

~~92~~ 90 *RL 8/5/2003 Addition error*

If a participant makes a correction to a form, the clinic coordinator should

- verify that the response is clearly written.
- In red ink, slash through the old response.
- The reviewer's initials, date of correction and the notation "participant correction" should be written next to the data field.

For example:

**YES** **NO**

☒ ☒ *RL 8/5/2003 participant correction*

### *Data Entry*

The data entry processes will differ at the two clinical sites. The BWH site will make copies of all forms that will be data entered (for their storage), and then provide the original forms to the DCC for data entry processing at the Channing. It is expected that there will be a weekly exchange of data forms from the BWH site to the Data Manager at the DCC, except during run-in periods where the exchange of data will happen more frequently. The Hopkins site will be entering their data forms locally, using the MS Access data entry programs developed by the DCC. Proper training materials and documentation on how to use the data entry system will be provided by the DCC.

To limit outliers in the data, range and logic checks are built into the system to discourage form discrepancies during entry. **Any out of range values will need to be resolved by the clinic coordinator/clinic staff prior to data entry.** The data entry technician should enter the data as is from the form, note their OMNI ID# in the box on the data form that says "Entered By", and also note the date of entry. The goal for data entry is to be current within two weeks in order for reports to be accurate and to minimize the number of corrections that will need to be made at one time.

*Data Entry Flow*

All data collection forms for a visit should be entered before the corresponding visit/flow forms. All forms including the visit/flow forms should be entered before the closeout forms.

For example: You just finished run-in for a participant….

| | |
|---|---|
| 1 | Enter all daily diaries not previously entered |
| 2 | Enter all data collection forms: |
| | Patient History |
| | BP 1 |
| | Brief Physical Activity questionnaire |
| | Medication questionnaire |
| | Case Conference form |
| 3 | Enter the Run-In flow form |
| 4 | Enter Close out form if relevant |

***Quality Control Methods Following Data Entry***

As the data entry technician enters the data, any values that do not pass the range or logic checks defined by the system, will not be allowed to be entered into the system. The clinic coordinator will need to contact the DCC Data Manager by phone or e-mail to resolve any of these types of issues.

***Data Edits to Database***

Most corrections to the database can be done directly at the sites. To have a correction made by the DCC, send an e-mail to the Data Manager with the participant ID, the name of the form, the date on the form, the data field in error and an explanation of the correction. The DCC will make the change and send an e-mail confirmation that the change has occurred. The clinic coordinator should also make these changes on the relevant participant data form (see "Data Edits of Forms" section above).

***Centrally-entered data***

Centrally-entered data will need to be sent to the DCC for entry. For the Johns Hopkins site, the only OMNI-Heart form that is entered (scanned) at the DCC is the Food Frequency Questionnaire (Willett FFQ). Before sending to the DCC, sites should make copies of the FFQ for onsite archiving for the length of the study. The original FFQ forms should be sent to the DCC. A shipping log (Form #36) specifying ID's of forms sent should accompany each mailing. A copy of this shipping log should be archived at the mailing site for reference and confirmation of form receipt. When receiving bundled mailings, the DCC staff will review the shipping log and assure that all reported forms were received. This should be noted on the shipping log, which will then be archived at the coordinating center. Any discrepancies will be immediately reported to the site, who will help resolve the problem. Resolution may include making additional copies of the archived data and re-mailing them to the DCC.

***Data Validation***

The primary measures of data integrity rely on the verification of data. Verification is a comparison of data before a transition (data entry) to the result after the transition to assure a one-to-one correspondence and assure that the transition process was "true". In order to assure the accuracy of the OMNI-Heart data, the DCC has set up a two step process. 1) Validation of the data by the DCC completed at the end of each cohort and as a part of a site visit. 2) Validation completed by the individual sites.

*Data Validation at the DCC*

Data validation will be done by the DCC to assure validity of the data. The DCC will request on an on-going basis as data is collected:

- All Blood Pressure forms for randomized participants
- A 10 % random sample (chosen by DCC) from randomized participants. This includes all clinical and diet forms entered into the OMNI-Heart data entry system.

