

9. EVALUATION PROTOCOLS

9.1 Demographic Information

Demographic information is collected during screening visit 1. The demographic questionnaire collects participant information including address and phone number, marital status, occupation, education, income, ethnicity and race. A copy of this form can be found in chapter 33, section 33.3. Socioeconomic status is determined from the demographic questionnaire using education and income. Emergency and medical contacts are also being recorded on the form. Additional information such as the best phone number for contact, the best time to reach the participant, whether the participant utilizes email and if it is acceptable to contact them at work are all included in the demographic questionnaire. Following completion of this questionnaire, file the form in the participant's chart for future use. The two-page form is administered at screening visit 1 following completion of the informed consent, height and weight measures and the study video.

9.1.1 Administering the Demographic Questionnaire (Done at screening visit 1)

- Copies of the Demographic questionnaire are located in the "Calerie Forms" file cabinet.
- Following the participant's completion of the informed consent, height and weight measures and the viewing of the study video, the demographic questionnaire may be administered.
- The demographic questionnaire is the first form to be completed.
- Ask the participant to complete the demographic questionnaire.
- Once the form has been completed, review the form for any errors and missing data.
- Initial the Demographics form to verify it is complete.
- Once finished, continue to administer additional screening visit 1 questionnaires.
- Retain page 1 of the Demographics form for the Participant binder.
- Fax or FedEx page two of the Demographics form to the CC for data entry and review.

9.2 Physical Exam and Vital Signs

9.2.1 Medical History

Rationale:

To ensure that all participants in CALERIE are healthy, and do not have any underlying medical conditions that may affect their participation in the study and/or any outcomes assessed during the study.

A complete medical history performed during screening will include a review of all major organ systems and all medications taken during 30 days prior to screening, as well as reproductive status, contraceptive and menstrual history for women, where appropriate. Use of an appropriate method of contraception will be verified at Month 1, 3, 6, 9, 12, 18 and 24 month visits.

At Screening:

1) **Study Manager:** Periodically ensure that the study physician is stocked with adequate study specific medical history forms (Appendix-Chapter 33.3).

2) **Study Physician:**

- Obtain a thorough medical history from each candidate at Screen Visit 2, using the medical history questionnaire.
- At the end of the interview review the medical history form with the candidate to ensure that all fields are complete.
- Return the completed medical history form to the study manager who will file it in the candidate's Screen Visit 2 paperwork.
- After the physical exam is completed write a remark on any medical history concerns that may affect participation.

3) **Study Manager:** Transfer study physician remarks to the screen 2 summary checklist and place in the screen visit 2 folder for the candidate's eligibility review by the multidisciplinary screening team. The Medical History Form will serve as the source document in the completion of the Medical History CRF.

During Baseline:

1) **Study Physician:** Complete the abbreviated medical history form to monitor any changes in health or reproductive status including contraception since the screening visit (when a detailed medical history was obtained).

- If there are any significant changes in or concerns about the participant's health status, document in the participants records and hand over the document to the study manager along with the abbreviated medical history form.
 1. Interval history / exam changes
 2. Changes that require the participant be terminated from the study
 3. Should be documented and relayed to the Study Coordinator and Principal Investigator
- If there are no concerns return the completed abbreviated medical history form to the study manger.

2) **Study Manager:** File the abbreviated medical history form in the participant's baseline visit folder and use as the source document for the completion of the Medical History CRF.

On Study

Study Physician and Study Manager task are the same for baseline.

Medications List

Rationale:

To document CALERIE participant medication usage with special attention to medications, that would affect their eligibility / participation in the study or that are specifically known to affect any of the study outcomes.

At Screening:

1) **Study Manager:**

- Remind candidates at screen visit 1 to bring in medications they are taking when they come in to meet with the study physician at Screen Visit 2.

- Periodically ensure that the study physician is stocked with adequate study specific medications forms (Appendix 33.3).

2) Study Physician:

- Conduct a comprehensive medication review including method of contraception for each candidate at Screen Visit 2, using the medications form and listing the medications the candidate is taking. Double check the collected information with the candidate to ensure that all fields are complete.
- If the candidate is on any medications that clearly excludes their participation in the study, inform the participant and Study Manager at this time.
- After this visit is completed document the candidate's medication use and the reason for exclusion.
- If candidate is not on any medication that may affect their participation in the study, return completed medication list to the study manager

3) Study Manager:

Ensure that the medication list is completed and file it in the candidate's Screen Visit 2 paperwork. The medication listing collected by the physician will serve as a source document to assist in the completion of the Medications CRF page by the study manager or study coordinator. Study physician remarks will be used in the summary file for the candidate's eligibility review by the multidisciplinary screening team.

During Baseline and Follow-up:

1) Study Physician:

Review the screening medication list at follow-up visits and make sure the list is current. All concomitant medications taken between visits are documented and updated on the medication list on an ongoing basis.

2) Study Manager:

Use the updated medication list as the source document for completing the Medications CRF during follow-up.

9.2.2 Physical Exam Procedures

1. **General Appearance:** Observe general appearance of the patient.
2. **Head, Ears, Eyes, Nose, Throat:** Head. Inspect the head for size. Evaluate hair for texture and hair loss. Ears. Examine external ear and external auditory canal. Test hearing: with eyes closed, instruct patient to acknowledge hearing the gentle rubbing of the examiner's fingers ~3-4 inches away from his right and left ear. Nose. Inspect nasal passages; note color of mucous membrane, inspect turbinates, note any drainage of sinuses, and inspect nasal septum. Eyes. Inspect eyes, eye lids, and eye brows for size, symmetry, and alignment. Note translucency and vascular pattern of sclera and palpebral conjunctivae. Test visual acuity (e.g. with a pocket screener). Inspect pupillary size and reaction to light and accommodation. Throat. Inspect mucous membrane of the entire mouth and examine tongue, palate, tonsils, and posterior pharynx for any lesions.
3. **Neck:** Note concavity of cervical spine, palpate for any focal area of tenderness, and test for range of motion. Evaluate the thyroid gland for consistency, tenderness, or enlargement. Auscultate for bruits
4. **Cardiovascular:** Palpate radial pulses and note character and amplitude. Inspect and/or palpate apical impulse. Auscultate heart sounds in five locations,

- note intensity of S1, S2, and identify any extra sounds. Observe for edema of foot, ankles, and legs.
5. **Lungs:** Note rate, pattern and comfort of respiration. Assess tracheal position. Evaluate symmetry of chest expansion. Auscultate lung sounds, note intensity, and compare both sides. Note the presence or absence of adventitious sounds.
 6. **Abdomen:** Inspect contour of abdomen, skin and subcutaneous tissue, and umbilicus. Auscultate in all four quadrants of the abdomen and note frequency and character of bowel sounds. Palpate all four quadrants of the abdomen for tenderness or evidence of any organomegaly. Palpate liver edge and percuss the liver span. Examine for the presence of inguinal or femoral hernias.
 7. **Lymph nodes:** Examine cervical and inguinal area for lymphadenopathies. Note size, location, tenderness, or enlargement of any lymph nodes.
 8. **Extremities/Skin:** Inspect and palpate skin and nails for color, texture, turgor, moisture, pigmentation, hair distribution. Feel with back of hand for warmth. Examine for signs of chronic arterial or venous insufficiency.
 9. **Neurological:** Examine mental status. Test all cranial nerves including test for hearing and visual acuity as described above. Test whether light touch, vibration and position sense are intact throughout. Check deep tendon reflexes.
 10. **Musculoskeletal:** Inspect the muscles for size, symmetry, atrophy, and fasciculation. Determine muscle power by gently trying to overpower contraction of each group of muscles.
 11. **Spine:** Observe for alignment, palpate vertebrae, assess range of motion.
 12. **Rectal exam:** Palpate the prostate gland in men > 40 years old
 13. **Breast exam:** mammogram, pelvic exam, and pap smear. Discuss/recommend to female participants that it be done through their primary physician according to guidelines.
 14. **Reproductive:** Discuss and document female participants' current reproductive status ie: length of menstrual cycle, history of surgical sterilization, pre or peri menopausal state, and if applicable, current method of contraception.

In the physical exam CRF form, the appropriate boxes corresponding to the different systems will be checked by the physician as either 1) abnormal 2) normal or 3) recommended/not recommended. If abnormal, the findings will be explained in the appropriate line.

9.2.3 Heart Rate

Rationale

To first establish a baseline heart rate and as measures of safety and effects of calorie restriction.

Equipment

- Watch with a sweep second hand or digital second display.

Participant Preparation

- Verify that the individual is comfortably **seated** in a chair, with legs uncrossed, and the back and arm supported.
- Verify the participant has not had caffeine or exercised in the last 30 minutes.

- Remind the participant to relax as much as possible and to not talk during the measurement procedure.
- Have participant rest for 5 minutes.

Heart Rate Measurement

- Heart rate is measured after the blood pressure measurements have been completed and the individual is in a rested state.
- The technician palpates the pulse on the participant's wrist (radial artery).
- The technician places their index and middle finger over the radial artery.
- The heart rate should be counted for 60 seconds and recorded on the Vital Signs CRF.

QC for this measure: The technician taking blood pressures will be trained at the Study Training Session. The CC will perform a statistical assessment by site to make sure that there is no an unexpected occurrence of observations that are multiples of 2, 3, 4, 5, 6, 10 and 20.

9.2.4 Resting Blood Pressure

Rationale

To first establish a baseline blood pressure measurement for each participant and then monitor for changes for purposes of outcome and data collection. The blood pressure readings are also being used to monitor safety and assess the effects of calorie restriction.

Equipment

- Stethoscope with bell
- Standard mercury sphygmomanometer
- Measuring Tape in metric units
- Trained, CALERIE certified technician
- Three Standard Size Blood Pressure Cuffs (Two of each size):
 - Small Adult
 - Adult
 - Large Adult

Participant Preparation

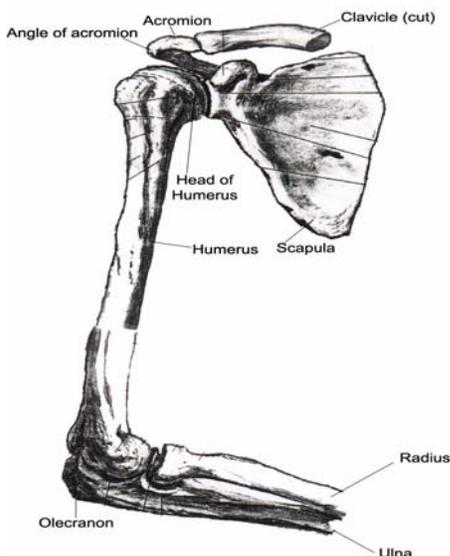
- Bring the participant into a quiet exam room, with the temperature of the room in the 68-75°F range.
- Explain the procedure to the participant.
- Verify the participant has not had caffeine or exercised in the last 30 minutes.
- Ask the participant to remove all clothing that covers the location of cuff placement.
- Measure the right mid-arm to ensure proper selection of cuff size.
 - Measurement of the bare arm is required for proper cuff selection.
 - The arm measurement must be taken with the participant standing, holding the forearm horizontal.
 - Measure the length of the humerus from the acromion process to the olecranon process (Figure 1).

- The midpoint of the humerus is marked on the dorsal surface of the arm.
- With the participant's arm relaxed at the side, the arm circumference is measured by drawing the tape snugly (without indenting the skin) around the arm at the level of the midpoint marking. Care must be taken to keep the tape horizontal.
- Using this measurement, select the appropriate size cuff from the chart below:

Arm Circumference	Cuff	Cuff Size
22 to 26 cm	Small Adult	12x22 cm
27 to 34 cm	Adult	16x30 cm
35 to 44 cm	Large Adult	16x36 cm

- Seat the participant comfortably in a chair, with legs uncrossed and flat on the floor. If necessary, place a book, footstool or other flat object beneath the participant's feet so they do not dangle. Place correctly sized blood pressure cuffs on each arm. Verify that the participant's back and arms are supported, such that the middle of the cuff on the upper arm is at the level of the right atrium (the mid-point of the sternum). Instruct the participant to relax as much as possible and not to talk or move excessively during the measurements.
- Position one of the participant's arms so that elbow and forearm are resting comfortably on the table with the palm of the hand turned upward. The bend of the elbow (antecubital fossa) should be at heart level.
- Palpate the brachial artery (just medial to and above the cubital fossa), and mark this location for stethoscope placement.
 - Locate the midpoint of the rubber ladder within the cuff (usually this is marked on the cuff).
 - Verify that the cuff is wrapped smoothly and snugly about the arm, with the bladder midpoint over the brachial artery, with mid-height of the cuff at heart level (bottom edge of cuff about 2.5 cm above the antecubital fossa).

Figure 1



- Explain to the participant that you will now leave them seated quietly in the room for 5 minutes and when you return you will perform the blood pressure measurements. Remind the participant not to talk when you re-enter for the measurements.

Resting Blood Pressure Measurement

The technician should prepare to take two blood pressure measurements in each arm at the first visit. The arm with the highest reading will be used for the remainder of the study. Only CALERIE certified technicians can perform blood pressure measurements for this study. Numerous blood pressure measurements are taken throughout the study at differing time points to assure valid readings.

The measurements:

- Connect the cuff to a standard mercury manometer. The manometer should be positioned so that the midpoint of the column is at eye level to the person measuring the blood pressure.
- When preparing to take the BP, the following criteria for use of the stethoscope must be met:
 - The earpieces should fit tightly enough to exclude outside sound but not so tightly as to cause discomfort. The earpieces should be placed in the ears with the tips down and forward.
 - The valve between the bell and the diaphragm should be turned in the correct direction. (Korotkoff sounds are best heard using the bell of the stethoscope.)
 - The bell of the stethoscope should be placed lightly on the skin overlying the brachial artery. Light pressure accentuates low-pitched sound and avoids compression murmurs. Pressing too heavily with the stethoscope causes turbulent flow in the artery and results in a murmur, which may prolong the apparent duration of phase 4.
- The cuff should be inflated to at least 30 mmHg above the point at which the radial pulse disappears.
- Place the bell of the stethoscope on the brachial artery just below and not touching the cuff or tubing and slowly (2 mmHg per second) deflate the cuff while listening through stethoscope.
- Record the first and fifth phases of Korotkoff, reading the pressure in mmHg to the nearest even number. The first sound heard in a series of at least two sounds is recorded for the systolic BP (Phase 1). For diastolic BP (phase 5), record the first silence and continue to deflate at a rate of 2mmHg/sec for at least 10 additional mmHg to confirm phase 5 reading by ensuring there are no further sounds.
- Have the participant raise their arm for 30 seconds between measurements and wait 1-2 minutes between readings.
- Repeat all steps above until 3 readings have been completed.
- If one of the readings differs from the others by 15 mmHg or more (either systolic or diastolic) then discard that reading and only use the remaining two. It is not necessary to conduct a fourth measurement.

Recording Blood Pressure Measurements

All blood pressure readings will be documented and should be recorded on the Vital Signs CRF. The average of the readings is calculated by the CALERIE CC. Once the

average is determined the pulse pressure is calculated by taking the difference between the averaged systolic blood pressure and the averaged diastolic blood pressure.

QC for this measure

The technician taking blood pressures will be trained at the Study Training Session. The CC will perform a statistical assessment by site to make sure that there is no an unexpected occurrence of observations that are multiples of 2, 5 and 10.

Please see Appendix XX for instruction on mercury calibrations.

9.2.5 Temperature and Respirations

Rationale

To first establish a baseline measurement and then monitor for changes as measures of safety and effects of calorie restriction.

Equipment

- Digital oral thermometer reading in degrees Celsius (Note: Please use the same brand throughout the trial)
- Watch with a sweep second hand or stop clock

Participant Preparation

- Have the participant remain in the seated position following the blood pressure and heart rate measurements.

Temperature Measurement

- Place the digital thermometer under the tongue, just to one side of the center and close the lips tightly around it.
- Leave the thermometer in place for the required amount of time or when the beep sounds letting you know that the reading has been completed. Times will vary depending on the model.
- Remove the thermometer from the participant's mouth and record the reading.
- The reading should be recorded in ° Celsius.

Respiration Measurement

- Count the number of times the chest of the volunteer rises over one full minute.
- The participant should not be aware that you are counting their respirations. This can cause a false measurement.

QC for this measure

The technician taking respiration measurements will be trained at the Study Training Session. The CC will perform a statistical assessment by site to make sure that there is no an unexpected occurrence of observations that are multiples of 2, 3, 4, 5, 6, 10 and 20.

Appendix XX

Maintenance Procedures for Standard Mercury Sphygmomanometer

The following checks should be conducted at least every month, and a log kept of the dates and the people carrying out the troubleshooting (see Table 7-2).

1. With the instrument placed flat on the table, and the inflation system disconnected, the level of mercury should read zero in the standard instrument. If the reading is either above or below the zero mark, mercury should be added or withdrawn until it reads zero. The top of the meniscus is on the zero line when the eyes are level with this line and the mercury is correctly adjusted.
2. The inflation system should then be reconnected, and the cuff rolled around a cylinder and secured. The valve should be closed on the Air Flow system, and the instrument inflated until the mercury rises to 240 mmHg. The valve should then be closed, at which time the mercury column should remain stable. If the column continues to fall, there is an air leak, and the following steps should be taken:
 - a. The system should be re-inflated until the column rises to 240 mmHg.
 - b. The tubing should be pinched at various locations to localize the area of the leak.
 - c. Appropriate replacement of the tubing, cuff or valve should be performed.
3. With the instrument inflated above full calibration, the screw cap should be examined for mercury leaks. If this happens, the screw cap should be tightened. If the leaks persist or the mercury is seen at the bottom of the tube, the silicone rubber that provided a seat for both ends of the glass tube should be replaced.
4. With time, the mercury will become dirty and an oxide may be deposited on the inside of the glass tube. The instrument should be laid nearly on its side (on a tray) so that the mercury will return to the reservoir and none can be seen in the glass tube. The tube should be removed carefully and cleaned out using the long pipe cleaner supplied with the instrument. The tube should then be replaced and the zero level rechecked. This cleaning must be done in a local instrument shop and is not to be attempted by clinical personnel.

9.3 In-Clinic Anthropometric Measures

9.3.1 Clinic Weight

Rationale

To obtain an accurate, reliable weight using a standardized protocol for the purpose of measured body weight to be utilized as outcome data. This weight will be the official clinic weight for the study.

Equipment

- Electronic Scale – Scale Tronix 5200 Model
- The same scale that displays the CALERIE study logo **must be** used to weigh participants for all outcome measures.
- **The scale MUST NOT be used to weigh participants enrolled in any other study than CALERIE!**
- Scales must be calibrated once per week and calibration logs kept at each site.

Participant Preparation

- Participant must be weighed in the morning after an overnight fast of at least eight hours and the time of last consumption will be noted.
- Participant must empty their bladder.
- Participant must remove shoes and clothing and asked to dress in a pre-weighed hospital gown.

Weight Measurement

- Tare the scale to zero before weighing the volunteer. If the scale does not tare to zero, follow the scale manual instructions for taring.
- Ask the participant to stand in the middle of the scale with arms hanging loosely at their side.
- The reading is taken when the digital readout remains constant and the participant is motionless.
- Record the weight to the nearest 0.1 kg.
- Have the participant step off of the scale and allow the scale to tare to zero. It should be within 0.1kg of zero. If it is not, then the weight just taken is not valid and the process should be repeated.
- Reweigh the participant once again as per above technique.

- Record both measurements and if the two measurements are $>.1$ kg apart, obtain a third measurement, following the above technique. The average of the 2 closest measures is then taken as the official clinic weight.
- For screening visit 1, use the two closest measurements to obtain an average. To obtain the average, use a standard calculator and add the two closest weights together and divide by 2. Take the average and subtract the weight of the gown.
- Use this weight to calculate the Body Mass Index (see section 9.3.3).
- Record all participant weights and the weight of the gown on the required CALERIE forms.
- No average is calculated at the site following screening visit 1. For the remainder of study visits, the average will be calculated through programming at the CALERIE CC.
- The scale will provide a printout following all weight measures. The printout should be taken following an individual's measurement and attached to the source document.

Quality Control Measures

The scale must be calibrated weekly. Use a standard 10 kg weight for calibration of the digital scales. For calibration, perform the following steps:

1. Place the 10 kg weight on the scale and record the weight on the scale display in column 1 of the calibration log.
2. Remove the weight from the scale. Step onto the scale and read your weight on the scale display. Recorded in column 2 of the calibration log.
3. Step off of the scale and put the 10 kg weight on the scale. Then, also stand on the scale. Read the total weight of you and the 10 kg weight on the scale display. Record the total weight in column 3 of the calibration log.
4. Once the three weights are recorded, compare the sum of weights in columns 1 and 2 to the total weight recorded in column 3. If there is a discrepancy of more than 0.1 kg, recalibrate the scale according to manufacturer guidelines found in the owner's manual.

Record calibrations in a log book kept at the sites. This calibration log should be available for the DCRI monitor at his/her visits. Please see Appendix 11-A for a copy of the scale calibration log.

Other QC items:

- CALERIE scales should be clearly marked, and they should not be used for any other on-going protocols at the sites.
- The CALERIE specific scale will be the only scale used for weighing CALERIE participants.

9.3.2 Height

Rationale

Obtain accurate data related to the stretch stature of volunteers and use this information to calculate Body Mass Index.