Additional validation will occur as a part of site visits. The DCC will request a random set of forms (from both randomized and non-randomized participants) from each site.

The site should copy the requested forms and complete the accompanying shipping log (form #36) and send to the DCC Data Manager. A summary error report and a detailed error report will be compiled for the site. The clinic coordinator and Data Manager will then work together to solve any discrepancies that may have occurred. The clinic coordinator is responsible for seeing that corrections are made to the forms if needed (see data edits on forms section). Corrected copies of the forms should be faxed or mailed to the DCC. Changes that need to be made to the database should be clearly noted on the form. The DCC will file all copies of the forms in the participant's chart.

*Data Validation by the Hopkins Site*

The Data Management system has several data validation reports available for the sites to validate their own forms. There are reports to view all screening data, all blood pressure data and all daily diary data for randomized participants. The clinic coordinator can print out the above reports for all randomized participants for the current cohort.

The following list is a guideline for the amount of data validation to be conducted at the individual sites:

- All screening data for randomized participants
- A random sample of daily diaries for randomized participants

The sites can also use the view feature in the Data Entry System to look at individual participant's forms. (See the OMNI-Heart Data Entry User's Manual for details.)

***Archiving***

For the Hopkins site, a copy of the MS Access Omni-Heart database will be transferred daily via e-mail to the coordinating center's data manager. Archiving will occur at the coordinating center, and will contain the previous day's data on-line and all historical data off-line. For reasons of safety and backup, archives of the Omni-Heart database will be stored on the Channing Laboratory computer network. The historical data is easily obtained if restoration is needed. In addition, all data collection forms need to be archived for the life of the study in hard-copy form so that copies may be sent to the coordinating center as needed for data management. Requests for copies of archived data will be made on a form-by-form basis by the DCC.

# Summary of Edits

# 9. Trial Monitoring Reports

***Introduction***

During the trial's course, the Data Coordinating Center produces a variety of reports to help the Steering Committee, Measurement Committee, Recruitment Committee, Clinic Coordinators, and the DSMB monitor the progress of the trial.

Additional reports, produced for the DSMB only, permit the DSMB to monitor the efficacy and safety of the interventions. These reports include not only standardized reports issued at regular intervals but also ad hoc reports as requested.

The reports prepared for the Steering Committee focus on the recruitment of participants into the trial. These reports allow the Steering Committee to ensure that recruitment is proceeding in a timely manner and to identify potential recruitment problems at an early enough stage that they can be corrected. In addition, the Steering Committee also receives reports summarizing the completeness and quality of the study database.

The Measurement Committee receives the same reports as the Steering Committee. The other committees receive reports relevant to their areas of expertise.

***Types of Reports***

*Recruitment/Follow-up Reports*

Recruitment and follow-up reports summarize recruitment activity and follow-up to date. These reports assist field sites in meeting recruiting needs and in scheduling eligible participants for upcoming screening visits.

*Baseline Data Reports*

These reports present the baseline characteristics of the randomized participants. Data are presented both by site and by treatment order. All of the information reflects baseline, pre-intervention data and therefore should be comparable across treatment groups.

*Quality Control Reports*

Quality control reports include a number of reports related to the integrity of the Omni-Heart database and adherence to trial protocol by both participants and sites. These include audit reports, counts (observed/expected) of data collection items and visits, with a particular focus on outcome variables.

*Laboratory QC and Results Reports*

Laboratory quality control reports summarize lab tracking, including receipt, receipt status, and the collection of process measures such as start and stop times for 24-hour urine samples

*Serious Adverse Events Report*

This report will list all serious adverse events that occur. An unblinded version of this report will be made available to the DSMB.

*Side Effects Report*

The side effects report summarizes side effects reported by Omni-Heart participants during the course of the study.

*Outcome Measures and Safety Issues Reports*

These reports are only sent to members of the DSMB. They comprise unblinded study data.