Equipment

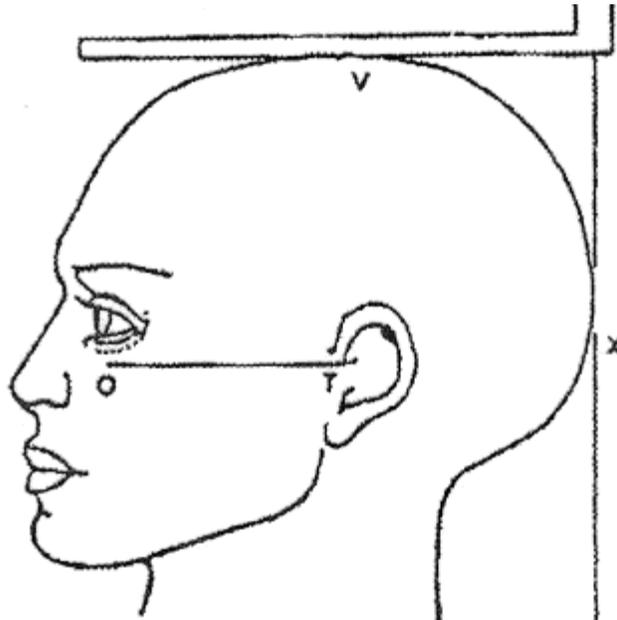
- Wall-mounted stadiometer in conjunction with a right-angled head board.

Participant Preparation

- Participant must remove shoes and any hair accessories or dressings that will keep the stadiometer head board from resting on the top of the head.

Vertical Height Measurement

- Ask the participant to stand erect with arms hanging naturally at their side. Heels, buttocks and upper part of back, but not necessarily the back of the head, must be in contact with the wall.
- Instruct the participant to take a breath and stretch as far as possible. The volunteer must hold their breath for the duration of the exam.
- Ask the participant to relax their head. While the participant is stretching, a second technician needs to assist by cupping the participant's head in their hands and gently applying traction bilaterally to the mastoid processes.
- While the second technician is continually applying traction, the first technician must create an imaginary line from the participant's orbitale (the most inferior edge of the eye socket) to the tragion (the notch superior to the tragus of the ear which is at the level of the superior aspect of the zygomatic arch). The horizontal plane is called the Frankfort Plane.



- Check to see that the participant's heels remain on the floor while the first technician lowers the head board slowly until firm contact is made with the vertex of the skull. (Note: The stadiometer head board must be raised and lowered slowly, or the calibration may be altered.)
- At the vertex of the skull, take the reading from the indicator. The reading must be to the nearest 0.1cm always rounding up.

- Record the reading on the CRF and repeat the procedure another time as described above.
- If the first two measures are not within 0.1 cm of each other, a third measurement must be obtained. Use the same technique described above.
- For screening visit 1, use the two closest measurements to obtain an average. To obtain the average, use a standard calculator and add the two closest weights together and divide by 2. The average is used to calculate the Body Mass Index (see section 9.3.3).

The second and the only other height measurements will be taken at baseline but will not be averaged at the site. The measurements are recorded and the average is calculated by programming at the CALERIE CC.

- Record the two measures that are within the range specified above (0.1 cm) on the CRF.

Quality Control Measures

The stadiometer must be calibrated at the beginning of each clinic day while participants are still being entered into the study. Sites must use a pre-measured pole and must verify that the pole height is reading accurately off of the stadiometer by following the steps described below.

1. Place the pre-measured pole on the floor and against the foot plate of the stadiometer.
2. Slowly lower the head board until it rests on top of the pre-measured pole.
3. Record the reading of the stadiometer.

Record calibrations in a log book to be kept at the sites. This calibration log must be available for the monitor at his/her visits. Please see Appendix 11-B for a copy of the stadiometer calibration log.

9.3.3 Body Mass Index (BMI) Calculation

Rationale

The BMI is used to assess the health status of volunteers as well as to correlate body weight and body fat. For this study it is also used to establish eligibility.

Equipment

- Texas Instruments TI-30XA Scientific calculator (the same calculator must be used by all sites to avoid differing rounding functions inherent to different calculators. Please also note that no hand calculations are permitted!)

Calculations

- Obtain the correct average height (cm) and average weight (kg) of the participant to 1 significant digit after the decimal point
- Convert the height to meters by dividing the number of centimeters by 100 (this gives three significant digits to the right of the decimal point):

$$\frac{\text{Cm of height}}{100}$$

- Take the square of the resulting number (m²) and save it (without rounding).

- To calculate the BMI: Divide the weight in kilograms by the square of the height calculated above (m²)

Definition of BMI:

$$\frac{\text{Kg of body weight}}{\text{m}^2 \text{ of body height}}$$

- This result should be recorded to one significant digit after the decimal point.
- Have a second CALERIE staff member repeat all steps above for verification of correct calculation procedure.

NHLBI Website:

Alternatively, BMI can be computed using the BMI calculator located on the NHLBI website.

- Cut and paste the following web address into the “Address” window of your browser.

<http://www.nhlbisupport.com/bmi/bminojs.htm>

- Obtain the correct average height (cm) and average weight (kg) of the participant to 1 significant digit as described above.
- Enter both numbers into the corresponding boxes on the NHLBI webpage, and click the “Submit” button.
- Read the calculated BMI and record to one significant digit after the decimal point.

9.3.4 Home Weights

This section provides detailed instructions on obtaining home weights and quality control procedures followed by study participants and clinical site personnel. Home weights will be collected daily during the DLW procedures at baseline, 6, 12, 18, and 24 months by Intervention participants. Those randomized to the Control group will record and provide their home weights at baseline, 12, and 24 months. Intervention participants will record their home weights starting Day 0 (dosing) of the DLW period continuing through the 14-day period to capture weight changes. Those in the Control group will start on Day 1 because they pick up their scale on Day 0. These daily weights will be recorded by all participants on a source document copied at the clinical site and sent to the Coordinating Center for calculating adherence.

At other times home weights will not be collected by the Coordinating Center but will be used by intervention participants and staff to monitor the participant's progress. The frequency of home weights will be determined by the participant and staff, however, it is planned these weights will be obtained at least weekly. More frequent measurement such as daily weighing may be recommended as a toolbox strategy.

All participants will receive a calibrated Lifesource UC-321 ProFIT/IntelliSCALE (A&D Medical, Milpitas, CA) scale at the baseline DLW. The first measurement on the home scale will be made at the clinic so that agreement between the weights from the home

scale and the weights from the clinic scale can be verified. If measurement shows a deviation of more than 0.1 kg from the clinic weight, the participant will get another scale.

Participants randomized to the intervention group will keep the scale at their home while those participants randomized to the control group will return their scale after the second baseline period. Scales will be distributed to the control group for each DLW but then collected from them afterwards. Control participants will neither be encouraged nor discouraged to weigh themselves in between DLW studies.

The clinic staff will be responsible for the pre-study and on-study scale calibration and distribution, participant training and communication, and review. Each participant will undergo an initial training on appropriate weight measurement and data recording procedures, scale maintenance and troubleshooting. Training will be repeated every 6 months.

9.3.4.1 UC-321 ProFIT/IntelliSCALE

9.3.4.2 General Scale Information

UC-321 is a portable scale designed for home and clinical use and powered by four type “AA” batteries. Maximum scale capacity is 150 kg, and precision of measurement is up to 0.05 kg (50 g). The scale has an “automatic-power-off” function to turn off the power in about 10 seconds after non-operation to extend battery life. Scale display has a “Low battery mark.” If this mark is displayed, batteries must be replaced.

The scale has four measurement categories - “WEIGHT,” “BMI,” “MEMORY,” and “TARGET.” All weight measurements in CALERIE will be taken in kilograms using the “MEMORY” mode. Up to 31 weight data measurements can be stored in memory. The 32nd data measurement is stored by deleting the oldest stored measurement. The difference from the last stored measurement and the current measurement is automatically displayed when the participant steps off the scale.

Complete scale Instruction Manual is enclosed as Appendix # to this MOP section.

9.3.4.3 Precision of Measurement Verification

Precision of measurement for all scales will be verified every 6 months. All sites will use a standard 10 kg reference weight acquired for the CALERIE study by the Coordinating Center.

9.3.4.4 Initial Precision of Measurement Verification

Within two weeks after receiving the scales from the Coordinating Center (or manufacturer), the Study Coordinator (or designee) will verify precision of measurement for each scale received:

Step 1: Place scale on a solid level flooring surface

Step 2: Place the 10 kg calibration weight on the scale and record the weight on the scale display in column 1 of the calibration log

Step 3: Remove the weight from the scale. Step onto the scale and read the weight of the technician on the scale display. Recorded in column 2 of the calibration log

Step 4: The technician then steps off of the scale and puts the 10kg weight on the scale. Then, the technician also stands on the scale. Read the total weight of the technician and the weight on the scale display. The total weight is recorded in column 3 of the calibration log

Step 5: Once the three weights are recorded, the sum of columns 1 and 2 is compared to the total weight recorded in column 3. If a discrepancy of more than .1 kg exists, the scale should be recalibrated according to manufacturer guidelines found in the owner's manual."

Step 6: Complete Site, Serial Number and Baseline sections of the Home Scale Certification Log (Appendix 2)

Step 7: Enclose a sample log in the carton with the scale

Step 8: Attach scale verification label (to be developed and provided by the CC – includes: Verified, Initials, Date) on the outer side of the carton

9.3.4.5 Month 6, 12, 18, and 24 Precision of Measurement Verification

Every six months, participants enrolled in the Intervention group will bring their scale to the clinic for measurement verification.

9.3.4.6 Six month check

Staff will check the calibration by following the steps above outlined in 1.2.1. If the home weight is more than 0.1 kg from the clinic weight, the participant will get another scale from the clinic and ship the "old" scale back to the manufacturer for calibration. There is a 3-year warranty for these scales and the manufacturer is responsible for repairs.

9.3.4.7 Control Group

Participants enrolled in the control group will return the scale to the clinic at the end of each DLW period. The clinic should provide the same scale back to the participant for each DLW period.

9.3.4.8 Home Weights Measurement – Clinical Staff Procedures

9.3.4.9 Baseline DLW Periods

9.3.4.10 First Baseline DLW Period

- Prior to meeting a participant, prepare the Daily Home Weight Log (Appendix #) by filling in the days and dates starting with the first day of home weight measurements
- Provide participant with calibrated scale

- Complete Participant ID and "Provided to Participant on" sections of the Home Scale Certification Log
- Enclose Log in the participant's binder
- Provide a participant with laminated home weight measurement instructions (Appendix #) and advise him/her to keep the instructions next to the scale
- Demonstrate scale features
- Provide a participant with verbal instructions on measuring home weights by reviewing written instructions with the participant
- Have a participant measure weight on the scale provided at least twice during the visit with a 20 – 30 minute interval between the measurements. Determine whether the measurement was properly performed and the results correctly read by a participant. Advise a participant on any corrective action. If necessary, have a participant measure weight one more time
- Provide a participant with the Daily Home Weight Log and verbal instructions on how to complete the log by reviewing written instructions provided on the opposite side of the Log
- Instruct a participant to keep the log and a pen with either black or blue ink next to the scale and record weight immediately after a weight was taken
- Instruct a participant to cross an appropriate day box if weight was not measured on a particular day
- Instruct a participant to verify records on Daily Home Weight Log versus the scale memory data weekly and make appropriate corrections in the Log, if necessary
- Instruct a participant to bring the completed Daily Home Weight Log to the clinic at the end of the first DLW period (when participant comes in for the first day) of the second baseline DLW period
- Contact a participant over the telephone weekly to check whether s/he experienced any difficulties with home weight measurements and data collection or verification. Re-emphasize the importance of home weight measurements

9.3.4.11 Second Baseline DLW Period

- Contact a participant over the telephone several days prior to the start of the second baseline DLW period and remind him/her about the upcoming visit and to bring the completed Daily Home Weight Log from the first DLW baseline period (this may be done as part of a visit reminder call)
- Prior to meeting a participant, prepare the Daily Home Weight Log by filling in the day and dates starting with the first day of home weight measurements
- Review the first baseline DLW period Daily Home Weight Log with a participant for completeness and clarify any records that are difficult to read. **DO NOT FILL IN ANY MISSING WEIGHTS BASED UPON PARTICIPANT'S RECOLLECTION OF THE MEASUREMENT RESULTS**
- If necessary, remind a participant of the importance of the daily weight measurements
- Inquire whether a participant experienced any difficulties with home weight measurements and data collection or verification and, if necessary, review weight measurement and log completion procedures with a participant
- If necessary, have a participant measure weight at clinic and determine whether the measurement was properly performed and the results correctly

read by a participant. Advise a participant on any corrective action. If necessary, have a participant measure weight one more time

- Provide a participant with Daily Home Weight Log and verbal instructions on how to complete the log by reviewing written instructions provided on the opposite side of the Log with a participant
- Remind a participant to keep the logs and a pen with either black or blue ink next to the scale and record weight immediately after the measurement was taken
- Remind a participant to cross an appropriate day box if weight was not measured on that day
- Remind a participant to verify records on Daily Home Weight Log versus the scale memory data weekly and make appropriate corrections in the Log, if necessary
- Contact participant over the telephone weekly to check whether s/he experiences any difficulties with home weight measurements and data collection or verification. Re-emphasize the importance of home weight measurements
- Control Group only:
 - Contact the participant over the telephone several days prior to his/her next visit to the clinic after the end of home weight measurement period and remind them to bring the completed Daily Home Weight Log and their scale
 - Collect scale from the participant
 - Review the Daily Home Weight Log for the second baseline DLW period with the participant for completeness and clarify any records that are difficult to read.

9.3.4.12 Month 6,12,18, and 24 DLW Periods (Control Group measures at Month 12 and 24)

- Contact the participant over the telephone several days prior to the visit and remind to bring the scale for precision of measurement verification to the clinic. If a participant did not mail or bring the completed Daily Home Weight Log for the previous DLW period, remind him/her to bring the Log (this may be done as part of a visit reminder call)
- Prior to meeting a participant, prepare the Daily Home Weight Log by filling in the days and dates starting with the first day of home weight measurements
- Inquire whether participant experienced any difficulties with home weight measurements and data collection or verification and, if necessary, review weight measurement and log completion procedures with a participant
- Verify precision of the scale measurement in accordance with the procedures described in Sub-Section 1.2 “Precision of Measurement Verification” of this MOP section
- Control Group only:
 - Provide participant with their calibrated scale on Day 1 of the 12 or 24 month DLW (attempt to use the same scale as the one the participant used last time)
 - Complete Participant ID and Date Dispensed sections of the Home Scale Log
 - Enclose Log in the participant’s binder

- Provide a participant with laminated home weight measurement instructions (Appendix 4) and advise him/her to keep the instructions next to the scale
- Demonstrate scale features to a participant
- Remind participant to verify records on Daily Home Weight Log versus the scale memory data weekly and make appropriate corrections in the Log, if necessary
 - Contact participant over the telephone or by email weekly to check whether s/he experiences any difficulties with home weight measurements and data collection or verification. Re-emphasize importance of home weight measurements
- Control Group only:
 - Contact the participant over the telephone several days prior to his/her first visit to the clinic after the end of home weight measurement period and remind to bring the completed Daily Home Weight Log and scale
 - Review the Daily Home Weight Log with the participant for completeness and clarify any records that are difficult to read. Collect record and scale

9.3.4.13 Home Weight Measurement – Participant Procedures

During the baseline visit the Study Coordinator provides a participant with verbal and written instructions on weighing themselves and recording their weight and reviews these instructions with the participant during follow-up visits. Written instructions should be provided to a participant on the laminated card.

9.3.4.14 Scale

- Read Instruction Manual before using the scale
- Do not share this scale with your household members
- Do not put any objects on the scale
- Do not expose scale to extreme temperatures, humidity, direct sunlight, shock, moisture and dust
- Keep the scale on the solid and leveled floor. Do not place the scale on a soft, wet or slippery floor
- Do not step onto the scale with wet feet. Make certain that feet are dry to prevent slipping or serious injury
- Gently step onto the center portion of the scale
- Do not place feet on the display window
- Do not hold the measurement switch for extended periods. This will shorten battery life
- Replace the batteries with new ones when “Low battery mark” is displayed. For batteries replacement, follow the instructions in the “Installing (or Replacing) Batteries” of the scale Instruction Manual
- Contact your study staff immediately if you experience any technical problems with the scale or your body weight measurement results on two consecutive days differ by more than 0.5 kg (500 g)

- Clean the scale with a dry, soft cloth or a cloth moistened with water and a mild detergent. Never use alcohol, benzene, thinner or other harsh chemicals to clean the scale
- Bring the scale to the clinic when requested by your study staff

9.3.4.15 Weight Measurement

- Weigh same time of day (ideally in the morning just after you get out of bed):
 - after you empty your bladder
 - in no clothes or under garments
 - barefoot
 - before eating and/or drinking anything
- Set the slide switch to "MEMORY." NEVER CHANGE THIS SETTING!
- Press the measurement switch gently. All display segments must be visible for several seconds
- Wait until the display 0.0 lb (0.0 kg) and steady symbol O are visible
- Step on the scale gently and stand still during measurement
- Read the weight the steady symbol O appears
- Step off the scale
- Record weight measurement result for an appropriate day on the Daily Home Weight Log provided by your study staff immediately after the measurement was performed

9.3.4.16 Daily Home Weight Log Maintenance

The following instructions are provided on the opposite side of the Daily Home Weight Log:

- A. Keep the Log and a pen with either black or blue ink next to the scale
 - Record weight measurement result on the Daily Home Weight Log provided by your study staff immediately after the measurement was performed
 - Cross an appropriate day box if weight was not measured on a particular day
 - At the end of each seven day period verify Log record vs. the memory record:
 - Gently press and hold the measurement switch
 - Weight data measurements are displayed in order from the last (most recent) to the first (oldest)
 - Verify the last seven weight measurements vs. the Log record
 - Press the measurement switch to power off the scale
 - Bring completed Log to the clinic at your next visit

9.3.4.16.1 Appendix 9-A UC321 Instruction

9.3.4.16.2 Appendix 9-B Home Scale Log

9.3.4.16.3 Appendix 9-C Daily Home Weight Log

9.3.5 Waist Circumference

Rationale

The waist circumference is the best surrogate marker for visceral adiposity and is an additional measure of body composition.

Equipment

- Gulick II Tape Measure

Participant Preparation

- Participant should lower or raise clothing so that the waist is exposed.

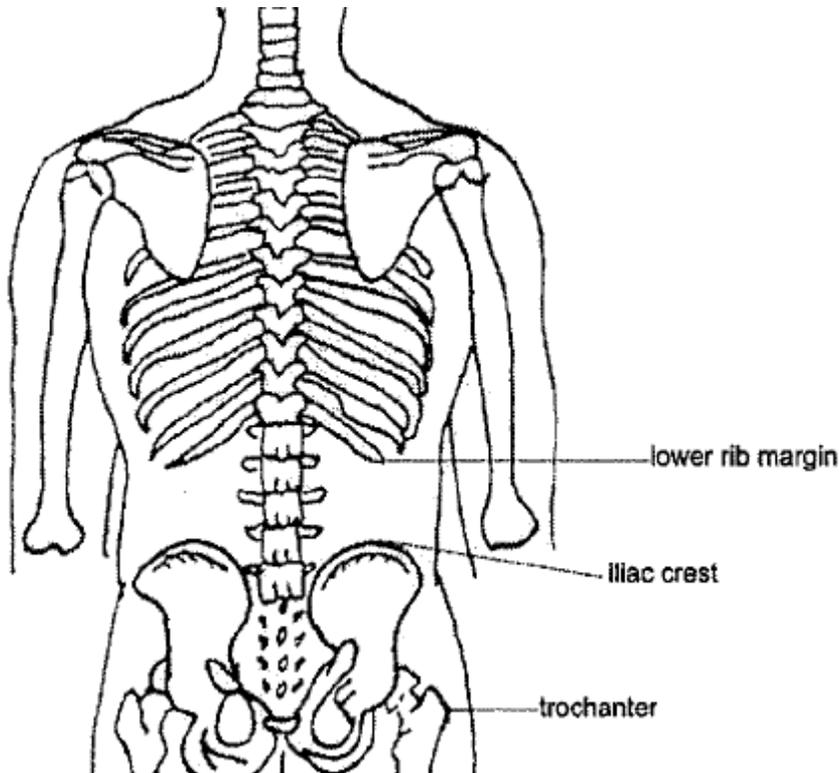
Waist Circumference Measurement

- The participant should stand in a straight, upright position with feet together.
- Ask the participant to relax and stand with arms at his/her side.

Natural Waist Measurement

- Find the natural waist (the narrowest part of the torso). This area is midway between the inferior border of the rib cage and the superior aspect of the iliac crest.
- Place the tape at the measuring point and locate the point on the tape where the zero aligns with the other end of the loop.
- Care should be taken to ensure that the tape measure remains horizontal, touches the entire circumference to be measured, and that tissue is not compressed.
- The measurement is taken at the end of normal expiration.
- Record the measurement to the nearest 0.5 cm.
- Repeat the steps described above and obtain a second measurement.
- Record the second measurement to the nearest 0.5 cm.

- If the two measurements differ by more than 1.0 cm, obtain a third measurement (or more if necessary) and use the two that are within 1.0 cm of each other.



Umbilical Point Waist Measurement

- An additional waist measurement will be obtained at the umbilical point.
- Locate the umbilical point on the participant.
- Place the tape at the measuring point and locate the point on the tape where the zero aligns with the other end of the loop.
- Care should be taken to ensure that the tape measure remains horizontal, touches the entire circumference to be measured, and that tissue is not compressed.
- The measurement is taken at the end of normal expiration.
- Record the measurement to the nearest 0.5 cm.
- Repeat the umbilical point measurement technique described above and obtain a second measurement.
- Record the second measurement to the nearest 0.5 cm.
- If the two measurements differ by more than 1.0 cm, obtain a third measurement (or more if necessary) and use the two that are within 1.0 cm of each other.

Quality Control Measures

The study tape measure should be calibrated weekly. Sites must have a pre-measured pole and need to verify that the pole length is reading accurately off of the Gulick tape measure. Record calibrations in a log book to be kept at the sites. This calibration log must be available for the monitor at his/her visits. Please see Appendix 11-C for a copy of the tape measure calibration log.

9.4 Metabolic Procedures

9.4.1 Resting Metabolic Rate using the Metabolic Cart

9.4.2 Core Temperature

Staff

Core Temperature Technician or Trained Inpatient Nurse

Test Conditions

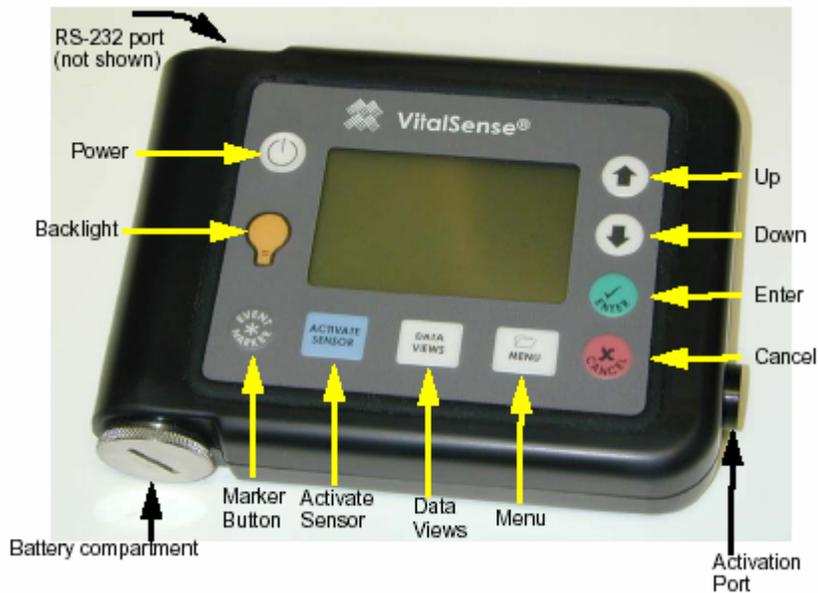
Core temperature will be measured and recorded every minute during the 24 hour period spent in the metabolic ward at Baseline, Months 6, 12, and 24 visits. At 6:00 p.m. the volunteers will swallow an 8.7 x 23-mm Jonah™ radio-capsule (Mini Mitter Co., Inc., Bend, OR) and will be fitted with a bandoleer type antenna system, connected to a portable monitor that records core temp. Minute by minute data will be submitted to the Coordinating Center, Average 24 hour, night (2:00 a.m. to 5:00 a.m.) and day (8:00 a.m. to 8:00 p.m.) temperatures will be computed from the submitted data.

Prohibited Procedures and Contraindications

- MRS procedures cannot be performed for 14 days following ingestion of the capsule.
- Core temperature cannot be performed in anyone whose body weight is less than 80 pounds.
- The sensor should not be given in the presence of any known or suspected obstructive disease of the gastrointestinal tract, including but not limited to diverticulitis and inflammatory bowel disease.
- The sensor should not be given if the participant who has had previous gastrointestinal surgery.
- The sensor should not be administered in any participant with hypermotility disorders of the gastrointestinal tract including but not limited to illus.

Preparation for the Measurement

Methods for configuring the Mini-Mitter Vital Sense core temperature device for data collection



1. **Verify Monitor Clock has been set.** If this is the first use of the device then follow the instructions below to set the monitor clock. Once you have set the clock, you should not have to reset it unless it is daylight savings time or the battery has died in the device since its last use. To avoid having to reset the clock each time, please change the battery when you hear the low battery alarm.

To set the clock, use the following instructions:

- a. From the main menu, use the arrow buttons to select *Adjust Time/Date* and press Enter.
- b. Use the arrows to navigate to the *hour*. (The selection will default to the hour when the Time/Date menu is selected.) Press Enter. Use the arrow buttons to increment and decrement the selection. Press Enter to input the selection.
- c. Use the arrows to navigate to the *minutes*. Press Enter. Use the arrow buttons to increment and decrement the selection. Press Enter to make your selection.
- d. Repeat this procedure to change the *seconds*.
- e. Use the procedure described above to change the *date*, beginning with the *year*.

2. **Erase any data memory** If you are unable to erase data memory, then the unit is malfunctioning and you should contact MiniMitter for further advice or send the device in for repair.

To erase data memory, use the following instructions:

- a. Prior to initiating a new session, the data memory should be erased.
- b. Use the arrow buttons to access *Erase Data Memory*.
- c. Use the arrow buttons to select OK. Memory erasure will take up to 30 seconds. The monitor front panel functions will be locked until the memory is clear.
- d. You will be prompted when the memory is clear.

3. **Turn on logging, set to degrees Celsius**

- a. If the logging is not turned on, the monitor will continue to communicate with the sensors but no information will be stored.
- b. Use the arrow buttons to select between ON and OFF.

- c. Select ON and press Enter.
 - d. Temperatures can be displayed in Celsius or Fahrenheit.
 - e. Use the arrow buttons to select Celsius and press Enter.
 - f. Confirm that you set the device to degrees Celsius
4. **Activate Sensor** If the sensor does not activate, choose another pill for activation. If it still does not work, send unit in for repair.
- a. DO NOT remove the Capsule Sensor from the package until it is to be activated.
 - b. Activate the Capsule Sensor prior to the participant swallowing the sensor. It cannot be activated once it has been swallowed.
 - c. First turn on the monitor. (Press the power button and hold for approximately ½ second.)
 - d. Press Activate Sensor.
 - e. Follow the directions on the display. Place the sensor lens against the Activation Port. Press Activate Sensor again.
 - f. During the activation prompts, DO NOT REMOVE THE SENSOR from the Activation Port.
 - g. You will be informed when the sensor has been successfully activated. Now remove the sensor from the Activation Port.

Confirm Activation of Sensor

Always confirm that the sensor is active prior to administering. Use the Data Views key to access and toggle among the various data views. Within one minute, you should see data begin to be displayed.

Core Temperature Measurement

Participant Placement of Core Temperature Device and Sensor

1. Provide participant with 8-ounces of room temperature water.
2. Following successful activation, have the participant swallow the Capsule Sensor with water.
3. Keep the Vital Sense Monitor within 1 meter of the participant's body at all times.
4. Affix a MRI warning wrist band to the subject with instruction that it is to be worn until the Capsule Sensor has been expelled.
5. Attach the bandoleer type antenna system and portable monitor to the participant.

Note: After ingestion, make sure the recorder unit reads a reasonable body temperature about 36-37 degrees C (it may be a little low at first due to water ingestion).

Note: For everyone, the 24-hr measurement will start at 8pm and end at 8pm the next evening. The data processing software should only look at temp measurements from 8pm (2 hours after ingestion) to 8pm the next evening. This gives time for the pill to enter the core of the body so that we get good core body readings. The initially low temp readings from water ingestion with the pill will not be seen in the data set since the actual data set would start at 8pm.

Note: A bad pill can be detected before it is swallowed. Make sure the pill reading is close to ambient temperature (about 22 degrees C) before it is ingested. If this is correct, your body temp readings will be correct. Otherwise, DO NOT ingest that pill and activate another pill.

Completing the Core Temperature Measurement

At 8:00 pm on the evening after ingestion of the pill, the test measurement will need to be completed. In order to complete testing, follow the steps described below:

1. Remove the antenna system and portable monitor from the participant 26 hours after the sensor was ingested.
2. Assess the participant for any adverse events that may have occurred during the 24 hour period, and then set up for data download.
3. Preview 24-hr data to determine any major sections of dropouts or unreasonable data points. If pill was passed, no further action (including taking a second pill) is taken. Submit the collected data per normal procedures.

Data Download, Storage of Equipment and Transfer of Data to CC

Data Download

1. Go to *Set-Up Monitor* on the main menu.
2. Access *Read* from the Main menu of the Vital Sense computer program. Click on *Read*.
3. You will be prompted to name the file where the data is to be saved and select a location. (this will need to be decided by the sites) This should be in a single agreed upon location on a regularly backed up network drive. There is an option to save the data as a Vital Sense Binary File (this is the default) or a text file (.txt). All files must be saved as a text file for this study and named by the following format:

CALXX-YYYY-ZZ.txt

Where

XX = site number

YYYY = participant number

ZZ = visit code as listed here.

00 = BASELINE2

06 = MONTH 6

12 = MONTH 12

24 = MONTH 24

These files will be processed electronically, so it is important to replicate this format exactly including dashes and no spaces. If there is a site specific need to capture any other information in the file name, this can be done after the visit code as long as the file extension remains .txt.

4. Name the file using the above convention, choose its location, and click on *Save*. You will be prompted on the progress of the data retrieval.
5. Once the data download is complete, a Data Collection Summary will appear. This is an index of the data collected. You now choose *Generate Report*.

6. This function will generate two types of files.
 - a. Choose the sensor that you want to appear in the report. Since the filename identifies the participant and timepoint, you should only select the sensor associated with that data.
 - b. Click on generate report.
 - c. Two output files will be generated. Both files will be named with the original Read Data filename.
 - d. A Microsoft Excel file with an .xls extension will be generated.
 - e. A plain text file with a .txt extension will also be generated.
7. Once the data is downloaded, verify that data is complete by viewing the spreadsheet. Then follow the steps described below to remove the sensor from the sensor list on the recorder unit.

Remove Sensor from List

This should be done immediately following verification of completed data.

1. Go to the Main Menu and select *Remove Sensor* from the *Sensor Option List*.
2. From the sensor schedule, use the arrow buttons to select the sensor that is to be removed and press *Enter*.
3. To cease tracking and remove the selected sensor, select OK and press *Enter*.
4. The selected sensor is now removed from the sensor schedule.

Turn off the monitoring unit

Store the monitor and capsules in a cool, dry place on site.

Data Transfer

Data Transfer of core temperature files should be completed according to the agreed upon schedule (Initially monthly). Before beginning the data transfer, all files should be downloaded and named in the correct format (see above for more information).

1. Group all the files to be sent to the CC in one location.
2. Put all the files together in a zip file and encrypt the data.
3. Transfer the file to Duke secure ftp site for your site.
4. Send an email to the data manager of the Galerie study at Duke indicating the number of files that were sent.
5. The data manager will reply when the file has been received and confirm the number of files received.
6. Once a file has been submitted to Duke, the data should not be resubmitted again unless requested. Files which have been submitted should be moved to an alternate directory so that they will not be confused with new data yet to be submitted.

Note: All site files will be saved on the Core Temperature computer to a secure and regularly backed up network drive.

Recordkeeping of the equipment

- All sites will keep a study log for the Core Temperature equipment. Please refer to Appendix XX for the sample log.
- Sensor numbers and the device serial number should be recorded for every participant.

Quality Control Procedures

The quality control for the device itself is built in. If a sensor is bad, the device will not activate the pill therefore you will not miss any readings due to a bad sensor. The technician will not be able to start a test without accurate recordings taking place.

The review of the report prior to downloading and saving will show if there were any missed readings. The site will note any missed readings or incomplete data and if this is not deemed due to the device or passing of the capsule, then the site should record who administered, monitored and completed the testing period. If the site notes that the same staff member is responsible for numerous mistakes, then the Study Manager will re-certify the technician on proper techniques. The CC will also note missed readings or incomplete test periods and if one site is having numerous mistakes or incomplete data, the CC will alert the site and request further training of site staff.

Troubleshooting

If any of the above procedures do not work or the device appears to be malfunctioning, you should contact your local Mini-Mitter Vital Sense representative for further instruction.

9.5 FOOD RECORDS

RATIONALE

To obtain optimally complete, plausible food intake records that will be used to derive reported energy and nutrient intakes and food patterns for all (control and CR) CALERIE participants. The food record will provide a six-day average of the nutrient content of all foods and beverages reported by the participants.

FOOD RECORD COLLECTION

A six-day food record will be collected at various time points in the study. Participants will receive instructions for the food record during Day 0 of the designated doubly labeled water (DLW) visits and be instructed to collect the food record during days 1-6 of DLW (which will almost always include 2 weekend days and 4 weekdays). During the DLW day-7 visit, the food record will be reviewed by the interviewer (preferable a nutritionist) for completeness and accuracy (see below).

Standardized interviewing and probing techniques will be used to elicit details of intake. Careful training of the staff who educates the participants on documentation of their food intakes will foster accurate recording.

MATERIALS

- Food Record Instructions
- Food record book
- Measuring cups and spoons

ROLES AND RESPONSIBILITIES

Staff at the CALERIE sites with specific responsibility for overseeing and conducting the 6-day food record include Interviewer, a Research Assistant, the Study Coordinator, and the Study Manager. These individuals have the following roles and responsibilities.

Interviewer

- Retrieves a blank copy of the 6-day food records and prepares it for the participant.
- Provides instructions to the participant on how to complete it.
- Ensure that the participant starts recording on Day 1 of the DLW study.
- Motivates the participant to provide complete and accurate information and explains the importance of the study.
- Reviews the 6-day food record with the participant on Day 7 of the DLW measurement, reviewing it for completeness and accuracy, and probing for all food consumed.
- Makes any notations of details in red on the record.
- Determine for each day whether the food record was missing, unreliable or reliable.
- Substitutes a replacement day for each day considered to missing or unreliable.
- Arranges to review the replacement day or days with the participant on Day 14 of the DLW measurement.

- Makes notations of details in red on the record.
- Reviews the record a second time to ensure it is accurate and legible.
- Gives the record to the research assistant.

Research Assistant

- Completes the CRF form for each 6-day food record using information provided by the Interviewer.
- Completes and updates the Food Record Log Sheet for each food record.
- Prepares the shipping manifest.
- Checks and verifies information entered in the shipping manifest.
- Initials and dates the shipping manifest.
- Ships the records to CCNRA.

Study Coordinator

- Informs the Interviewer of upcoming 6-day food record for the CALERIE participants.

Study Manager

- Checks and verifies information recorded on the CRF before it is sent to the CC.
- Assures that proper procedures are followed.

TRAINING OF INTERVIEWERS

Interviewers (preferably nutritionists) who will be responsible for food record instruction and debriefing will complete training and certification by the Nutrition Reading Center or by an interviewer who has been trained by the Nutrition Reading Center prior to contact with the participants. The training sessions will consist of information dissemination, role playing with evaluation, discussions, and training exercises.

Certification

The interviewers will be asked to complete certification exercises. First, they will be asked to complete calculation exercises. Secondly, they will be asked to complete exercises related to debriefing. Finally, the interviewer will be asked to retrieve three three-day diet records. These will be checked by the trainer and feedback given. The Reading Center and the Coordinating Center will keep records of the certifications.

Recertification

To maintain certification status for nutrition data collection, the interviewer must debrief at least six study participants in a six-month period. The interviewer must also complete any additional exercises deemed necessary by the trainer. If the interviewer does not debrief records for 1 year, the interviewer must attend a training session and debrief two three-day records and the calculation and debriefing exercises must be completed.

ROLE OF INTERVIEWERS AT SITES

The task of the dietary interviewer will be:

1. To conduct food interviews in person with study participants.
2. To provide instructions for study participants to complete food records.

3. To maintain supplies needed for debriefing.
4. To adhere to all procedures outlined during training.
5. To perform other duties as needed.

A major objective of a study using diet records is to maintain reproducibility by the use of quality controls. The accuracy and reliability of the data is aided by standardized interviewing and probing techniques by each interviewer, by careful training of the interviewers, and by periodic monitoring and retraining.

The interviewer is involved in a very important act of communication. The interviewer must make sure that the questions asked are clear and unbiased, that the participants understand the questions and give answers that are relevant and complete and that those answers are accurately and fully recorded in the record. Only if the interviewers working on the study have learned to ask the questions in the same way and make sure that the answers are correctly recorded in the same way, can the information gathered in the interviews be combined to give a true picture of the nutritional intakes of the participants.

Throughout your contacts with study participants, it is important that you maintain your professionalism, create an environment in which the participant feels comfortable to respond freely, and establish rapport with the participant. By accomplishing these goals, you will be more successful as an interviewer. All members of a research team must strive to maintain and project a sense of professional integrity and honesty to all participants and to others that they may interact with.

Maintaining Confidentiality

In order for the interviewer to obtain valid and meaningful answers from the participants, the participants must be made to feel that they can speak freely to the interviewer. To achieve this, each interviewer promises that only members of the research staff will see the record that the participant provides and that this information will not be revealed to others. Each person working on a study must be continuously aware of the responsibility to safeguard the rights of all the individuals participating in the study. As an interviewer, you are in a position to hear confidential information from the study participants. Your protection of this information is essential. This means that you must protect not only the information you get in direct answer to the questions you ask in the interview, but also the information that you gather through casual conversation before or during the interview.

Never divulge names or other information about the participant except to the research team. Refrain from any discussions about study participants, which might be overheard by people not on the study staff or that is not relevant to the purpose of the study. All the members of the research team are under the same legal, moral and ethical obligations to protect the privacy of the participants in the study.

In order to help maintain privacy, code numbers will be used to identify participants whenever possible.

Establishing and Maintaining Rapport

When you first make contact with a participant, your initial task is to establish rapport. Your tone of voice, introductory remarks, and the way you answer questions will strongly influence the rapport that develops between you and the participant. What you say and how you say it should set the tone for the friendly, cooperative, but businesslike relationship that will continue to develop throughout the interview. The impressions formed in the first few minutes usually become the basis of the rapport the interviewer develops with the participant, and may influence how cooperative the participant will be during the interview.

Making a professional impression depends on several things: your appearance, your voice, and your body language. Cleanliness and neatness are very important. A cheerful, but natural and professional sounding voice is what you want to strive for. Through your posture and facial expressions you can communicate interest in the participant and the interview. By sitting up straight, leaning towards the participant, making eye contact and smiling you are expressing interest to the participant.

Being professional requires that you are confident about your job as an interviewer. Be sure that you are familiar with all interview materials and techniques before you work with clients. It is essential that you communicate the importance of the study and the importance of the participation of the participant. Your conviction of the importance of the study will influence the participant's willingness to cooperate.

An interviewer can give positive reinforcement to the participant to help maintain rapport. If their attention is diverted, it is important to bring them back to task with reminders of the importance of accurate answers. Letting them know how much longer the interview will last may help. If they are very talkative, it may be necessary to remind them that there are time constraints, but this must be done tactfully.

An interviewer should never correct or be critical of spelling or grammar, or of the lack of understanding of the task on the part of the participant.

Probing Techniques

The quality of the dietary interview depends a great deal on the interviewer's ability to probe meaningfully and successfully. Probing is the technique used by the interviewer to obtain more information. Probing is necessary when food descriptions and preparations are incomplete, when verifying amounts actually consumed, and when verifying times in which no foods are reported. To know when to probe, it is important to review each food reported in the food record and to pay particular attention to the flow or "sense" of the intake day. Probing for complete information takes time and care, but if the information is not complete, the foods will not be able to be coded properly. The interviewing tools should be used during this probing.

The interviewer must also probe for forgotten foods and for added foods. Added foods are things such as condiments that may or may not provide nutritional value. If there are no additions to the foods this should be documented correctly. That is, no additions in preparation or no additions at the table, or both. This allows the coder to understand that the information was probed and not just missed. It often helps to have a participant recall what they did that day to see if this triggers a memory about foods consumed. For example, if they went to the movies, they may have bought food to eat during the movie.

If you are probing to account for a gap in a day's reporting, be careful to avoid probes that contain assumptions about normal meal patterns. Never assume that the first thing a respondent eats in a day is breakfast. Instead, relate the probes to a period of time or an activity. You might say "I notice you had cereal at 8 am and then soup at 5 pm. Did you have anything to eat or drink between these times?" Or you might say "I notice you said you saw a movie in the evening. Did you have any food or drinks while you were at the movie?"

Probes should be formulated in such a way that the respondent can freely choose an answer. The interviewer should not imply that a certain response is preferred or expected. For example, rather than asking "So you added sugar?" it would be better to ask "Did you add anything to the cornflakes or did you eat them plain?" This gives the participant the opportunity to choose from all possibilities. The best approach to formulating a neutral probe is to begin with a general question, such as "What flavor was it?" If you do not receive an adequate response, then a more specific probe can be used, such as "Was it vanilla, chocolate, or some other flavor?" By ending the probe with "or some other flavor" you have not limited the possibilities. In other words, the neutral probe suggests a range of possible responses rather than a specific answer. Some examples follow.

Non-Neutral Probes

What did you eat for breakfast?
Did you eat popcorn at the movies?
Were your eggs fried?
Did you have dessert at lunch?

Did you put milk on your cereal?

Did you put mayonnaise on your sandwich?

Neutral Probes

What was the first thing you ate when you got up?
Did you eat or drink anything at the movies?
How were your eggs prepared?
Was there anything else you ate or drank after you ate your sandwich?

Did you have anything else with your cereal?

Did you add anything to your sandwich or did you eat it plain?

Sometimes a participant responds "I don't know". This may mean that they did not understand the question. It may also mean that the respondent needs time to think about a response. Try to ascertain what the respondent is saying and attempt to get a more specific response without antagonizing the respondent. If you are unable to get the information, make a note to that effect.