***Distribution of Reports***

*Monthly Steering Committee/Measurement Committee Reports*

These are generally distributed by uploading to the WWW site and notifying committee members by e-mail prior to the meeting or conference call.

- Recruitment/Follow-up Reports
- Baseline Data Reports
- Quality Control Reports
- Laboratory QC and Results Reports
- Side Effects Report

*Monthly Recruitment Committee Reports*

Distribution will be via the WWW site with notification to investigators when updates occur.

- Recruitment/Follow-up Reports

*End of Cohort Reports*

These are distributed to the Steering and Measurement Committees at the end of each cohort after all data have been entered.

- Recruitment/Follow-up Reports
- Baseline Data Reports
- Quality Control Reports
- Laboratory QC and Results Reports
- Side Effects Report

*Reports for DSMB Meetings*

These are prepared and distributed about 2-4 weeks prior to each DSMB meeting.

- Recruitment/Follow-up Reports
- Baseline Data Reports
- Quality Control Reports
- Laboratory QC and Results Reports
- Side Effects Report
- Outcome Measures and Safety Issues Reports

# Summary of Edits

# 10. Safety Monitoring

### *Blood Pressure*

In order to prevent a prolonged period of untreated hypertension (outside the eligibility range of OmniHeart), several blood pressure safety procedures are observed.

- At PSV, individuals taking any anti-hypertensive medications are excluded, and those who report having taken them in the past must have been off of them for at least two months.
- Individuals with a history of cerebrovascular or cardiovascular disease are excluded, as are those with congestive heart failure
- Blood pressure is monitored regularly throughout the study, and "escape levels" are established to identify, and ensure proper follow-up of individuals with an elevated blood pressure that might warrant drug therapy. Participants may also be referred to a physician if deemed appropriate based on symptoms and clinical judgment even though the BP is below the escape thresholds.
- Individuals who complete the study with persistently high, but still allowable, blood pressure readings are referred for counseling and possible treatment as part of the close-out visit.
- If escape levels are reached or a participant is referred for BP management for some other reason, a BP Escape Tracking Record (Form #23) is filled out. This form is used to document responses of the OmniHeart investigators and contacts with personal providers to each escape level blood pressure. Once the form is complete, a copy is sent to the DCC.

### *OMNIHEART Blood Pressure Escape Criteria*

The following blood pressure escape levels and protocols have been established to ensure that participants are offered appropriate evaluation and therapy when clinically indicated. The actions taken when these escape levels are reached vary somewhat for screening, run-in, and intervention. In all cases, participants may be immediately referred for evaluation if a clinician believes such action is appropriate based on his or her own clinical judgment.

*Screening*

Screening criteria for excluding participants from further participation based on elevated blood pressure levels are discussed in sections 7 and 8 of the protocol. In the event that the mean SBP at any one visit exceeds 180 mm Hg or the mean DBP exceeds 110, the participant is not only excluded from the study but is referred to a physician to determine if medication is needed. If the participant does not have a personal physician, qualified personnel at the clinical center may make the recommendation for treatment.

*Run-In Feeding*

Two escape levels apply during run-in and intervention feeding. They differ in terms of the frequency with which a follow-up measurement is required. Also, a repeat elevated blood pressure triggers an automatic exclusion during run-in but only a referral during intervention feeding.

**Escape level #1:** The mean blood pressure recorded at any single visit exceeds either a SBP of 180 mm Hg or a DBP of 110 mm Hg.

**Action:** Participant may be excluded immediately and referred to a physician for further evaluation. Alternatively a second blood pressure measurement must be obtained within four days and prior to randomization. If this second measurement exceeds 170/105 mm Hg, the participant is automatically excluded and referred to a physician for follow-up.

**Escape level #2:** The mean blood pressure recorded at any single visit exceeds either a SBP of 170 mm Hg or a DBP of 105 mm Hg.