Conducting the Interview

The interview should be conducted in a private area. The participant should be seated next to the interviewer so that both can clearly see the diet record that is being reviewed and measuring aids such as rulers, thickness bars, measuring utensils, and 2-dimensional models should be available throughout the interview to use if needed. The interview will take approximately 45-60 minutes to complete. The interview should contain the following components:

1. The interviewer should introduce herself/himself.
2. The interviewer should state the purpose of the interview and the importance of the participant's participation as well as to assure them that the information they are providing is confidential.
3. The period of the food record assignment should be reviewed. The six-day period begins with the time the participant gets up on the first day and ends when they go to bed on the sixth day. All foods, drinks, and supplements consumed should be written in the record. The interviewer should check to be sure that the food record is within the study window.
4. The interviewer should be prepared to answer any questions that the participant may have about the study or the interview.

PARTICIPANT PREPARATION/TRAINING ON THE FOOD RECORD

The interviewer will provide the participant with necessary education, training and tools necessary for completion of the food record. The interviewer will meet with the participant in person during their DLW visit (Day 0) to give detailed instructions on the completion of the food record.

The following information and materials will be provided to the participant:

- Food record book with specific instructions
- Two-dimensional food measures (measures for wedges, circles, squares & rectangles, ruler)
- Measuring cups (set of 4)
- Measuring spoons (set of 4)
- The dates the food record should be completed

Food Record Instruction

Introduction

- Greet the participant with enthusiasm and warmth.
- Discuss and review the importance of the food record.

Food Record Instructions for the Participants

- Remind the participant that the most important thing to remember about keeping a record for six days is to write down everything that they eat and drink and emphasize the importance of writing down all foods and beverages immediately after consuming them. Explain to the participant the importance of eating as they normally would during the food record period to help us get an accurate estimate of what they usually consume.
- Review the food record book with the participant. Point out the location of the food record instruction pages, measurement page, supplement page, recipe/food label space and food record pages and review all instructions and examples provided in the food record book. The food record book with instructions can be seen in Appendix .

- Provide the participant with the 2-dimensional model handout (Appendix) which provides circles, squares and rectangles, and wedges for the participant to use to help provide more accurate portion estimates.

Closing

- Make sure the participant has a food record book and a 2-dimensional shape handout.
- Review the six-day food record assignment.
- Reschedule days if necessary.
- Ask the participant to call the office if they are unable to complete the assignment as assigned.
- Remind participant to bring the food record and any food labels to the next appointment.
- Thank the participant for their help.

FOOD RECORD BOOK

A food record book will be provided to the participant at each measurement time point. A copy of the food record can be found in Appendix . The food record book will collect information on the following variables:

- Date/Day of week
- Time point (BL1, BL2, M6, M12, M18, M24)
- Time of intake
- Meal code
- Food & Beverage description
- Amount
- Where food was prepared (Place codes)
- Recipes
- Food labels
- Supplements

Meal Codes

The food record will contain a column to collect information on the meal, defined by the participant. The following code abbreviations will be given to the participant:

- B – Breakfast
- L – Lunch
- D – Dinner
- Sn – Snack
- Bv - Beverage (separate from a meal or snack)
- O - Other

Place Codes

Participant's Home (H)

Any food/drink from a grocery store or market that is brought home for consumption. Include food from a grocery store or market that is brought to a

- dormitory for consumption. Also include any food/drink prepared or brought from home regardless of where it is consumed.
2. Friend's Home (F) Any food/drink from someone else's home, whether store bought or homemade. This includes pot luck or covered dish meals.
 3. Work (W) Any food/drink that is obtained from a participant's work place.
 4. Restaurant (R) Any food or drink from a restaurant, including fast food restaurants. This includes food eaten in, carried out, or delivered. The name of the restaurant should also be recorded.
 5. Other (O) Food/drink that does not fit into the other categories

Supplements

The participant will be instructed to record any intake of supplements during the food record time point. This will serve as both a check to see if they are taking the study-assigned supplements (multivitamin with minerals and 500 mg of elemental calcium in the form of calcium citrate) as well as to check to if the participant is taking any further nutritional supplements that may not be part of the study protocol. If the participant indicates that a supplement was taken on a particular day, be sure that the following information is documented:

- Brand name if known
- Kind (multivitamin with or without minerals, vitamin C, Vitamin E, Iron, Calcium, etc.)
- Type (regular, chewable, children's, high potency, stress tab, prenatal, etc.)
- Dosage (mg., mcg., IU, etc.) and number of tablets or capsules taken each time.
- Time and place they were consumed.
- Other foods and beverages consumed with them.

If the participant has not recorded the dosage or other pertinent information, ask if the participant still has the supplement container at home. If so, ask if it would be okay to call to get the information and ascertain the most convenient time to call.

The study-assigned supplements (multivitamin with minerals and 500 mg elemental calcium from calcium citrate) the participant recorded will not be entered into the Nutrition Data System for Research (NDS-R) by the Reading center. Other recorded dietary supplements that contain minimal calories will not be entered into NDS-R. Meal replacements and other calorie-containing nutrition products will be entered into NDS-R. These items will be reviewed by the interviewer and decided on a case-by-case basis if they should be entered into NDS-R and notation will be made on the supplement page if any recorded supplements should be entered into NDS-R by the Reading Center.

FOOD RECORD COLLECTION AND REVIEW

General Instructions for debriefing

Each food intake day should be reviewed for complete descriptive details and amounts consumed. The following information is confirmed and documented:

1. Day of the week and date.
2. If supplements were taken. If so, then the brand, type, dosage, time consumed, place, and any foods and beverages consumed with it are probed and documented.
3. Time food was eaten. The time recorded is the time the participant began the eating occurrence. If the participant has written down the time she ate each food during the same meal or snack or has specified when the occurrence ended, the extra times are deleted.
4. Place where the food was prepared. We are interested in where the food was prepared not where it was eaten. If the food was from a restaurant, the interviewer should probe the name and type of restaurant. It is possible that there can be more than one place code per eating occurrence. When this occurs, the retriever should draw an arrow in the place column to indicate which foods were prepared in each location.
5. Whether the food is a meal or snack. There should be only one time recorded for each meal or snack.
6. Complete description of each food. This should include brand names, cooking methods, fats and other items added to the food either in cooking or at the table.
7. The amount actually consumed in acceptable units.
8. A response to the question as to whether the amount of food consumed is typical or if the participant was ill. The interviewer will record if the participant stated that food record day was usual (U), more than usual (MU) or less than usual (LU).

Obtaining descriptive details

The interviewer should refer to the interviewer checklist (Appendix), if needed, when probing for food description details. The interviewer checklist which is a food-specific list of appropriate probes and defaults, will be provided to the sites by the Reading Center and will be used as a reference as needed by an interviewer. The interviewer should be prepared to write, preferably with a colored pen, so that it is clear what notations were made by the interviewer and which the respondent made. Only acceptable abbreviations (Appendix) should be used. If necessary, ask the respondent to slow down so that appropriate notes can be made.

The following example describes the probing method:

Participant Records	Interviewer probes	Participant replies	Interviewer probes	Participant replies
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Cereal	What kind?	Cornflakes	Brand?	Kellogg's
Milk	Percent fat?	2%	Flavor?	White
Sugar	What kind?	White		
Toast	What kind?	White	Commercial, Homemade, Bakery?	Wonder
	Additions?	Butter	Regular or diet?	Regular
			Butter or margarine?	Margarine
			Stick, tub, squeeze?	Tub
			Brand?	Fleischmann's
		Regular or diet?	Regular	

It is important to probe for all additions to items on the dietary record. An example of the details needed follows, using fats as the item.

1. In appropriate foods, always probe if fat was added in preparation or at the table.
2. Probe for the type of fat.
3. Do not write "no added fat" or "no additions". Do specify "no fat in preparation (NFP) and / or "no fat added at the table (NFT).
4. If the participant does not know if fat was added, document "unknown if fat in preparation" and/or "unknown if fat added at the table".
5. If the participant does not know what type of fat was added, state "unknown type of fat added in preparation" and/or "unknown type of fat added at the table"
6. If the participant knows the type of fat, but not the brand or variety, document this information. (e.g. unknown type of shortening, unknown type of margarine, etc.)
7. If the participant is able to give detailed information, probe for the following:
 - A. Meat fat-typically, meat or meat bones used to season vegetables. Probe for the type of meat, e.g., ham, bacon, fatback, etc. If the meat is eaten, attempt to quantify.
 - B. Solid shortening-probe for brand and variety (regular or butter flavor).
 - C. Oil-Probe for brand and type
 - D. Mayonnaise-Probe brand name, if real or mayonnaise type, if regular, low fat, fat free, or cholesterol free.
 - E. Salad dressings-Probe type (scratch, bottled, or mix). Probe brand and type (regular, light, non-fat). If homemade, probe for ingredients, especially the fat.
 - F. Butter-Always confirm that it is real butter. Probe for regular stick vs. tub (whipped). If the participant has written butter and is unsure if it was real butter, put quotation marks around the word butter.
 - G. Margarine-Probe for brand, form (stick, tub, squeeze) and type (regular, whipped, diet, spread, light, extra light, fat free, etc.). A label book with pictures might help in identifying brand names.

Probing for Preparation

Depending on the food that is consumed, a variety of probes may be necessary to describe the preparation of the item:

- **Cooking Preparations:** Was the food fried, grilled, broiled, boiled, baked, microwaved, steamed, stewed, roasted, etc. If a participant says that a food was barbequed, be sure to find out if they mean grilled or if they mean that barbeque sauce was added, or both. If the food is a leftover, find out how it was prepared both times.
- **Special Preparations:** Probe to determine if meat was trimmed, untrimmed, or partially trimmed. For poultry, find out if it was prepared with the skin or if skin was removed. If the skin was removed, was it before or after preparation. Determine if there was a breading or coating of any kind on the food.
- **Homemade:** Homemade and scratch do not mean the same thing. Often a participant will say that a food is homemade when they mean that it was made from a mix, or it was microwaved at home. If it is a mix, probe for ingredients added to the mix. If it is a commercial product, try to get the brand name. If it is a scratch recipe try to get as much information as possible about variable ingredients such as fat, milk, etc. Remember that things such as biscuits or cookies may come from a bakery or may be made from refrigerated dough. Commercial products may be changed such as adding meat to a commercial spaghetti sauce.
- **Form of the Food:** When a volume measure is reported, it may be necessary to probe for the form of the food, such as solid, cut pieces, chopped, melted, etc. You will need to determine how to probe for the form of the food based on the food and what other foods it was eaten with. For example, cheese on nacho chips- was it cubed, sliced, grated, or melted cheese. Volume measures are marked as Fluid Ounces or FO and weight measures are in Ounces (oz) or grams (gm).

Quantifying Amounts

The interviewer confirms all quantities reported.

The following is an example of probing for amounts:

Participant Records	Interviewer Probes/Verifies	Participant Replies
Cornflakes-1 cup	Is this the amount you ate? (points to the 1 cup measure)	Yes
Milk- ½ cup	Is this the amount you added To the cereal? (points to ½ Cup measure) Did you finish all the cereal And the milk?	Yes No, half of the milk Was left in the bowl.
Toast-2 slices	Did you eat all of it?	Yes
Margarine-missing amount	How much margarine did You add to the toast?	2 teaspoons

There are internal edit limits set for each food in the NDS-R. These limits can be found on the Interviewer Checklist. Anytime a food quantity is recorded in the food record in an amount equal to or greater than the edit limit, the interviewer should verify the amount with an explanation as to how it was verified. (i.e., I used cups). Remember that is important to also confirm unusually small amounts, such as a pork chop that is only 1/16th of an inch thick. Remember that it is very difficult to visualize portion sizes.

Always be sure that you record the amount that was actually consumed and not what was served. If a person eats multiple servings of a food, be sure to label the measurement as each or total. Also, be sure that both servings are the same size. An example is pizza- a person ate 2 slices. If the participant says that it was 4 inches long and 2 inches wide, ask if this is the size of each slice or the total amount. If this is for each slice, confirm that both slices were the same size and ask if they were wedges or rectangles. Then write 2 wedges 4 inches long and 2 inches wide each.

The following guidelines can be used when verifying amounts:

1. The interviewer must confirm all quantities. Food models are to be used when needed. Do not assume that the participant has measured the food item, even if a quantity is given. When a participant states a cup, they may mean a drinking cup as opposed to a measured cup.
2. Confirm that the portion stated in the food record was the portion consumed and not the portion served.
3. When confirming quantities, never give the participant the impression that you do not believe them. Word your questions in such a way that either allows them to confirm what was written or allows them to visualize what was consumed. It is extremely difficult for anyone to visualize the quantity consumed. Stress that you understand how difficult it is and tell the participant that you are just trying to make sure that you understand what was written. If necessary, write a note on the record to let the coder know that the amount was probed and confirmed.
4. Use the food models in any way that may help the participant to visualize portions. For example, if ice cream or mashed potatoes were eaten, it might be easier to visualize if the measuring cups are turned upside down so that they look more like the item consumed.
5. When food quantity is given using dimensions, give the shape of the item. It might seem obvious to you, but write it down anyway. For instance, pizza might be a wedge or it might be a rectangle.
6. Clearly state whether the dimensions given are the dimensions of **each** serving or slice or for the **total** amount consumed.
7. In order to enter the foods into the computer, the following dimensions are needed for each of the following shapes:

Three dimensional items:

Cube- length x width x height

Triangle-length x width x height

Sphere-diameter

Cone-diameter at greatest point and length

Cylinder-diameter and height or thickness

In some cases a two dimensional description is acceptable (in foods with a fairly standard thickness such as a brownie). It is believed that the standard thickness would provide a better description than the participant could give and therefore NDS-R may only ask for two dimensions. However, it is best to train the participant to give their best estimate of height, width and length so the dimensions are available if needed for entry.

For the following foods, a thickness or height is not required:

- Circle-tomato slice, cookie (if standard cookie), onion slice. Diameter needed.
- Wedge-pizza (indicate whether thick or thin crust). Length and width needed.
- Rectangle-pizza. Length and width needed.
- Cylinder-regular size hot dog or hot dog bun, baked potato, banana, croissant. Length needed. Potatoes can be described either by diameter and length or by diameter alone if spherical.
- If a participant consumes a commercial product that comes in a standard size, it is not necessary to probe the dimensions. For example-a saltine cracker- just probe for the number eaten. These can be entered in the computer as each.

8. Liquid- Confirm if the quantity given included ice in the measurement. Confirm that the quantity was the quantity consumed and not the quantity served.
9. It is very important for the interviewer to be able to visualize the quantity given. If you do not clearly understand what the participant meant or if the description does not sound logical, have the participant draw a picture or probe for further information.
10. Be aware that some participants give the quantities consumed by the entire family. This is especially common with recipes or in describing the amount of fat added to or used for frying foods.
11. Unless otherwise stated, it will be assumed that the meat quantities described will be for the edible portion of the cooked meat, fish or poultry, unless it is a quantity from a restaurant. If the participant has given the raw weight or description or given the size with the bone, please write that information next to the quantity. If the participant is having a difficult time describing a meat quantity, a comparison could be made to a McDonald's Quarter Pounder which has approximately 3 ounces of cooked meat while the regular hamburger has a little over 1 ounce of cooked meat.

12. If the participant consumes food from a national fast food restaurant that is known to be in the database, it is not necessary to get individual quantities of each component of the food. For these food items, confirm if the food was ordered as it is normally served, or if anything was taken off or added to it. We must know the size of the serving, that is small, medium, etc., and how many servings were actually consumed.

After reconfirming an unusually large or small quantity, put a check in the verification box and write a short explanation of how it was verified. For example-used a measuring cup or spoon. Be sure to indicate each or total when required.

Use of Food Measurement Models

The food models can help the participant with the very difficult task of estimating portions. Each study site will have food models available to the participant during the interview and encourage them to use them. Here are some helpful hints:

- Measuring cups and spoons- the participant should describe the amount in level cups or spoons. If they are describing heaping cups or spoons, ask them to equate that to level measures. Sometimes it is helpful to turn a measuring cup upside down to make it look like a serving of mashed potatoes or other food.
- Glasses and bowls-If a participant points to a glass or bowl do not assume that it was filled. Ask the respondent to point to the correct measuring line. If a bowl is heaping, again ask the participant to quantify in level measurements.
- Ruler and thickness bars- Either of these can be used for thickness or height.
- Shapes - these are helpful when the participant is having trouble describing the dimensions with just the ruler. These are two-dimensional, so remember to find out the thickness where necessary.

Reliability and Incomplete Food Records

After the food record has been debriefed, the interviewer must make a judgment regarding the reliability of each day of the information gathered. The interviewer will record if the participant stated that food record day was usual (U), more than usual (MU) or less than usual (LU). However, for each food record day, the interviewer must also record whether the food record day was reliable (R), unreliable (UR) or missing (M).

- A food record day will be considered **reliable** if it is felt that the foods reported by the participant are accurate and true and if the food record data (including food description, amounts, and time of consumption) are coherent and complete for most food items consumed.
- A food record day will be considered **unreliable** for the following reasons:
 - The interviewer feels the food record day is incomplete or inaccurate. For example, the participant has not completed the food record for the full day, cannot recall whole meals or snacks, or has given unusable or incomplete information on other aspects of the food record such as amounts, food details, or times of consumption then the food record.
 - If the participant states that the food record day was highly unusual due to illness or occasion and the interviewer agrees that the day recorded appears to be

highly unusual based on input from the participant as well as other days recorded.

- If the participant has given inaccurate or extreme amount values for one or more food items, which leads the interviewer to suspect the reliability of other portion estimates.
- The participant acknowledges or is seen filling in the food record after the fact.
- A food record day will be considered **missing** if the record for that day is missed, skipped or lost for that assigned day.

Repeating Food Records

The need to repeat any or all of the food record will be judged on a day to day basis. The participant will be asked to replace a food record day if the food record day is missing or unreliable. The best effort will be made to collect a replacement food record day with the same day of the week as initially assigned (a Tuesday for a Tuesday, etc.). If this is not possible due to scheduling, then the best effort will be made to replace a weekend day with another weekend day and a weekday for another weekday. If repeat days are necessary, then these will be assigned to be completed during Days 8-13 of the ongoing DLW measurement. The interviewer should make arrangements for debriefing the repeat food record days in person during the day 14 DLW visit.

If the participant refuses to complete another day, the days that have been completed will be used.

Record Editing

After the record has been reviewed with the participant, the interviewer should go back over each day of the food record to fill in any missing information while it is still fresh in the mind of the interviewer. This may include clarifying a description, a time, an amount, etc. Any extraneous information should be crossed out and contradictory information should be clarified.

When the food records have been returned to the study site, they are checked for completeness of information and legibility. The records should be checked as soon as possible after retrieval so that the interviewer will still have the interview fresh in her mind. Sick days or unreliable days should be clearly marked. All times should be recorded, including am and pm. Writing should be legible with only approved abbreviations being used. If information is missing, the participant can be contacted to get the information. Do not guess at what the participant meant. When referring to a previous item do not write "see above". Instead, rewrite the pertinent information. The record should then be sent to CCNRA for coding.

DATA TRACKING AT STUDY SITES AND DATA TRANSFER FROM SITES

Once the interviewer has checked the food record for completeness and legibility, the food record will be given to a designated research assistant at that site. The research assistant will copy the food record, complete the Case Report Form, complete the Food

Record Log Sheet, and complete the Shipping Manifest before sending the food records by Fed Ex to the Reading Center. These steps are described below.

Case Report Form

A case report form (CRF) will be completed by a designated research assistant and used to collect information on the food record assignments and completeness. The CRF (Appendix) will contain information the following data:

- Center Number, Participant Number, Participant's Initials
- Whether or not the assigned food record was completed and coded reason if not completed
- Protocol time point (BL1, BL2, M6, M12, M18, M24)
- Date and corresponding DLW day of food record collected, reliability, and repeat days if necessary

Food Record Log Sheet

Each site will designate a research assistant to keep a Food Record Log Sheet (Appendix). The Food Record Log Sheet will be completed each time the interviewer gives the research assistant a completed food record and each time a food record is sent to the Reading Center. The Food Record Log Sheet will be kept at each site and will keep a log of the following information:

- ID of the participant
- Participant's initials
- Protocol time point (BL1, BL2, M6, M12, M18, M24)
- Dates of collected food record
- Dates of replacement days
- Interviewer's initials
- Date sent to CCNRA
- Initials of person sending
- Other comments

Shipping manifest and data transfer from sites to Reading Center

A designated research assistant will prepare a shipping manifest (Appendix) to send to the Reading Center. The shipping manifest will be sent along with the food records to the Reading Center.

The shipping manifest will contain the following information:

- ID of participant
- Date of birth as a secondary identifier
- Total number of food record days sent
- Dates collected
- Interviewer's initials
- Dates of unreliable days

- Date sent to CCNRA
- Initials of person sending
- Comments

The food records will be sent by Fed Ex from the sites to the CCNRA within 2 weeks of the time that data was collected and verified. A copy of the food record and all food labels and recipes will be made and kept at the site where it was collected. The original record will be sent to:

CCNRA
c/o Marcia Schmidt MS, RD, LD
2800 Winslow Room 4222
Cincinnati, OH 45206

9.6 Body Composition

9.6.1 DXA Quality Assurance Manual of Procedures for DXA Operator

CALERIE Study

**DXA Quality Assurance Manual of Procedures
for
DXA Operators**

**Hologic QDR 4500-A, Delphi-W and Discovery
Bone Densitometers
Operating with Windows Based Software**

**UCSF DXA Quality Assurance Center
Department of Epidemiology and Biostatistics**

**Version 1.1
November 30, 2006**

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Table of Contents

1.0 Introduction	52
2.0 Study Logistics	53
2.1 Division of Quality Assurance Responsibilities	53
2.1.1 Clinical Center Responsibilities	53
2.1.2 DXA Quality Assurance Center Responsibilities	54
2.2 Training and Certification of CALERIE DXA Operators	55
2.2.1 On-Site Training of DXA Operators at Start-Up	56
2.2.2 On-Site Visits During Follow-Up	56
2.3 Precision Assessment of Chief Operator	56
2.4 Review of DXA Scans	57
2.4.1 Flagged Scans	57
3.0 DXA Scan Acquisition	58
3.0.1 Participant Preparation for Scan	58
3.1 Participant Data	58
3.1.1 Patient Biography	58
3.2 Spine Scans	61
3.2.1 Spine Acquisition	61
3.2.2 Spine Follow-up Scans	61
3.3 Hip Scans	62
3.3.1 Hip Acquisition	62
3.3.2 Hip Follow-up Scans	62
3.4 Forearm Scans	63
3.4.1 Forearm Acquisition	63
3.4.2 Forearm Follow up Scans	64
3.5 Whole Body Scans	64
3.5.1 Whole Body Acquisition	64
3.5.2 Whole Body Follow-up Scans	65
4.0 Scanner Quality Control	65
4.1 Cross-Calibration of Scanners	65
4.2 Phantom Scans	66
4.2.1 QC Spine Phantom Scans	66
4.2.2 Whole Body Phantom Scans	66
4.2.3 Whole Body Air Scan - Windows Based Software	67
4.3 Machine, Software, and Service Problems	67
4.4 Hardware/Software Change Control	68
5.0 Data Management	68
5.1 Hard Copies of Scans	68
5.2 Electronic Scan Archive	68
5.3 Transfer of Data to the DXA Quality Assurance Center	68
5.4 Return Materials Sent by the DXA Quality Assurance Center	69
APPENDIX A. Study Forms sent to DXA QA Center	70
APPENDIX B. Study Forms sent out by DXA QA Center	70

1.0 Introduction

The purpose of this manual is to describe the DXA bone mineral density (BMD) and body composition quality assurance program for the clinical centers participating in the CALERIE study. It provides information specific to the Hologic QDR 4500, Delphi-W and Discovery scanners and is intended as a supplement to the appropriate Hologic user's guide.

To use this manual effectively, it is essential to have read and understood the entire Hologic QDR user's guide for your scanner. The study densitometry operators are required to have participated in a Hologic QDR training session and should be familiar with all instrument features and procedures discussed in the appropriate Hologic user's guide.

During the study, any questions regarding procedures that arise should be directed to:

Russell Scott
UCSF DXA Quality Assurance Center
185 Berry Street, Lobby 4
5th floor, Suite 5700
San Francisco, CA 94107-1762
Email: rscott@psg.ucsf.edu

Telephone: 415-514-8096 Fax: 415-514-8150

If Russell Scott is not available, please contact:

Cyndy Hayashi
UCSF DXA QA Manager
Email: Cynthia.Hayashi@ucsfmedctr.org
Telephone: 415-514-8091

IMPORTANT: Unauthorized changes in scanner model, software or personnel can have a large impact on the integrity of study data. If, for any reason, changes in any of these areas are anticipated, please contact the DXA Quality Assurance Center in San Francisco before any changes occur for further instructions.

2.0 Study Logistics

Table 1 summarizes the bone density scan acquisition schedule. Hip, spine, whole body and forearm scans will be obtained at three clinical visits on all participants: Baseline, 12 month, and 24 month. All participants will have an additional whole body scan at baseline + 28 days.

Note: The calorie restriction (CR) group will have the following additional whole body scans: Month 6, Month 6 + 14 days and Month 18.

Table 1. Scan Acquisition

BMD Scan	Bsl	Bsl+28 days	Month 6	Month 6 + 14 days	Month 12	Month 18	Month 24
Hip	X				X		X
Spine	X				X		X
Forearm	X				X		X
Whole Body	X	X	X (CR)	X (CR)	X	X (CR)	X

Table 2. Site Information at Baseline

SITE	SCANNER TYPE	SOFTWARE VERSION
PBRC	4500 A	11.2
Washington U.	Delphi W	12.4
Tufts	Discovery A	12.3.3

2.1 Division of Quality Assurance Responsibilities

2.1.1 Clinical Center Responsibilities

The clinical centers must ensure the overall quality and completeness of the DXA data and that all protocols and procedures are strictly followed. Specific responsibilities include the following:

1. Require that operators are properly trained and certified. If there are state requirements for DXA operators, these must be met;

2. Identify a chief densitometry operator to train and supervise other operators. This person will be the primary contact person for any communications regarding technical issues from the UCSF DXA Quality Assurance group;
3. Identify one, or preferably two, additional operators who will be available and trained to perform CALERIE scans when the chief operator is not available;
4. Perform and review daily QC scans and schedule cross-calibration scans of traveling phantoms;
5. Assure that proper archiving and back-up procedures for participant scans are performed and that archives are stored securely on appropriate archiving media until the end of the study;
6. Send participant scan materials to the DXA Quality Assurance (QA) Center daily (baseline and 6-month visits) or weekly (12-month, 18-month, 24-month visits) as specified in Section 5.3.
7. Send scanner performance data monthly to the DXA QA Center as specified in Section 5.3.
8. Assure proper functioning of hardware/software and request service from Hologic;
 - a. Notify Hologic and the QA Center of any machine or software problems or if the QDR scanner is being relocated
 - b. Record machine/software problems and service on the Hologic Repair/Service/Upgrade Form. Provide copies of any Hologic service reports to the QA Center.
 - c. Perform 5 QC phantom scans before (if possible) and after service
 - d. Perform 5 QC phantom scans before and after scanner relocation
 - e. Regular preventive maintenance by Hologic
9. Contact the QA Center with any urgent questions or problems that cannot be dealt with in the normal mailings;

2.1.2 DXA Quality Assurance Center Responsibilities

The following are the responsibilities of the QA Center:

1. Write and maintain the MOP;
2. Promptly review the participant scans for proper acquisition. Provide feedback to the clinical centers on the quality of scan acquisition. Request repeat scan from the clinical center if necessary.

3. Analyze the participant scans and maintain a study wide database of the analyzed scans;
4. Notify the clinical center and CoC promptly regarding excessively low BMD and/or excessive bone loss;
5. Review certification scans and return results/comments to each clinical center;
6. Certify operators to obtain scans in CALERIE;
7. Promptly review the QC phantom and air scan data received from each clinical center in order to identify surges or drifts in machine performance;
8. Identify possible sources of error, and suggest possible solutions. **(However, the QA Center will not be responsible for the solution of a hardware or software problem; that will rest with the clinical center and Hologic.)**

Any questions or correspondence regarding the manual or the technical aspects of the DXA measurements should be directed to:

Russell Scott
UCSF DXA Quality Assurance Center
185 Berry Street, Lobby 4
5th floor, Suite 5700
San Francisco, CA 94107-1762
Email: rscott@psg.ucsf.edu

Telephone: 415-514-8096 Fax: 415-514-8150

If Russell Scott is not available, please contact:

Cyndy Hayashi
UCSF DXA QA Manager
Email: Cynthia.Hayashi@ucsfmedctr.org
Telephone: 415-514-8091

2.2 Training and Certification of CALERIE DXA Operators

To obtain consistent results, the densitometry operators must be aware of possible sources of error that may affect data collection and analysis. Only those operators who have been certified by the QA Center are allowed to perform the scanning for this study.

Each clinic should have at least two people, preferably three, who are trained and certified for the CALERIE study. One person should be identified as the primary operator for CALERIE who will obtain the majority of the scans. This will reduce variability in the scan acquisition. However, it is essential to have another trained

operator available for the CALERIE study to acquire scans when the primary operator is absent.

Anyone performing scans for the CALERIE study must meet the following certification requirements:

1. Read and understand both the appropriate Hologic user's guide and this MOP
2. Successfully complete a Hologic QDR training course. This requirement may be waived at the discretion of the QA Center IF the operator attends the QA Center on-site training and provides satisfactory certification scans to the QA Center.
3. Certification by ISCD is recommended for all operators and required for the chief operator at each site.
4. Attend the QA Center on-site training.
5. Receive a satisfactory review of submitted certification scans by the QA Center.

In order to become certified to perform scans for the CALERIE study, each operator must send printouts of 5 example scans done at each skeletal site to the QA Center for review. Scans should have any private patient information removed or blacked out. The scans should be sent to the address listed on the previous page. If five example scans are not available for sending (we understand that some sites may not perform forearm scans on a regular basis), the QA Center will assess CALERIE study data for certification purposes.

The QA Center is responsible for deciding if an operator is certified and for notifying the clinic. Since the Hologic central training sessions are held infrequently, there may be a delay between when a new operator is hired and when certification is complete. Non-certified personnel may not scan participants without authorization by the QA Center.

2.2.1 On-Site Training of DXA Operators at Start-Up

The DXA Reading Center will provide on-site training of the DXA operators at each clinic during study start-up. A two-day training session will review general techniques and the specific procedures for CALERIE. The training can be provided for up to 4 operators. It is essential that DXA operators for CALERIE attend the on-site training.

2.2.2 On-Site Visits During Follow-Up

Two on-site visits will be scheduled during the CALERIE study. This will be an opportunity to review DXA techniques for the previously trained operators and to train new operators if needed.

2.3 Precision Assessment of Chief Operator

A precision assessment of whole body scan acquisition will be performed at baseline by each chief operator. Thirty participants at each site will be scanned twice for whole body, with re-positioning in between scans. Instructions will be provided by the QA Center.

2.4 Review of DXA Scans

The quality of scan acquisition will be ensured by a centralized review.

1. An original printout of the unanalyzed baseline scan should be maintained in the site study binder. This will be used as a reference during the acquisition of follow-up scans.
2. Unanalyzed scan data will be sent to the QA Center. For the baseline and 6-month visits, scan data must be sent on a daily basis, using “next day 10AM delivery” service. At subsequent follow-up visits (12-months and later), the scans may be sent on a weekly basis, using “next day delivery” service.
3. If a scan is determined to be unacceptable, the QA Center will send a request to rescan the participant. It is the responsibility of the operator to rescan the participant according to QA Center comments. During the baseline and 6-month visits, the QA Center will notify the clinic within one working day of receipt of the scans if any scan needs to be re-acquired.

Procedures for compiling and forwarding scans to the QA Center are outlined in Section 5.0.

2.4.1 Flagged Scans

Any scans that were difficult to acquire or are questionable should be sent immediately to the QA Center for evaluation. The operator should comment on why he/she believes the scan to be questionable. The QA Center will provide feedback to the operator on all flagged scans. If the participant needs to be rescanned, the QA Center will notify the operator within one working day.

2.4.2 Participant Safety

When analyzing the hip and spine scans, the QA Center will determine if any T-scores are below

-2.0. In addition, for the 12-month and 24-month hip and spine scans the QA Center will evaluate bone loss compared to baseline. Excessive bone loss (EBL) is defined as a rate-of-change greater than 5% at the 12-month visit or greater than 10% at the 24-month visit at the total hip or total spine.

The QA Center will notify the DXA chief operator and the CALERIE Study Manager at the clinical center and the CALERIE CoC, using the Notification of Low BMD or Excessive Bone Loss (EBL) form (Appendix B), of low bone density or excessive bone

loss based on the criteria above. The QA Center will include copies of the relevant scans with the notification.

3.0 DXA Scan Acquisition

This section describes in detail the specific procedures to be conducted for the CALERIE study with respect to entering the patient biography and scanning the participant.

Standard scanning procedures for the hip, spine, forearm and whole body bone density measurements are described in detail in the Hologic user's guide. Some of the information from the Hologic guides is repeated in this document for emphasis. Please note, however, that some of the scanning evaluation protocols for this study differ from those detailed by Hologic.

Use the Array mode for all participant scan acquisition. Do NOT use the Fast Array mode. If the image generated in Array mode is too grainy or has a "moth eaten" look, the technologist may use High Definition, if available. An extremely grainy image indicates that the tissue thickness or quality of the tissue is too great for the x-rays to penetrate in enough quantity to render a good image for analysis. The scan mode used on baseline should be maintained throughout the study.

3.0.1 Participant Preparation for Scan

The participant will be transported to the DXA facility by one of the study coordinators who will give the clinic weight and other participant data (participant ID number, birth date, sex, height, and ethnicity) to the DXA technician. The participant will be instructed to void before the DXA measurement and change into hospital scrubs or gown.

For consistency of results, we ask that the participant remove EVERYTHING and change into a patient gown. The DXA operator should check that no metal or plastic objects remain on the participant. This includes hair clips and pins, bras, snaps, zippers and buttons, as well as hip and back braces. The participant must remove any jewelry, earrings, other piercings, bracelets, watches, or rings.

All participants should refrain from taking any calcium or mineral supplements (vitamins) the day of their DXA exam since undigested tablets may interfere with the spine scans. If the participant has taken a calcium supplement, the operator should proceed with the scan but make a note in the Participant Scan Log to bring this to the attention of the QA Center. Any studies involving barium or radioisotopes should not be performed 4 weeks prior to the scheduled DXA exam.

3.1 Participant Data

Be sure to completely fill out the Participant Scan Log Sheet (see Appendix A).

3.1.1 Patient Biography, Patient Confirmation, and Scan Comments Screens

Be sure to use zero (0) and one (1) and not the letter "O" or letter "I" when entering numerical data into the Patient Biography fields.

The Study Coordinator will send a DXA Biography Form with the participant listing the Participant ID number, birth date, sex, weight, height, ethnicity, and visit number to be used in the Hologic biography. This form must be received before scanning the participant. All biography information must match the official study information.

FOLLOW-UP VISITS

Care should be taken **NOT** to create a duplicate biography when the participant returns for repeat measurements. After baseline, you should never have to click "New Patient". Conduct a search for the appropriate patient biography by entering the Participant ID number. Always confirm the patient's date of birth as a cross check that you have selected the correct patient biography.

The following fields should be updated in the patient biography for the follow-up visits:

- Weight-as provided by the study coordinator
- Height-as provided by the study coordinator
- Operator scan code: initials
- Scan Comments field with the appropriate visit number

PATIENT BIOGRAPHY SCREEN (See Figure 1)

Last Name: Enter the Participant ID number as given by the study coordinator, with CAL added at the end. Example: 01-0001CAL. (Adding these letters will avoid conflict with other studies on the scanner – that might happen to use the same ID numbers as CALERIE.)

Patient ID: Enter the Participant ID number, with CAL added at the end. (Same as the entry in the Last Name field)

Sex: Female or Male

Ethnicity: As given by the study coordinator. The categories available on the Hologic scanners are: White, Asian, Black, and Hispanic. These categories are used to determine the T-score for the scans. If the field is left blank, the Hologic software will use the white (Caucasian) database to determine T-scores.

DOB: It is important that the DOB match the study records. Cross check with the participant that the correct date of birth is being used for the study. If there is an error, contact the CALERIE study coordinator at your site immediately.

Weight and Height: As given by the study coordinator. (Update at follow-up visits)

<u><i>6-Month</i></u>	<u><i>6</i></u>
<u><i>6-Month + 14 days</i></u>	<u><i>7</i></u>
<u><i>12-Month</i></u>	<u><i>12</i></u>
<u><i>18-Month</i></u>	<u><i>18</i></u>
<u><i>24-Month</i></u>	<u><i>24</i></u>

3.2 Spine Scans

The appropriate Hologic user's guide should be consulted for the proper spine scanning procedures. Clarifications and exceptions for the CALERIE Study are noted below.

3.2.1 Spine Acquisition

1. Verify that the participant's spine is aligned with the longitudinal axis of the table by standing at the head of the table and looking down the length of the table. The participant's arms should be by their sides. Do not place the hands over or behind the head since this may induce a lordotic curve in the spine.
2. Use the Hologic positioning block under the participant's knees to reduce lordosis. The legs should be at approximately ninety degrees. Always use this same block and block position for all future scans.
3. The participant should be made as comfortable as possible to reduce the chance of unwanted movements. If the participant is very kyphotic, an additional pillow under the head may be used to reduce the stress on the lower back.
4. Observe the scan acquisition on the screen. Use the rescan feature freely following the instructions in the appropriate Hologic user's guide to re-center the spine if needed.
5. Scan from the middle of L5 (include a portion of the iliac crest for reference) up to the middle of T12, so that you will include all vertebrae from L1 to L4. Be sure to collect sufficient data for accurate identification of vertebral levels. If you are unsure of the levels, acquire data through T11.
6. At the end of the scan, enter the visit number in Scan Comments. Then go to Report and generate a printout of the image for reference on follow-up scans.

3.2.2 Spine Follow-up Scans

Refer to the baseline printout for positioning of the participant and scan modes selected; this is to ensure consistent scanning of the same area. Careful positioning and visual comparison of the current scan with baseline are essential for producing precise measurements. Use the rescan feature as soon as any positioning errors are detected during the current scan.

3.3 Hip Scans

The appropriate Hologic user's guide should be consulted for the proper hip scanning procedures. Clarifications and exceptions for the CALERIE Study are noted below.

3.3.1 Hip Acquisition

1. The **LEFT hip is the preferred** hip. Reasons to scan the right hip instead of the left: history of fracture of the left hip, surgery to replace all or part of hip joint, existing disease (severe osteoarthritis, osteonecrosis, anatomical malformations) that prevents the left side from being scanned or analyzed properly.
2. Use the Hologic hip positioning device. Keep the participant's hands out of the scanning area by placing them comfortably on the participant's chest.
3. Align the femoral shaft with the longitudinal axis of the table. Ensure rotation of the hip by holding the knee and the ankle when positioning the leg.
4. After proper rotation, firmly secure the foot using the hip positioner's Velcro strap.
5. The participant should be made as comfortable as possible to reduce the chance of unwanted movements.
6. Instruct the participant to remain quiet and still until the end of the measurement. You must rescan the participant if there is any movement during the scan.
7. At the end of the scan, enter the visit number in Scan Comments. Then go to Report and generate a printout of the image for reference on follow-up scans.

3.3.2 Hip Follow-up Scans

Refer to the baseline printout for positioning of the participant and scan modes selected; this is to ensure consistent scanning of the same area. Careful positioning and visual comparison of the current scan with baseline are essential for producing precise measurements. Use the rescan feature as soon as any positioning errors are detected during the current scan.

The following fields should be updated during the follow-up visits:

- Weight- As given by the study coordinator.
- Height- As given by the study coordinator.
- Operator scan code
- Scan Comments field with the appropriate visit number

If the participant has experienced a hip fracture or surgery on the side that was scanned at baseline, do NOT obtain a scan of either hip at the follow-up visit(s).

3.4 Forearm Scans

The appropriate HOLOGIC user's guide should be consulted for the proper forearm scanning procedures. Clarifications and exceptions for the CALERIE Study are noted below.

3.4.1 Forearm Acquisition

When performing forearm scans, attention must be paid to the following points:

1. Center the table. Use a chair without wheels.
2. Scan the non-dominant forearm. If this forearm has been fractured or contains hardware, scan the other forearm.
3. With the elbow bent and resting on the table, measure the distance from the ulnar styloid to the table in centimeters and record the measurement on the Data Transmittal Form. Divide this number by 2 to calculate half of the distance down from the ulnar styloid and mark it on the participant's arm. This is the region to be scanned.
4. Note: The scanner arm is positioned differently for right vs. left forearm. If scanning the left forearm, the participant will be seated facing the head of the table. Start the scan at the midpoint of the forearm. If scanning the right forearm, the participant will be seated facing the foot of the table. Start the scan in the carpal bones and stop the scan when you reach the midpoint of the arm. The participant's arm should be bent at about 105 degrees. Use the cross hairs of the laser to position the forearm straight on the table.
5. Hologic recommends the use of the forearm positioner. Many participants may find this device uncomfortable. The QA Center will allow operators to refrain from using the positioning device only if they can produce high quality reproducible scans. The forearm must be straight and centered in the scan field. Use the Hologic Palm Mouse for support of the hand.
6. If the Hologic forearm positioning device is being used, ensure that the anatomy scanned is inside the window. Do not scan including any plastic part of the positioning device.
7. Make sure that the participant's head is kept clear of the scanner arm.
8. The participant should be seated as comfortably as possible to reduce the chances of unwanted movements. Instruct the participant not to move until the end of the measurement.

9. At the end of the scan, enter the visit number in Scan Comments. Then go to Report and generate a printout of the image for reference on follow-up scans.

3.4.2 Forearm Follow up Scans

Refer to the baseline printout for positioning of the participant; this is to ensure consistent scanning of the same area. Careful positioning and visual comparison of the current scan with baseline are essential for producing precise measurements. Use the rescan feature as soon as any positioning errors are detected during the current scan. Make sure you acquire the same amount of forearm on follow-up.

If the participant has experienced a wrist or forearm fracture or surgery on the side that was scanned at baseline, do NOT obtain a scan of either forearm at the follow-up visit(s).

3.5 Whole Body Scans

The appropriate Hologic user's guide should be consulted for the proper whole body scanning and analysis procedures. Clarifications and exceptions for the CALERIE Study are noted below.