**Action:** Participant may be excluded immediately and referred to a physician for further evaluation. Alternatively a second blood pressure measurement must be obtained within four days and prior to randomization. If this second measurement exceeds 170/105 mm Hg, the participant is automatically excluded and referred to a physician for follow-up.

If the participant does not have a personal physician, qualified personnel at the clinical center, ideally blinded to randomization assignment, may make a recommendation for treatment.

*Intervention Feeding*

**Escape level #1:** The mean blood pressure recorded at any single visit exceeds either a SBP of 180 mm Hg or a DBP of 110 mm Hg.

**Action:** A second blood pressure measurement must be obtained within four days. If this exceeds 170/105 mm Hg, the participant is referred to a physician for follow-up.

**Escape level #2:** The mean blood pressure recorded at any single visit exceeds either a SBP of 170 mm Hg or a DBP of 105 mm Hg.

**Action:** A second blood pressure measurement must be obtained within seven days. If this exceeds 170/105 mm Hg, the participant is referred to a physician for follow-up.

If the participant does not have a personal physician, an investigator at the center, ideally blinded to diet status may make a recommendation for treatment.

In the event that a participant is referred to a clinician for evaluation, the clinical center should seek to obtain a set of up to five end-of-intervention blood pressure measurements. Care should be taken, however, that this does not delay or otherwise interfere with appropriate clinical care. If blood pressure medication is not initiated, the participant continues in the trial.

### *Referral for Non-Blood Pressure Reasons*

Abnormalities noted in laboratory or physical assessments that require medical evaluation result in referral to other medical care sources unless they arise as a direct result of participation in OMNIHEART. If clinical problems arise from OMNIHEART participation, the problem may be dealt with at the clinical center or through referral as is most appropriate.

### *Morbid Events Affecting Blood Pressure*

Participants who suffer a morbid event with a lasting effect on blood pressure (e.g., myocardial infarction, stroke) are considered terminated as of the date of the morbid event. ***Similarly, participants who are placed on exclusionary medications or special diets by their physicians are also considered terminated as of the date these medications or diets began. In each of the above cases, the participant's end-of-intervention blood pressures are calculated as outlined in section 4.11 of the Protocol and he/she is excluded from further participation in the study.****

### *Approach to Participants Placed on Anti-Hypertensive or Cholesterol-Lowering Medications*

During the course of the trial, some randomized participants may start either anti-hypertensive medication or cholesterol-lowering medication.

### *Food Safety*

Clinic staff are instructed in procedures for handling, preparing, and distributing foods. These procedures focus on preventing contamination of foods and on safe preparation, storage, and consumption practices. Participants are instructed to immediately report symptoms that may arise from food-borne illness. Such reports trigger clinics to investigate whether other participants have experienced similar symptoms, to review their own procedures, and to determine if further action is required. In order to avoid food-borne illness, participants are provided instructions on food storage and preparation.

### *Adverse Events, including Serious Adverse Events*

Throughout the run-in and intervention feeding periods, the Daily Diary (Form #24) is used to capture information about symptoms from the study foods and about intercurrent medical events. Symptoms of lactose intolerance and to other gastrointestinal symptom will typically be addressed by a study dietitian. The daily diary is also meant to capture intercurrent medical problems that would be classified as a serious adverse event. Serious adverse events include any of the following:

Fatal or life-threatening event
In-patient hospitalization
Prolongation of existing hospitalization
Significant or persistent disability
Congenital abnormality or birth defect
Any other event that may adversely affects the rights, welfare or safety of the participant.

If a serious adverse event occurs, the staff member should notify the principal investigator or designated study clinician, should gather some basic information, and should complete Form 12 (Serious Adverse Events). The study clinician should review and sign this form and if appropriate contact the participant. The study clinician should then complete the bottom of Form 12 and the corresponding local IRB form used to document serious adverse events. The clinician should submit the report to the local IRB according to their guidelines and send copies to the DCC and the NHLBI project officer. The DCC will collate these documents and report to the Steering Committee and the DSMB.