3.5.1 Whole Body Acquisition

When performing whole body scans, attention has to be paid to the following points:

1. Position the participant at the top of the table with just enough space to give air points at the beginning of the scan. ***It is extremely important that the participant is correctly positioned on the exact center of the table.*** The arms should be at the sides with hands placed palm down. If the hands do not fit in the scan field, do not tuck the hands under the thighs. The hands may be placed in lateral position and taped, with paper tape, if necessary.
2. Go to the end of the table and place your hands under the participant's ankles. The legs should be straight; invert the feet until the toes touch. Secure the feet with a piece of paper tape.
3. If during scanning it is apparent that part of the participant's body lies outside the scan field, stop the scan and reposition the participant.
4. Do not use pillows or other positioning/support aides.
5. If the participant is very tall, you may clip off part of the feet. If the participant is properly positioned using the full usable length of the table on all visits, you will clip off a consistent amount of the feet in follow-up scans.
6. Instruct the participant to breathe normally, being careful not to move or talk until the end of the measurement.

7. At the end of the scan, enter the visit number in Scan Comments. Then go to Report and generate a printout of the image for reference on follow-up scans.

3.5.2 Whole Body Follow-up Scans

Refer to the baseline printout for positioning of the participant and scan modes selected; this is to ensure consistent scanning of the same area. Careful positioning and visual comparison of the current scan with baseline are essential for producing precise measurements. Stop, reposition and start the scan again as soon as any positioning errors are detected during the current scan.

4.0 Scanner Quality Control

Monitoring of machine performance throughout the study is the joint responsibility of the clinical centers and the QA Center. Table 3 lists the quality control procedures and schedule.

Table 3. Quality Control Scanning Schedule

Phantom	Scanning frequency
Local Hologic Tissue Bar	1 time/week
Local Hologic Spine Phantom	Daily (at least 3 times/week)
Local Hologic Whole Body Phantom	3 time/week
Whole Body Air Scan	Minimum 1 time/week

4.1 Cross-Calibration of Scanners

In order to assess accurately the absolute variations in scanner performance between clinical centers, cross-calibration phantoms will be circulated and scanned at each clinical center during the first few months of the study. Each clinic will receive two phantom shipments. One shipment will include Hologic hip, spine and block phantoms. The other shipment will have a Hologic whole body phantom. A detailed protocol will accompany the phantoms.

4.2 Phantom Scans

Perform the QC spine scan in the morning prior to any participant scans, as outlined in the appropriate Hologic user's guide. The operator performing the scan is responsible for checking the results and repeating the scan if the values fall outside the acceptable range. If the results fall outside the acceptable range on the second scan, Hologic should be called.

Whole body quality control consists of Hologic whole body phantom scans, whole body air scans and tissue bar scans. The Hologic whole body phantom comes with instructions from the manufacturer. The instructions for the whole body air scans are in Section 4.2.3 of this manual.

The tissue bar comes with instructions from Hologic. For Windows based software see Appendix C1, Analyzing Body Composition for the Whole Body Scan, in the QDR for Windows user's guide. If you do not have this appendix, call Hologic Helpdesk at 1-800-321-4659.

Create only ONE patient biography for your whole body phantom. Depending on the version of Hologic software, there should be a biography for the whole body phantom and one for the whole body air scan. Some of the more recent scanners will perform the whole body air scans automatically after the tissue bar is scanned. In this case, operators do not need to create a biography for this scan. Avoid duplication of phantom biographies by using the patient menu to select the appropriate biography prior to scanning the phantom.

4.2.1 QC Spine Phantom Scans

1. Ensure alignment with the scanner axis by using the laser cross-hairs. Make sure that the BMD, BMC and AREA values of your scanner are within normal limits. If the most recent scan falls outside the limits, repeat the scan.
2. Original printouts of the spine QC plots (BMD, BMC and AREA) are to be sent to the QA Center for review monthly. The date range for the plots should cover at least the previous 6 months to the present. After the first six months of the study, include the entire length of the study in the QC plots.
3. A System Backup should be done weekly. Hologic normally recommends you use a 4-disk rotation. Store your backups in a secure area.

4.2.2 Whole Body Phantom Scans

- Whole body phantom scans cannot be added to the QC database; the phantom is scanned as a participant. Create a biography as you would for a participant.
- Scan the phantom three times a week according to the instructions provided by Hologic and Appendix C of this manual.

- COPY the whole body phantom scans to the traveling CD/disk, then Archive to the primary and secondary CD/disk before deleting scans from the hard drive.
- The QA Center will retrieve the scans from the traveling CD/disk, analyze the scans and plot the desired variables. The clinical centers will be notified of any detected problems.

4.2.3 Whole Body Air Scan - Windows Based Software

A Whole Body scan of “air” should be performed at least once a week. The “air” scan will assess the proper functionality of the scanner and indicate any potential problems with the x-ray beam

To prepare for the air scan, clear the entire tabletop of any objects and clean the pad of any debris. Only the table pad should remain on the table. This is critical since the test can detect items as thin as a single piece of Scotch tape.

Performance of the air scan differs substantially across the scanners and software in use at the three CALERIE sites. The process is automated with the newer scanners or 12.0 and later versions of software. We are therefore providing specific instructions on performance of the air scans in an Appendix to this MOP (Appendix C). The instructions will also be reviewed in detail during the on-site training.

Once the air scan has been performed, you will need to fill out the WB Air Scan Worksheet (see Appendix A). Find the SD values for HiBone. Record these values for lines 10 through 19 (10 values in all) on the worksheet. Also record the Global SD for HiBone.

You will also need to send the electronic file of the air scan to the DXA QA Center. COPY the WB AIR QC SCAN to your traveling CD/disk and archive to the clinic CD/disk. The traveling CD/disk will be sent to the DXA QA Center once a month.

IMPORTANT:

- In the event that the Global SD exceeds 3.0, immediately fax the worksheet to Russell Scott at UCSF (415-514-8150) and call Hologic.
- If the SD for any of the individual lines 10 through 19 exceeds 2.0 units, immediately fax the worksheet to Russell Scott at UCSF (415-514-8150). The DXA QA Center will review the data and decide if further action is needed.

4.3 Machine, Software, and Service Problems

If your machine needs to be repaired or if any adjustment has to be made that possibly might affect your data:

1. Do a System Backup before any work is done on the scanner.

2. If possible, contact the QA Center before the repairs or adjustments are made to find out whether additional measures are required.
3. Perform 5 scans of the Hologic daily QC spine phantom before (if possible) and after the repairs or adjustments are made.
4. Send a copy of the repair technician's notes and a copy of the Hologic Repair/Service/Upgrade Log (see Appendix A) to the QA Center with the monthly QC data transfer. The repair log should contain complete information on all repairs/changes done on your machine. Please keep a repair log with your machine.

4.4 Hardware/Software Change Control

Unauthorized hardware/software changes must be avoided. If for any reason you think you have to change the hardware/software, or your Hologic service representative recommends a hardware/software change, contact the QA Center BEFORE any changes are made.

Future hardware/software upgrades will be checked by the QA Center in conjunction with Hologic technical support personnel to assure that the upgrade will not adversely affect the study. The QA Center will provide a recommendation to the CALERIE Steering Committee who will make the final decision on any upgrades. All hardware or software upgrades must be approved by the CALERIE Steering Committee **BEFORE** installation at the clinical centers.

Record hardware/software upgrades on the Hologic Repair/Service/Upgrade Log.

5.0 Data Management

5.1 Hard Copies of Scans

The clinical center is responsible for maintaining original hard copies of all unanalyzed baseline scans performed during the study. Keep the original printouts in the participant's scan printout folder or the study binder.

5.2 Electronic Scan Archive

Each clinical center should maintain primary and secondary archive disks. These disks remain at the site. At the end of each day, the operator should archive all study data to the primary and secondary archives.

Participant and QC data should be sent on a “copy” disk or CD.

5.3 Transfer of Data to the DXA Quality Assurance Center

Send daily for all baseline and 6-month visit scans, using “next morning by 10AM delivery” service. For the 12-month and later visits, scan data may be sent on a weekly basis, using “next day service.” Include:

1. Participant Scan Log Sheet. Use the form to “flag” individual scans with special concerns.
2. Copy disk/CD with unanalyzed scan data.

Send monthly using “next day service”:

1. QC Data Transmittal Form
2. Spine Phantom QC Plots. Send a printout of the most recent plots of the QC database (spine BMD, BMC, and AREA). The plots are reviewed at the QA Center and problems are reported back to the clinical center.
3. Export of QC data (label the disk with site name, date and “QC Data”)
4. Whole body phantom scans and “air” scans on CD/disk.
5. Whole Body Air QC Scan Worksheet
6. Hologic Repair/Service/Upgrade Form
7. Copy of any Hologic service reports for that time period

Pack the materials carefully. The copy disk(s)/CD should be in a protective mailer or bubble wrap to avoid damage. Data should be sent using a service capable of tracking packages (e.g. FedEx). Ship these items to the following address:

Russell Scott
UCSF DXA Quality Assurance Center
185 Berry Street, Lobby 4
5th floor, Suite 5700
San Francisco, CA 94107-1762
Email: rscott@psg.ucsf.edu

Telephone: 415-514-8096 Fax: 415-514-8150

5.4 Return Materials Sent by the DXA Quality Assurance Center

The QA Center will return the traveling CD/disk(s) to the clinical centers in monthly shipments.

As needed, the QA Center will send:

1. Requests to repeat a scan due to poor acquisition
2. Notification of excessively low BMD or EBL
3. Feedback/comments on scan acquisition
4. Recommendations for service, additional phantom scans, etc., as necessary based on the quality control data.

APPENDICES

APPENDIX A. Study Forms sent to DXA QA Center

- 1. Participant Scan Log Sheet**
- 2. QC Data Transmittal Form**
- 3. Hologic Repair/Service/Upgrade Form**
- 4. Whole Body Air QC Scan Worksheet**

APPENDIX B. Study Forms sent out by DXA QA Center

- 5. Notification of Low BMD or Excessive Bone Loss (EBL) and CALERIE Guidelines for Management of Low Bone Density or Excessive Bone Loss**
- 6. DXA QA Data Action Form**

Master copies of these forms will be available electronically. These forms must be photocopied at the clinical center as needed. Original forms should be maintained at the clinical site. Copies of the forms should be sent to the QA Center.

APPENDIX C. Whole Body Air Scans – Instructions [TO BE ADDED AFTER DEC 15]

- Hologic software versions 11.X**
- Hologic software versions 12.X**

9.6.2 CALERIE DXA Forms



CALERIE Biographical Information for DXA Scan

The DXA Operator must enter specific information, listed below, into the DXA scanner for each CALERIE participant. To insure that this information is accurate, we ask that the clinic coordinator complete this form and provide it to the DXA Operator when each participant is scanned.

Please provide the following information:

For the Baseline Visit

Participant six digit Study ID#: _____

Participant Ethnicity: The Hologic scanner provides the following choices for race/ethnicity. Please circle one. "Other" will default to the white (Caucasian) reference database.

White Black Hispanic Asian Other _____

Participant Date of Birth (MMM/DD/YYYY): _____

Participant Weight: _____ **lb**

Participant Height: _____ **inches**

Follow up visits:

Participant Weight: _____ **lb**

Participant Height: _____ **inches**

Study Coordinator (circle one) yes or no

I have checked that this participant has not had any examinations involving a radioisotope or radiographic contrast medium, like barium, within 4 weeks prior to the scheduled DXA appointment.

9.7 Physical Activity Procedures

9.7.1 Maximal Oxygen Uptake Test Procedures

Maximal oxygen uptake ($VO_2\text{max}$) is the maximum amount of O_2 that a subject can take up during strenuous exercise. It reflects the maximal capacity of the cardiovascular system to supply the working skeletal muscles with oxygen and the ability of working muscle to use O_2 . $VO_2\text{max}$ tests will be performed under medical supervision for the first test for each subject. Once the exercise ECG is documented to be free of diagnostic abnormalities indicative of occult coronary artery disease, subsequent testing can take place under the supervision of the appropriately trained personnel, according to the site's normal procedures. The test will be performed at Baseline, Month 12 and Month 24.

Maximal oxygen uptake will be measured while subjects exercise on a motorized treadmill and breathe through a low resistance mouthpiece while wearing a nose clip. Expired gases will be collected and analyzed using the site's dedicated $VO_2\text{max}$ metabolic cart or appropriate alternative as selected by the site and approved by the QC Committee. The cart will be calibrated before and after each test according to the manufacturer's instructions (refer to the next section of this MOP where this is outlined in detail). A minimum of two technicians are required to be present for a $VO_2\text{max}$ test. One technician should operate the ECG monitor, treadmill, and RPE. The other should monitor the metabolic cart, BP, HR and participant safety.

Metabolic Cart Calibration:

1. The metabolic cart should warm up for a minimum of 30 minutes before beginning calibration.
2. For calibration of gases, one will use a two-point calibration (i.e., one against room air and one against commercially prepared precision gas). The room air values are 20.94 for O_2 and 0.04 for CO_2 . The commercial gas values are usually in the vicinity of 16.0% O_2 and 4.0% CO_2 (calibration gases vary somewhat, but should generally be in this range as this is similar to the subject's expired air). Repeat the calibration procedure if the computer read outs for CO_2 or O_2 are > 0.02 from what the cal gas or ambient gases are reported to be by the supplier. For example, if the ambient O_2 reads 20.91, instead of 20.94, the calibration should be saved and then repeated and saved again.
3. Flow volume calibration should be done at approximately the following rates (<30, 80, 120, 200, 300 L/min).
4. For testing, one will set-up the metabolic cart to record data as 15s averages (i.e., four data points per minute).

Pretest Assessment:

1. Subjects will be fasting for a minimum of 90 minutes, not have undergone any invasive skeletal muscle testing or exercise functional measure the day of testing, and not have taken beta adrenergic blockers within 24 hours of testing. Subjects should be instructed in advance of these guidelines.
2. Subjects will be monitored prior to, during and following the test using ECG. A minimum of three leads will be used unless the participant is at moderate or high

- risk according to ACSM guidelines, in which case a 12-lead ECG will be performed.
3. Details of the testing procedure will be explained to the subject.
 4. Once the participant is connected to the ECG, they may be seated in a chair stationed next to the treadmill.
 5. BP is measured at rest, after the subject has been standing for two minutes.
 6. Calculate the participants age-predicted maximal heart rate, where predicted $HR_{max} = 208 - (0.7 \times \text{age})$

Inform Subjects About Particulars of the Test:

1. Demonstrate how to use the equipment.
2. Explain the test protocol. For example: The objective of the test is to continue exercising to exhaustion. The technicians will provide verbal encouragement and support to assist the participant in reaching a maximal effort and satisfying the maximal oxygen uptake criterion. The test is incremental, which means that it will become progressively harder and harder. The speed and/or grade of the treadmill will be increased each two minutes. The participant is not allowed to hold-on (grip) to the treadmill during the test. The subject may stabilize by applying a light touch (e.g., two fingers) to the handrails.
3. The Borg's Rate of Perceived Exertion Scale (i.e. 20 point scale) will be administered in the last 30 sec of each workload. The participant is asked to point to a number that represents their exertion at that point in time with the instructions that "6 represents how you feel sitting in the chair and 20 represents how you feel if you cannot take another step."
4. Describe any unusual sensations the subject may experience: shortness of breath, chest pain, dry mouth and throat, dizziness and tell them to notify the technician with hand signals if these occur during the test.
5. Determine a hand signal for when the participant wants to stop (a firm thumbs down).

Fitting Mouthpiece, Collecting Resting VO₂ Data and Beginning Test:

1. Have the subject stand on the treadmill with their feet either side of the belt.
2. Fit the mouthpiece and nose clip to the participant. Ensure that the mouthpiece is operational (check valves movement on inspiration and expiration) and there are no air leaks around the nose and mouth.
3. Check that the ECG monitor is operational.
4. Collect three minutes of VO₂ data while the subject is standing at rest, or until the VO₂ values stabilize.
5. If the resting VO₂ is < 2.5 or > 5.0 ml/kg/min, equipment malfunction is likely -- resolve the problem before starting the test.
6. Average the VO₂ data from the last full minute of the resting VO₂ data collection as baseline.
7. During the last 30s of the resting period, have the participant stand with their feet on either side of the belt. Slowly start the belt at <1mph and have the participant step onto the moving belt. In the last 5s, count down...5...4...3...2...1...and speed up to 3mph while at the same time pressing "Start Exercise" on the metabolic cart.

Familiarization (required before the subject's first test only and after the resting VO₂ is obtained):

1. Encourage the participant to undertake some non-strenuous stretching of the calf muscles, hamstring, etc.
2. Begin the familiarization session in the same manner that the exercise test will be commenced. That is, the participant will begin with both feet positioned either side of the treadmill belt and holding on to supporting handrails. Start the belt at <1mph and have the participant step on the treadmill after a 5s count-down "...5...4...3...2...1...go." Once the participant is walking, increase the speed of the treadmill up to 3 mph. The participant is now required to walk normally with no assistance from the handrails.
3. Allow the participant to exercise for about two minutes.

Testing Proper

1. The grade and speed are adjusted according to the Cornell protocol (outlined below) until the subject is physically unable to continue. Encourage the subject to complete the final stage. The RER **should be ≥ 1.10 at this point.**
2. During test, record:
 - Heart rates every minute by rhythm strip during the last ten seconds of the stage.
 - Blood Pressures are measured before the end of every other stage starting with stage 2.
 - Rate of Perceived Exertion every minute in the last 30 seconds of each workload
 - Note arrhythmias (VPC's, couplets, triplets, VT, SVT).
 - ST depression
 - Symptoms of heart disease (chest pain, lightheadedness).

Protocol: Cornell (Am J Cardiol 72:715-720, 1993)

All stages are 2 minutes.

Stage 1: 1.7 mph / 5%
 Stage 2: 1.7 mph / 10%
 Stage 3: 2.0 mph / 10%
 Stage 4: 2.5 mph / 12%
 Stage 5: 3.0 mph / 13%
 Stage 6: 3.4 mph / 14%
 Stage 7: 3.8 mph / 16%
 Stage 8: 4.2 mph / 16%
 Stage 9: 4.8 mph / 17%
 Stage 10: 5.0 mph / 17%
 Stage 11: 5.0 mph / 18%
 Stage 12: 5.5 mph / 18%

Test Completion and Recovery:

1. While the test is in progress, explain to the participant that every second is important. Tell them that when they feel as though they are nearing the end, they should ask themselves, "Can I go another 10 seconds?" Let them know that as soon as they signal to stop (thumbs down), the speed and grade will immediately start to decline.

2. Immediately lower the grade to 0%
3. Remove the mouthpiece, nose clip and head piece.
4. Take an immediate post test BP.
5. The subject should actively cool down for two to three minutes at 0% grade and 3 mph.
6. Ask the participant why they had to stop exercising and record the answer on the testing form.
7. Ask the participant their peak RPE at the moment the test was terminated. Ask participant if they had any chest pain or pressure at any time during test or recovery period.
8. BP's are taken every three minutes during recovery until the recovery is terminated (see 9).
9. When the subject's BP and HR are back to within 10% of the baseline the test may be terminated.
10. Print the "Gas Calibration Report", which should include the pre- and post-test calibration reports.

Processing the Test:

1. A trained technician will process the test data.
2. Remaining data from the test is collected and recorded on the testing form.
3. Maximum HR from the ECG printout is measured and results are transferred to the record sheet.
4. The two highest consecutive 15-second VO_2 measurements within the last two minutes of exercise are averaged and recorded and considered the " VO_2 max." At least 30 seconds of data must be included during the final workload for these data to be considered for the VO_2 max determination.
5. In addition, "peak VO_2 " is considered the highest VO_2 determinations over any 15-second period and recorded on the worksheet.
6. Change in VO_2 between workloads (i.e., during the plateau) is calculated as the difference between the average VO_2 during the final 30 seconds of successive workloads, where at least 30 seconds of data are available.
7. Max RER, VE, HR, BP, VE/ VO_2 , speed and Grade are calculated and recorded. All data from the metabolic cart should be printed in 15s averages.
8. Time the test was stopped and the reason the test was stopped should be recorded.
9. Comments should be recorded on the testing form and should include any significant information from the test.
10. The test will be reviewed and signed by a qualified physician and kept in the subject's binder. Also, on the initial test, the physician will determine the need for direct medical supervision on subsequent tests by so indicating on the CRF.
11. The technician will indicate on the testing form the following information:
 - Positive, Negative Adequate, or Uninterpretable (reasons for Uninterpretable tests will be indicated on the report form). All tests are formally read by the study physician.
 - Maximal, near maximal or submaximal test refer to next section for definition of each
 - Type of arrhythmia
 - Chest pain, dizziness, light-headedness, etc.
 - HR and BP

- Exercise tolerance
- Reason for test termination

Determining VO₂max criteria. The test is scored as a max test if two or more of the following are met:

- a) Plateau in VO₂. VO₂ is said to reach plateau if it changes \leq 150 ml/min between the final two completed workloads
- b) RER \geq 1.1
- c) HR max \pm 5 bpm of age-predicted maximum.

Reasons to Stop a test (Based on ACSM's Guidelines for Exercise Testing and Prescription):

1. Progressive angina (stop at 3+ level or earlier on a scale of 1 to 4).
2. Ventricular tachycardia.
3. Any significant drop (20 mm Hg) of systolic blood pressure or failure of the systolic blood pressure to rise with an increase in exercise load.
4. Lightheadedness or signs of circulatory insufficiency.
5. Greater than two mm horizontal or down sloping ST depression or elevation (in the absence of other indicators of ischemia) for more than three beats in a row.
6. Onset of second or third degree A-V block.
7. Increasing ventricular ectopy, multi-form PVC's, or R on T PVC's.
8. Excessive rise in BP: systolic BP > 250 mm Hg or diastolic BP > 120 mm Hg.
9. Chronotropic impairment.
10. Sustained supraventricular tachycardia.
11. Exercise-induced left bundle branch block.
12. Subject request to stop.
13. Failure of the monitoring system.

VO₂max Measurement Quality Control

Maximal oxygen uptake, commonly referred to as VO₂max, is the most widely recognized measure of cardiopulmonary fitness. It is physiologically reflective of the capacity of the cardiovascular and pulmonary systems to transport oxygen to working skeletal muscle, as well as of the capacity of the working muscles to utilize oxygen during exercise. VO₂max is used as an index of physical fitness at baseline and to determine changes in physical fitness over the intervention. VO₂max is measured as an absolute value (L/min) and is commonly expressed relative to body mass (ml/kg/min). VO₂max will be expressed as both an absolute and relative value for CALERIE.

The VO₂max tests should be held to certain criteria in order to achieve physiological peak. These criteria generally include:

- a) Having a respiratory exchange ratio \geq 1.10
- b) Achieving a max HR within five beats of the age predicted maximum. A near maximum test achieves at maximum HR within 5 bpm of age-predicted maximum. A sub-maximum test is anything less than this.
- c) Achieving a plateau in oxygen uptake with increasing work. A VO₂ is considered to plateau if the VO₂ increases less than 150 ml/min in the last two complete stages of an exercise test to exhaustion (American College of Sports Medicine: Guidelines for Exercise Testing and Prescription, 6th Edition, 2000).

Generally, meeting two out of the three criteria is a marker for an acceptable test. It is also important that each of the CALERIE sites follow the specified protocol and document which of the above criteria were met on the report form.

The QC items identified below represent common standard quality control items. Under all conditions, tests should be performed only under the direct supervision of a trained health care provider with knowledge of the following: indications for and contraindications to the test; normal end points and abnormal responses or complications requiring test termination; and principals and details of exercise testing, including subject preparation, safety, instrumentation, and procedures. The QC items assume the equipment at each site has been calibrated according to directions and schedule of manufacturer and that all of these calibrations have been documented in study documentation. Study technicians will be required to recognize a maximum test and indications/contraindications for testing as described in ACSM certification.

A resting VO_2 is measured for several reasons:

- a) Resting VO_2 , measured after the participant is in a resting position, standing or sitting is a good and facile check of whether the instrumentation is working correctly. If the resting VO_2 is outside the range of 2.5 to 5.0 ml/kg/min the instrumentation should be rechecked to make sure that all is in working order.
- b) The resting VO_2 is relatively insensitive to baseline psychological reaction that a subject may have to testing. That is, although the HR, BP, RR and RER may be elevated due to nervousness, unless the subject is moving, the resting VO_2 should be only slightly abnormal.

The exercise device and the metabolic cart should be calibrated **before and after** each test. If the pre and post calibrations do not agree, then the test should be considered invalid and the test repeated for the subject. The calibration reports should be kept with other study documentation. Calibration logs must be kept in the CALERIE regulatory binder.

Summary of QC procedures for this test.

1. Resting VO_2 as a check of proper instrument operation
2. Gas Calibration of cart before AND AFTER each test (logs kept in binder)
3. Treadmill speed and grade calibrated at start and at yearly intervals
4. CC tally the number of incomplete tests, invalid tests, incomplete worksheets, and # of near max and sub max tests (i.e. failure to meet 2 of 3 criteria) for each site
5. Report to QC committee on a quarterly basis for the first year and then at six-month basis thereafter.
6. Calibration data for cart (from before and after every test) and treadmill (done yearly) is kept at the sites and should be checked during the monitoring visits.

9.7.1.1 Peak VO₂ CALERIE ETT Form

Name: _____ Subject No: _____
last first
 Testers: ____ / ____ / ____ Date: ____ / ____ / ____ Time: ____ : ____



I. Stress Results

Cornell Protocol

Fasting > 90 minutes?
 Y N

	Comments: <i>(enter all that apply)</i>	Arrhythmias: <i>(enter all that apply)</i>	
1 Discomfort (reproduces symptoms)	10 Ectopy supressed	1 PAC's	12 Ventricular Trigeminy
2 Discomfort (not typical of symptoms)	11 Discomfort subsided	2 Atrial bigeminy	13 Ventricular Couplets
3 Claudication	12 Prolonged discomfort	3 PJC's (premature junctional beats)	14 Ventricular Triplets
4 Dyspnea	13 Hypotension	4 Automatic atrial tachycardia	15 VT non sustained (>3beats and <30sec)
5 Dizziness	14 Hypertension	5 Paroxysmal AV junctional tachycardia	16 VT sustained (>30 sec.)
6 Musculoskeletal pain	15 RBBB	6 Afib/flutter non-sustained	17 Wide complex tachycardia
7 ST changes	16 LBBB	7 Afib/flutter -sustained	18 Ventricular fibrillation
8 Fatigue	17 Paced rhythm	8 SVT - undetermined etiology	19 1st degree AV block
9 Syncope		9 PVC's (uniform)	20 2nd degree AV block
		10 PVC's (multiform)	21 3rd degree AV block
		11 Ventricular Bigeminy	22 Cardiac arrest

	TIME	MPH	% Elevation	HR	BP	RPE	COMMENTS	ANGINAL DISCOMFORT	ARRHYTHMIAS	TREATMENTS
Supine					/					
Standing										
Stage 1	sec	1.7	5			/20		/10		
Stage 2	sec	1.7	10		/	/20		/10		
Stage 3	sec	2.0	10			/20		/10		
Stage 4	sec	2.5	12		/	/20		/10		
Stage 5	sec	3.0	13			/20		/10		
Stage 6	sec	3.4	14		/	/20		/10		
Stage 7	sec	3.8	16			/20		/10		
Stage 8	sec	4.2	16		/	/20		/10		
Stage 9	sec	4.8	17			/20		/10		
Stage 10	sec	5.0	17		/	/20		/10		
Stage 11	sec	5.0	18			/20		/10		
Stage 12	sec	5.5	18		/	/20		/10		

Stress Results continued

Comments: <i>(check all that apply)</i>		Arrhythmias: <i>(enter all that apply)</i>		Treatments: <i>(check all that apply)</i>	
1 Discomfort (reproduces symptoms)	10 Ectopy suppressed	1 PAC's	12 Ventricular Trigeminy	1 Atropine	10 Cardioversion
2 Discomfort (not typical of symptoms)	11 Discomfort subsided	2 Atrial bigeminy	13 Ventricular Couplets	2 Adenosine	11 Defibrillation
3 Claudication	12 Prolonged discomfort	3 PJC's (premature junctional beats)	14 Ventricular Triplets	3 Verapamil	12 Brevibloc
4 Dyspnea	13 Hypotension	4 Automatic atrial tachycardia	15 VT non sustained (>3beats and <30sec)	4 Vagotonic maneuver	
5 Dizziness	14 Hypertension	5 Paroxysmal AV junctional tachycardia	16 VT sustained (>30 sec.)	5 Procainamide	
6 Musculoskeletal pain	15 RBBB	6 Afib/flutter non-sustained	17 Wide complex tachycardia	6 Lidocaine	
7 ST changes	16 LBBB	7 Afib/flutter -sustained	18 Ventricular fibrillation	7 Bretylium	
8 Fatigue	17 Paced rhythm	8 SVT - undetermined etiology	19 1st degree AV block	8 Nitroglycerin	
9 Syncope		9 PVC's (uniform)	20 2nd degree AV block	9 IV fluids	
		10 PVC's (multiform)	21 3rd degree AV block		
		11 Ventricular Bigeminy	22 Cardiac arrest		

II Recovery Results

Comments: <i>(enter all that apply)</i>		Arrhythmias: <i>(enter all that apply)</i>		Treatments: <i>(enter all that apply)</i>	
1 Discomfort (reproduces symptoms)	10 Ectopy suppressed	1 PAC's	12 Ventricular Trigeminy	1 Atropine	10 Cardioversion
2 Discomfort (not typical of symptoms)	11 Discomfort subsided	2 Atrial bigeminy	13 Ventricular Couplets	2 Adenosine	11 Defibrillation
3 Claudication	12 Prolonged discomfort	3 PJC's (premature junctional beats)	14 Ventricular Triplets	3 Verapamil	12 Brevibloc
4 Dyspnea	13 Hypotension	4 Automatic atrial tachycardia	15 VT non sustained (>3 beats and <30sec)	4 Vagotonic maneuver	
5 Dizziness	14 Hypertension	5 Paroxysmal AV junctional tachycardia	16 VT sustained (>30 sec.)	5 Procainamide	
6 Musculoskeletal pain	15 RBBB	6 Afib/flutter non-sustained	17 Wide complex tachycardia	6 Lidocaine	
7 ST changes	16 LBBB	7 Afib/flutter -sustained	18 Ventricular fibrillation	7 Bretylium	
8 Fatigue	17 Paced rhythm	8 SVT - undetermined etiology	19 1st degree AV block	8 Nitroglycerin	
9 Syncope		9 PVC's (uniform)	20 2nd degree AV block	9 IV fluids	
		10 PVC's (multiform)	21 3rd degree AV block		
		11 Ventricular Bigeminy	22 Cardiac arrest		

Recovery	TIME	HR	BP	COMMENTS	ANGINAL DISCOMFORT	ARRHYTHMIAS	TREATMENTS
Rec 1	sec		/		/10		
Rec 2	sec		/		/10		
Rec 3	sec		/		/10		
Rec 4	sec		/		/10		
Rec 5	sec		/		/10		
Rec 6	sec		/		/10		
Rec 7	sec		/		/10		
Rec 8	sec		/		/10		
Rec 9	sec		/		/10		
Rec 10	sec		/		/10		
Rec 11	sec		/		/10		
Rec 12	sec		/		/10		

Exceeded 12 recovery stages? <i>(If Yes, see pages 6 and 7)</i>	<input type="radio"/> Yes <input type="radio"/> No
--------------------------------------------------------------------	----------------------------------------------------

III Additional Findings

Chest Discomfort <i>(check all that apply)</i>
<input type="radio"/> None <input type="radio"/> Typical anginal pain <input type="radio"/> Atypical anginal pain <input type="radio"/> reproduces patient's symptoms <input type="radio"/> not typical of patient's symptoms

Reason(s) for Termination: <i>(check all that apply)</i>
<input type="checkbox"/> THR reached <input type="checkbox"/> MPHR reached <input type="checkbox"/> ST changes <input type="checkbox"/> Chest discomfort <input type="checkbox"/> Hypotension <input type="checkbox"/> Hypertensive response <input type="checkbox"/> Dyspnea <input type="checkbox"/> Planned <input type="checkbox"/> Dizziness <input type="checkbox"/> Syncope <input type="checkbox"/> Musculoskeletal pain <input type="checkbox"/> Fatigue (generalized or leg) <input type="checkbox"/> Claudication <input type="checkbox"/> Automatic atrial tachycardia <input type="checkbox"/> Paroxysmal AV junctional tachycardia <input type="checkbox"/> Atrial fib/flutter (non-sustained) <input type="checkbox"/> Atrial fib/flutter (sustained) <input type="checkbox"/> Ventricular couplets <input type="checkbox"/> VT non-sustained (>3 beats and <30 seconds) <input type="checkbox"/> VT sustained (>30 seconds) <input type="checkbox"/> Wide complex tachycardia <input type="checkbox"/> 2nd degree AV Block <input type="checkbox"/> 3rd degree AV Block <input type="checkbox"/> Cardiac arrest <input type="checkbox"/> Ventricular fibrillation <input type="checkbox"/> SVT - undetermined etiology
Other (free text):

IV. Pre Study ECG

ECG (check one) Normal Abnormal Not Available
If Abnormal

Rhythm <i>(check all that apply)</i>	P Wave <i>(check all that apply)</i>	Axis <i>(check one, if applicable)</i>	Conduction <i>(check all that apply)</i>
<input type="checkbox"/> AIVR <input type="checkbox"/> Atrial fibrillation <input type="checkbox"/> Atrial flutter <input type="checkbox"/> AV sequential pacing <input type="checkbox"/> Ectopic atrial tachycardia <input type="checkbox"/> Nodal rhythm <input type="checkbox"/> NSR <input type="checkbox"/> Paced rhythm <input type="checkbox"/> Sinus bradycardia <input type="checkbox"/> Sinus tachycardia <input type="checkbox"/> SVT <input type="checkbox"/> Ventricular pacing	<input type="checkbox"/> LAE <input type="checkbox"/> RAE	<input type="radio"/> Normal <input type="radio"/> LAD <input type="radio"/> RAD	<input type="checkbox"/> 1° AV Block <input type="checkbox"/> 2° AV Block - Type I <input type="checkbox"/> 2° AV Block - Type II <input type="checkbox"/> 3° AV Block <input type="checkbox"/> Incomplete LBBB <input type="checkbox"/> LBBB <input type="checkbox"/> Left Ant Hemiblock (LAD > -30°) <input type="checkbox"/> Left Post. Hemiblock (RAD > +120°) <input type="checkbox"/> Nonspecific IVCD <input type="checkbox"/> RBBB <input type="checkbox"/> Incomplete RBBB <input type="checkbox"/> WPW
Arrhythmias <i>(check all that apply)</i>	QRS Complex <i>(check all that apply)</i>	ST-T Waves <i>(check all that apply)</i>	
<input type="checkbox"/> Couplets <input type="checkbox"/> PAC's <input type="checkbox"/> PJC's <input type="checkbox"/> PVC's <input type="checkbox"/> Ventricular tachycardia	<input type="checkbox"/> Anterior MI <input type="checkbox"/> Inferior MI <input type="checkbox"/> LVH <input type="checkbox"/> Lateral MI <input type="checkbox"/> Posterior MI <input type="checkbox"/> RVH	<input type="checkbox"/> Early repolarization <input type="checkbox"/> Low voltage <input type="checkbox"/> LV ischemia <input type="checkbox"/> Nonspecific ST-T changes <input type="checkbox"/> Poor R wave progression <input type="checkbox"/> Prolonged QTc <input type="checkbox"/> Secondary repolarization changes (LVH, RBBB) <input type="checkbox"/> Secondary repolarization changes (RVH) <input type="checkbox"/> ST elevation (persistent) c/w LV aneurysm <input type="checkbox"/> ST elevation c/w acute infarction <input type="checkbox"/> ST elevation c/w acute pericarditis <input type="checkbox"/> Subendocardial injury <input type="checkbox"/> Transient ST elevation c/w variant angina	

IV. Interpretation (to be filled out by M.D.)

ECG Interpretation: <i>(check one)</i>		
<input type="radio"/> Positive	<input type="checkbox"/> When interpretation was Initially positive In stress or recovery? (check one) <input type="radio"/> Stress <input type="radio"/> Recovery Heart rate was _____ bpm ST depression - _____ mV ST change type initially? (check one) <input type="radio"/> Depression <input type="radio"/> Elevation In Leads: (check all that apply) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> aVR <input type="checkbox"/> aVL <input type="checkbox"/> aVF <input type="checkbox"/> V1 <input type="checkbox"/> V2 <input type="checkbox"/> V3 <input type="checkbox"/> V4 <input type="checkbox"/> V5 <input type="checkbox"/> V6	<input type="checkbox"/> Maximum net exercise ST Depression Max ST depression - _____ mV In Leads: (check all that apply) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> aVR <input type="checkbox"/> aVL <input type="checkbox"/> aVF <input type="checkbox"/> V1 <input type="checkbox"/> V2 <input type="checkbox"/> V3 <input type="checkbox"/> V4 <input type="checkbox"/> V5 <input type="checkbox"/> V6 Resting ST depression \geq .05mV in above leads? <input type="radio"/> Yes <input type="radio"/> No ST depression is downsloping? <input type="radio"/> Yes <input type="radio"/> No
		<input type="checkbox"/> Maximum net exercise ST Elevation Max ST elevation + _____ mV In Leads: (check all that apply) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> aVR <input type="checkbox"/> aVL <input type="checkbox"/> aVF <input type="checkbox"/> V1 <input type="checkbox"/> V2 <input type="checkbox"/> V3 <input type="checkbox"/> V4 <input type="checkbox"/> V5 <input type="checkbox"/> V6 Resting ST elevation \geq 0.05 mV in above lead(s)? <input type="radio"/> Yes <input type="radio"/> No
<input type="radio"/> Negative	Adequate or Inadequate (check one) <input type="radio"/> Adequate (peak HR is within 5 beats of THR) <input type="radio"/> Inadequate (THR not reached, no exercise ECG changes)	Variable horizontal ST depression, nondiagnostic? <input type="radio"/> Yes <input type="radio"/> No
<input type="radio"/> Uninterpretable	Uninterpretable due to: (check all that apply) <input type="checkbox"/> Resting and further exercise ST elevation only in leads with pathologic Q waves and/or residual ST segment coving from prior MI <input type="checkbox"/> Exercise induced conduction disturbance <input type="checkbox"/> Exercise induced conduction disturbance (not Right Bundle Branch Block) <input type="checkbox"/> Rest and Exercise IVCD <input type="checkbox"/> Rest and Exercise IVCD (not Right Bundle Branch Block) <input type="checkbox"/> Rest and Exercise paced ventricular rhythm <input type="checkbox"/> Resting IVCD/paced rhythm disappears with exercise but significant ST segment changes are present on the exercise ECG. <input type="checkbox"/> Baseline ST changes <input type="checkbox"/> Paroxysmal atrial tachycardia <input type="checkbox"/> Increased ventricular arrhythmia <input type="checkbox"/> Lead fell off <input type="checkbox"/> Patient fell <input type="checkbox"/> Artifact <input type="checkbox"/> LVH repolarization <input type="checkbox"/> Digoxin effect	

V. Additional Comments

Interpreted by: _____

Interpreting MD (check one)

9.7.2 Muscle Strength and Endurance Testing

Muscle strength is assessed using an isometric handgrip strength test and isometric and isokinetic knee extension and flexion tests. Muscle endurance is assessed using isokinetic knee flexion and extension. The strength and endurance tests are performed at baseline and at the 12- and 24-month time points during the study. Within the sequence of tests performed at each time point, the strength and endurance tests should not be performed within 24 hours of (before or after) the maximal treadmill exercise test.

9.7.2.1 HANDGRIP STRENGTH

Equipment

Jamar Hydraulic Hand Dynamometer (Asimow Engineering Company, Los Angeles, CA).

Procedures

1. Set the handle position:
 - Baseline tests: The dynamometer handle should be positioned so that the proximal interphalangeal joints (i.e. the joints just distal to where a ring is worn) are flexed at 90 degrees.
 - Follow-up tests. The dynamometer handle should be placed in the same position as was used for the subject's baseline test. This requires that the baseline test handle position is looked-up prior to the test appointment.
2. Read and record the "zero" force value for the dynamometer while being careful to not squeeze the handle. If the value is discrepant from 0 by more than 1 kg, the instrument should be serviced. Use a different dynamometer for the test if possible.
3. Determine of handedness:
 - For baseline tests, ask the subject which hand is dominant (right, left, or ambidextrous) and record. . This step is not necessary for follow-up tests.
4. Position the subject:
 - Standing position.
 - Head should be neutral (facing straight ahead).
 - Upper arm should be vertical (neutral shoulder position).
 - The elbow should be held at 90 degrees flexion.
 - Wrist is neutral.
5. Explain the test:
 - The test objective is to squeeze the dynamometer as hard as possible in a brief maximal effort of no more than 3 seconds. . The right and left hands are tested alternately until a total of three tests have been performed on each hand.
 - A quick maximal effort should be made with each trial . No movement from the initial position should be made during the maximal effort. . Although a powerful exertion should occur rapidly, jerking of the dynamometer or of the arm or other body parts is not permitted.
6. Perform the test:
 - Set the force-recording needle on the dynamometer dial to zero.

- Assure that the subject is in the correct starting position and tell the subject to perform the test when ready.
- During the effort, encourage the subject verbally by saying “harder! harder!” or “push! push!”
- After each trial, record the force value (kg) indicated on the dynamometer dial and reset the dial to zero.
- Alternately perform the test on each hand for a total of 3 tests per hand.
- At least 30 seconds of rest should occur before repeat testing on the same hand.
- The single highest score recorded on each hand is used as the grip strength value.

Data Report and Summary

Data are manually recorded on the “Strength Tests” form. All calculations (i.e. determination of the maximal values for the right and left hands and the calculation of force per unit body weight) are automated and are done at the Coordinating Center.

Quality Control and Calibration Verification

Quality control information for the hand dynamometer strength measures is collected in three ways. First, prior to each test, the dynamometer is inspected to be sure that the force gauge indicates zero when the dynamometer is not being squeezed. The “zero” force value is recorded on the data form for each test. This information is entered into the central CALERIE database along with the data from each test and is therefore readily available for quality control reports.

As a second quality control measure, the high force “gain” calibration of the dynamometer is checked every 3 months during the study by hanging a weight of known mass (30-50 kg) from the handle of the dynamometer. The same calibration weight is used for all calibrations within a given site. Verification of the gain calibration is documented in a site-specific calibration logbook for the dynamometers. If the zero value deviates by more than 1 kg, or if the high force calibration is off by more than 3.0% of the known force, the calibration verification procedure is repeated two more times. If the calibration is still problematic, the instrument will be serviced by appropriate personnel or replaced.