### *Data, Safety and Monitoring Board*

An external Data and Safety Monitoring Board (DSMB) reviews the trial's progress at least on an annual basis. Their review includes unblinded interim results. The DSMB can recommend that the NHLBI terminate the trial early if participants are being subjected to undue risk or if the trial's objectives are met and further follow-up would serve no added scientific purpose.

### *Laboratory Abnormalities*

Participants are provided with a copy of local laboratory studies. Also, they are informed of any clinically significant, local laboratory abnormality, whether or not these constitute an exclusion to OMNIHEART. These laboratory data are supplied to the participant and, with his/her permission, to his/her physician for follow-up.

# 11. Participant Closeout

# Participant Closeout

## *Purpose*

This chapter contains instructions for closing out participants prior to randomization, early termination after randomization, closing out randomized participants at the end of the cohort and end of trial close-out.

## *Closeout Prior to Randomization*

If a participant refuses to participate in the study or becomes ineligible prior to randomization, they need to be closed out of the OMNI Heart data entry system.

**Eligible participants who decline enrollment:** If a participant declines enrollment in the study, they can be closed out by using the Participant Closeout/Termination Form, (Form #18, Section A.). Check the primary reason that most accurately describes why the participant did not enroll.

**Participants who become ineligible prior to randomization:** If refusal/ineligibility is determined prior to randomization, the participant can be closed out by using the Participant Closeout/Termination Form (Form #18, Section B.). Check the primary reason that most accurately describes why the participant is ineligible.

## *Early Termination After Randomization*

**Post-Randomization termination:** If a participant terminates study participation after being randomized they can be closed out by using the Participant Closeout/Termination Form (Form #18, Section C.). Check the primary reason that most accurately describes why the participant is terminating their study participation.

Note also that for anyone who drops out of the study after having completed week four of the first intervention period, for whatever reason, OMNI Heart personnel should try to obtain as many of the five end-of-feeding period blood pressure measurements as possible, along with a fasting blood draw for that intervention period and any remaining interventions for that participant.

### *End of Cohort Closeout*

At the conclusion of each cohort, closeout activities take place in the context of a group session. Study participants receive a summary of their average screening blood pressure measurements and the average of all their blood pressure measurements during the three diet periods. The participants are not informed of their intervention group status and individual blood pressure measurements until the end of the entire study. While the structure and content of the close-out activities is left largely up to the individual sites, the following must occur:

- Provide summary of screening blood pressure averages and the average of all their blood pressure measurements during the three diet periods
- Distribute education materials including, but not limited to:
  - -The DASH Eating Plan
  - -Your Guide to Lowering Blood Pressure
- Give certificate and/or letter of appreciation
- Review "What's Next in OMNI Heart?" handout (Appendix 1)

### *End of Trial Closeout*

#### Data Management

The final closing out of participants from the OMNI Heart data management system will occur when all data collection forms from a participant are collected and entered into the OMNI Heart data entry system. The Intervention Flow Form (Form #20) for PIII should be completed and entered.

#### Unblinding

At the conclusion of the entire trial, the clinical centers will provide additional information to participants beyond that provided at the end of cohort closeout. Such information can be provided in the context of a meeting or mailing. In either instance, include a summary of trial results and information specific to the individual. A general description of the diet in lay terms is provided. At this time, participants also receive a listing of their individual blood pressure responses to each intervention.

***Appendix 1.***

# What's Next in Omni Heart?

April 2005

- Last group will finish feeding
- Last data will be sent for analysis
- Last blood and urine samples will be sent for analysis

May to October 2005

- Study results will be analyzed

November 2005

- You will receive a detailed report with your personal results, including:
  - Your blood pressure on each diet
  - Your cholesterol and triglyceride levels on each diet
  - Your weight
  - Your diet assignments

- Final Farewell Reception. You will be invited to a reception to hear the study results, discuss what they mean, and ask questions.

Spring - Summer 2006

- A reprint of the main trial results will be mailed to you.