A third quality control measure is to compare the two highest force values for each hand. If the two force values for a given hand are discrepant by more than 10 kg, this suggests that (a) a force values was misread/misreported, (b) the subject did not give uniform effort with each trail, or (c) the instrument gave a spurious reading secondary to being bumped or jerked during the test. Reports for this quality control measure are easily generated since the required force data are routinely entered into the common CALERIE database. Reports of the frequency of tests that violate this quality control measure are routinely assessed.

9.7.2.2 ISOMETRIC/ISOKINETIC KNEE EXTENSION AND FLEXION

Equipment:

Washington University: Biodex System 3 dynamometer (Biodex Medical Systems, Shirley, New York)

Tufts University: Biodex System 3 dynamometer (Biodex Medical Systems, Shirley, New York)

PBRC: Cybex II Isokinetic Dynamometer, (Cybex Division of Lumex, Inc, Ronkonkoma, NY USA)

Procedures:

1. Weigh the subject and record or enter into the dynamometer computer.
2. General warm-up: have the participant exercise for 10 minutes at a light to moderate intensity on a cycle ergometer.
3. Set up the computer information and dynamometer for data collection.
 - a. For baseline tests, determine and document all details regarding the equipment setup (i.e. positions of the seat, dynamometer, etc.).
 - The backrest should be reclined at 85°
 - The seatback should be positioned so there is 1 – 2” of space between the edge of the seat bottom and the back of the lower leg
 - The femoral epicondyle of the knee joint should be aligned with the pivot center of the dynamometer
 - The lever arm should be positioned so that the pad is attached to the lower leg in the region of the smallest diameter just proximal to the malleoli.
 - b. For follow-up tests, set up the equipment according to specifications that were documented during the baseline test.
4. Query the subject about knee pain and conditions (i.e. recent knee injury, chronic pain, etc.) that might contraindicate the test or affect test results. Document the issues of concern and which tests, if any, were omitted as a result of the problem.
5. Secure the subject to the seat with knee, lap, and shoulder straps.
6. Explain the test to the subject.
 - a. The right and left legs are each assessed at different speeds.
 - b. For knee extension tests, the subject should kick up as hard and fast as possible with each repetition, letting the leg return to the starting position between repetitions, until the desired number of repetitions has been performed.
 - c. For knee flexions, the subject should pull down and back on the lever arm as hard and fast as possible for every repetition, while extending lightly between repetitions to return the lever arm to the starting position.
 - d. All repetitions for each test should be performed continuously (i.e. no rest between repetitions).
 - e. The subject is permitted practice trials before items a-d, but not e-f below.
 - f. Explain that there is a tendency to breath hold during the test but this should be avoided.
 - g. For the 180°/sec, 30 repetition tests, it is important to explain to the subject that they must not pace themselves and that maximal effort should be put into every repetition. Pacing defeats the purpose of this “muscle fatigue” test.
 - h. Knee flexion repetitions should be performed immediately after knee extension repetitions such that the concentric knee extension is immediately followed by a concentric knee flexion.

7. Weigh the lower leg for use in gravity corrections of test results
 - a. Lock the position of the movement arm at 30° before full extension. Thus, for these tests “full range of motion” (60°) is considered from 90° (leg hanging perpendicular to the floor) to 30° (from full extension) where 0° is considered full extension.
 - b. Tell the subject to fully relax the leg.
 - c. Read and record (or store in the computer) the leg weight.
 - d. Only one gravity correction needs to be performed for each leg for all tests within a given testing time point.
8. Have the subject performs a velocity-specific warm-up of three submaximal effort repetitions followed by a single repetition at maximal effort. The subject is permitted practice trials before items a-d, but not e-f.
9. Perform the following tests in the listed sequence. First perform all of the tests on the right leg, then on the left leg. A concentric knee extension repetition should be followed immediately by a concentric knee flexion repetition for the 5 repetition and 30 repetition bouts. Additionally, a 5 minutes of rest should separate c and d from e and f.
 - a. Concentric 60°/sec knee extension; 5 repetitions
 - b. Concentric 60°/sec knee flexion; 5 repetitions
 - c. Concentric 180°/sec knee extension; 30 repetitions
 - d. Concentric 180°/sec knee flexion; 30 repetitions
 - e. Isometric knee extension at 45°; three, 5-second repetitions with a 30 second rest between repetitions
 - f. Isometric knee flexion at 45°; three, 5-second repetitions with a 30 second rest between repetitions
10. Execute the test (the following procedural sequence is used for each of the above test components).
 - a. Activate the data collection program (or chart recorder)
 - b. Tell the subject to start the extension(s) or flexion(s) (as appropriate for the test component)
 - c. During the test, provide continual instruction and verbal encouragement until all repetitions have been completed.
 - d. Tell the subject when to stop and relax

Data Report and Summary

All results are adjusted (by the dynamometer computer) for gravity effect torque by subtracting the lower leg weight from flexion torque values and by adding lower leg weight to extension torque values.

1. Muscular strength
 - Peak torque from the isometric tests and power, work and peak torque data from the isokinetic tests is interpreted as muscular strength data. The results are expressed in absolute terms and relative to body weight.
2. Muscular endurance
 - Muscle fatigue index is calculated from the 180°/second isokinetic test as the percent decrease in peak torque during the 30 repetition set as follows:
 - Muscle fatigue index (% decrease in peak torque) = $100 - [(mean\ of\ the\ last\ 5\ repetitions) / (mean\ of\ the\ highest\ consecutive\ 5\ repetitions) \times 100]$.

- Total work is defined as the total of the five repetitions and average power is the average of the five repetitions in items a & b.

Quality Control and Calibration Verification

Calibration is verified on a monthly basis according to the manufacturer's instructions. If the equipment fails the manufacturer's recommendations for calibration verification, the verification procedure is repeated two more times. If the calibration is confirmed to be in error, the manufacturer or other suitable service personnel is contacted to service the instrument. All calibration records are kept in a calibration logbook at each study site.

Performance measures are also used for quality control assessments. First, since muscle fatigue occurs during repeated maximal effort contractions, torque data from both of the isokinetic tests are evaluated for the presence of fatigue patterns. More specifically, in the 60°/sec assessments, the average peak torque from the first two repetitions should always be greater than the average peak torque from the last two repetitions. Likewise, the fatigue index values from the 180°/sec tests should always be positive. The frequency with which the expected fatigue pattern is not seen is easily extracted from the common CALERIE database and summarized for review.

Force data from the isometric tests is also used for quality control assessments. For each assessment, the two greatest peak torque values should be discrepant by ≤ 10 kg. Reports of the frequency of which this criterion is not met are routinely generated from the common CALERIE database.

9.7.3 Stanford 7-Day Physical Activity Recall

Seven-Day Physical Activity Recall (PAR) Questionnaire

Participant _____ Study Time point _____

Interviewer _____

Today's Date _____ Day (circle one): Mon Tues Wed Thurs Fri Sat Sun

- | | | |
|------------------------------------------------------|--------------------------------|--------|
| 1. Were you employed in the last seven days? | 0. No (Skip to Q#3) | 1. Yes |
| 2. If yes, which days? | Mon Tues Wed Thurs Fri Sat Sun | |
| 3. What two days do you consider your non-work days? | Mon Tues Wed Thurs Fri Sat Sun | |

		<i>DAYS</i>						
		1	2	3	4	5	6	7
Day: (Mon...)								(yesterday)
Date: (mm/dd/yy)								
Sleep: In Bed / Up Total time								
Work: Start / End Total time								
M O R N I N G	Moderate							
	Hard							
	Very Hard							
A F T E R N O O N	Moderate							
	Hard							
	Very Hard							
E V E N I N G	Moderate							
	Hard							
	Very Hard							

PAR Questionnaire – Page 2

4. Compared to your physical activity over the past three months, was last week's physical activity more, less or about the same?

1. More 2. Less 3. About the same

KEY	Rounding:	10-22 min	=	0.25 hr
Place asterisk (*) to the right of a work-related activity		23-37 min	=	0.50 hr
& the time spent doing it.		38-52 min	=	0.75 hr
		53-1:07 hr:min	=	1.0 hr
		1:08-1:22 hr:min	=	1.25 hr

INTERVIEWER:

Please answer questions below and note any comments on interview.

5. Were there any problems with the 7-Day PAR interview? 0. No
1. Yes (If yes, please explain.)

6. Do you think this was a valid 7-Day PAR interview? 0. No (Please explain)
1. Yes

7. Please list below any activities reported by the subject that you don't know how to classify.

8. Please provide any other comments you may have in the space below.

SEVEN-DAY PHYSICAL ACTIVITY RECALL (PAR) LIST OF ACTIVITIES

INTENSITY	JOB	HOME	SPORT OR RECREATION

LIGHT	<ul style="list-style-type: none"> * Typing * Standing * Driving 	<ul style="list-style-type: none"> * Ironing, sewing * Light auto repair * Indoor Painting 	<ul style="list-style-type: none"> * Leisurely walking * Softball * Bowling * Playing a musical instrument

MODERATE	<ul style="list-style-type: none"> * Lifting or carrying light objects (up to 5 lbs) * Painting outside of house 	<ul style="list-style-type: none"> * Sweeping, Mopping, Vacuuming * Clipping hedges * Raking * Mowing lawn with power mower * Cleaning windows * Pushing stroller with child 	<ul style="list-style-type: none"> * Brisk walking (on level ground) * Shooting baskets * Throwing frisbee * Cycling leisurely on level ground * Swimming laps (easy effort) * Weightlifting

HARD	<ul style="list-style-type: none"> * Construction work * Lifting or carrying objects (5-15 lbs) * Climbing ladder or stairs 	<ul style="list-style-type: none"> * Scrubbing floors * Shoveling dirt, coal, etc. * Mowing lawn with non-power mower * Carrying child (5-15 lbs) 	<ul style="list-style-type: none"> * Brisk walking (uphill) * Backpacking (on level ground) * Brisk cycling on level ground without losing breath * Tennis (doubles) * Downhill skiing * Swimming laps (moderate effort)

VERY HARD	<ul style="list-style-type: none"> * Carrying heavy loads such as bricks or lumber * Carrying moderate loads up stairs (16-40 lbs) 	<ul style="list-style-type: none"> * Digging ditches * Chopping or splitting wood * Gardening with heavy tools 	<ul style="list-style-type: none"> * Jogging * Basketball (in game) * Soccer (in game) * Backpacking (uphill) * Cycling (uphill or racing) * Tennis (singles) * Cross-country skiing * Swimming laps (hard effort) * Aerobic dancing * Circuit training (using a series of Nautilus machines without stopping)

PAR INTERVIEW INSTRUCTIONS

Important Points:

- ** The PAR interview will be administered by the Study Coordinator or designated backup. The PAR interviewer should NOT be a member of the research team who is involved in administering the intervention to the participant being interviewed.
- ** The interviewer should practice conducting the PAR interview ~3 times before interviewing a study participant.
- ** Stress that this is a recall of actual activities for the past week, not a history of what the participant usually does.
- ** Emphasize that we are NOT asking about many physical activities that are considered light activities, such as desk work, standing, light housework, strolling, and stop-and-go walking such as grocery or window shopping. Clarify that we are interested in occupational, household, and sports activities that make them feel similar to how they feel when walking at a normal pace, and more vigorous activities.
- ** Allow the participant to determine the appropriate intensity category. The categories on the List of Activities should serve as a guide. However, the interviewer has the final say about the category assignment, based upon interrogation of the interviewee. (The only exception is running, which should always be classified as “very hard”)
- ** Remain neutral, do not encourage or praise the participant. Do not reply or, if you do, use a neutral word such as OK. If an interviewer accidentally says “good,” correct the mistake by adding, “You remembered really well.”
- ** It is helpful to restate what the participant reported.
- ** Cue and prompt as necessary.

Interviewer’s Role:

The role of the interviewer is to gather accurate information about each participant’s physical activity during the past week. It is important to ask appropriate open-ended questions, have good timing, prompt often without leading the participant, and provide cues and definitions when necessary. Examples of open-ended questions that help a participant recall his or her day might be, “What were you doing Tuesday morning? You said that you got up at 6:00 a.m. Did you go anywhere after that? ... Did you watch any particular TV show? ... What did you make for dinner? ... What did you do that evening?” If a participant is going into excessive detail, remind him/her that he/she does not need to account for every minute. A good interviewer controls the pace and structure of the interview but does not control the participants’ answers. Be impartial and allow the participant to decide how he or she is going to answer. For example, when a participant is asked to choose the intensity of a physical activity, only the participant should decide how to rate it. Be aware of your own opinions so that you do not manipulate the information. Remember to record what is heard, not what you think it should be.

Assessing Physical Activity:

It is necessary to consider the frequency, intensity, time, and type (F.I.T.T.) of the physical activity. The PAR interview focuses on collecting data on intensity, time, and type of activity. The PAR differentiates between occupational physical activities, such as stocking shelves, waitressing, and construction work, and leisure activity (i.e., all other physical activities that are not done during paid work hours.) Most participants spend the majority of their waking hours in light activity. Many tiring household or occupational tasks do not have a very high energy cost. Store clerks may report feeling fatigued from standing all day, but the energy cost is minimal. With occupational tasks, it is necessary to clarify the time spent in physical activity by asking about breaks. Time spent in lunch, coffee breaks, and standing breaks can be subtracted from physical activity time. For example, a store clerk reports stocking shelves for 8 h and is asked if he or she took any breaks. After recalling time spent on lunch and just standing around, the clerk reports spending 6 of the 8 doing moderate physical activity.

Recalling events is easier when working backwards from the present day to 1 wk ago from today. Record yesterday above column 7, and work backwards in time so that column 1 is 1 wk ago from today. Inform the

participant that you will begin asking questions about yesterday and work backwards through the previous 7 d. Before starting the interview, briefly explain to the participant what is involved in the interview process.

Intensity:

Ask only about activities that are at least the intensity of walking, but include walking. Ask what the intensity was for every activity. The exception is running, and only running. If a person states that he or she jogged or ran, then that activity goes in the very hard category. It is not necessary to give the intensity guidelines. If a person categorizes running or jogging as moderate or hard, it is placed in the very hard category. This does not apply for walking because it is difficult to know if it was a stroll, normal, or brisk walk. For all other activities – baseball, swimming, surfing, painting, digging, etc. – provide the intensity guidelines for comparison. Walking and running provide good frames of reference for classifying activities, and participants should be able to compare subjectively the physical activity he/she did to running or walking. For most activities, the rate at which it is performed can make a significant difference in the energy cost. Use comparisons to walking and running so the participant can rate how hard he/she did the activity.

List of Activities:

Provide the participant with the “PAR List of Activities” during the interview. This list is to be used as a guide to help the participant remember activities that they may have performed during the past 7 days. The interviewer may use the list to help prompt the participant. There may be other activities that the participant reports that do not appear on this list. It is important that the participant decide which intensity category is most appropriate for each activity (it may differ from the intensity category on the List of Activities).

Duration & Scoring:

The interview needs to be sensitive to walking. Although people walk many times during the day, not all walks are counted (e.g. we do not add up each time a person walks to the refrigerator). The specific rule for walking is that only walks of 5 min or longer are counted. However, that 5-min bout of walking can only be counted if another 5-min bout occurs in the same intensity category during in the same period of the day (morning, afternoon or evening), such that the total during that period adds up to a total of 10 minutes.

For any activity to be counted, it must add up to at least 10 min by the end of the day period (morning, afternoon, or evening). The general rule is that a participant must do at least 10 min of an activity in 1 activity category during one period of the day for it to be counted; this amount is recorded and rounded to 15 min.

Rounding: 10 and 20 min are rounded to 15 min = .25 h
25 and 35 min are rounded to 30 min = .50 h
40 and 50 min are rounded to 45 min = .75 h
55 and 65 min are rounded to 60 min = 1.0 h

Evaluating the Interview:

Evaluate the interview by answering the questions on page 2 of the worksheet. List any activities reported by the subject that you do not know how to classify. Be detailed. Ask the name of the activity, the duration (not including breaks), and how the activity compares to walking and running.

Special cases:

If the last week was totally atypical (e.g. the subject was in the hospital or in bed, involved in a family or work crisis, or traveling), it is permissible to go to the previous week for the survey. Do not take this action lightly; use it only in unusual circumstances.

PAR CALCULATIONS

- 1) Add the number of hours spent in sleep, moderate, hard, and very hard activities. NOTE, add nap times to sleep time. Time spent in Light Activity is calculated by difference:

$$\text{Light hr} = 24 \text{ hr} - \text{sleep hr} - \text{moderate hr} - \text{hard hr} - \text{very hard hr}$$

- 2) Assign the following MET intensities to each activity category:

<u>Activity</u>	<u>METs</u>
Sleep	1
Light	1.5
Moderate	4
Hard	6
Verv Hard	10

- 3) Calculate MET-hr:

Hrs spent in each activity category for the past 7 d are multiplied by their respective MET values and then summed and expressed as MET-hrs.

Sample Data from the 7-Day Recall:

Sleep:	<u>60.0</u> h	x	1 MET	=	60 MET-hr
Light:	<u>99.5</u> h	x	1.5 METs	=	149 MET-hr
Moderate:	<u>3.5</u> h	x	4 METs	=	14 MET-hr
Hard:	<u>2.5</u> h	x	6 METs	=	15 MET-hr
Very Hard:	<u>2.5</u> h	x	10 METs	=	25 MET-hr
TOTAL (per wk)					263.25 MET-hr (per week)
TOTAL (per day)					263.25 MET-hr/wk ÷ 7 d/wk = 37.6 MET-hr/d

- 4) Calculate total daily energy expenditure (TDEE, in kcal/d):

a. Use subject's measured RMR to determine 1 MET: $(\text{RMR, kcal/d}) \div (24 \text{ h/d}) = \underline{\hspace{2cm}} \text{ kcal/h}$

$$\begin{aligned} \text{If RMR} &= 1600 \text{ kcal/d:} \\ 1 \text{ MET} &= 1600 \text{ kcal/d} \div 24 \text{ hr/d} = 66.7 \text{ kcal/hr} \end{aligned}$$

b. Calculate TDEE by multiplying 1 MET by the # MET-hr/d:

$$\text{TDEE} = 66.7 \text{ kcal/hr} \times 37.6 \text{ MET-hr/d} = 2507$$

N.B. The following calculation is the published method for calculating energy expenditure (in kcal/d) from MET-hr of activity using the PAR Questionnaire. However, the examples below illustrate why this calculation, which generally works well in normal-weight individuals, often is inappropriate for overweight individuals:

In normal-weight person: 1 MET = 1 kcal/kg/hour

e.g. 70 kg person would expend:

1 kcal/kg/hr x 70 kg x 24 hr/d = 1680 kcal/d at rest

1 kcal/kg/hr x 70 kg x 263.25 MET-hr/wk ÷ 7 d/wk = 2633 kcal/d with activity

BUT, this calculation often overestimates EE for overweight individuals:

e.g. 85 kg person doing the same activities would appear to expend:

1 kcal/kg/hr x 85 kg x 24 hr/d = 2040 kcal/d at rest

1 kcal/kg/hr x 85 kg x 263.25 MET-hr/wk ÷ 7 d/wk = 3197 kcal/d

PAR INTERVIEWER SCRIPT

(Interviewer's script is shown in **bold**):

1. Introduction: **“The questions that I will be asking you refer to the physical activities you've engaged in during the past week.”**
2. Work: **“I am going to start by asking you a few questions about your employment.”**
(Ask employment questions on top of PAR worksheet.)
3. Weekend Days: **“What 2 d of the week do you consider to be your weekend days? Most people consider Sat. and Sun. to be their weekend days, but it may be different for you.”**
{Some participants state that they do not have weekend days because they work all week or never have 2 d off; in this case, ask what 2 d are most like weekend days. If only 1 d is given as a weekend day, then ask what other day is most like a weekend day}
4. Sleep: **“Now I'd like to look at the time you spent sleeping in the past week. By sleeping, I mean the time you went to bed one night and the time that you got out of bed the next morning. You may not necessarily have been asleep the entire time you were in bed. You may have been reading or watching television. Today is (Monday), so yesterday was (Sunday). What time did you go to bed (Sunday) night? What time did you get up (Monday) morning?”**
{Determine hours spent in bed to the nearest ¼ h. The participant does not need to be asleep the entire time, because lying down and sleeping burn approximately the same number of kilocalories. Time spent in sexual activity is not counted as sleep. Start with yesterday and work backward through the previous 7 days. Do this for each day of the 7 -d recall. Calculate total time spent sleeping after completing the interview.}
5. Work Hours: {If Applicable} **“Now I'd like you to tell me what hours you worked each day during the past week.”**
{Record start and end times on worksheet. Calculate total time spent working after completing the interview.}
6. Physical Activity: **“I am going to ask you about the physical activities you engaged in during the past 7 d, starting with yesterday and going back 7 d. In doing so, please remember, this is a recall of actual activities for the past week, not a history of what you usually do. We are not considering light activities, such as desk work, standing, or light housework. We are considering occupational, household, recreational, and sports activities that make you feel similar to how you feel when you are walking at a normal pace, and more vigorous activities. For example, slow stop-and-go walking such as window shopping, is not included; however, walking at a normal pace to do an errand is included.”**
7. PAR List of Activities: {Provide the participant with the PAR List of Activities} **“These are examples of activities that you may have engaged in. Remember that we are not considering Light Activities, which include the majority of our daily activities.”**
8. Intensity Guidelines: **“I will ask you to categorize the intensity of each physical activity you do into one of three groups: moderate, hard, or very hard.
The moderate category is similar to how you feel when you're walking at a normal pace.
The very hard category is similar to how you feel when you are running.
The hard category falls in between.
In other words, if the activity seems harder than walking but not as strenuous as running, it should go in the hard category.”**

PAR INTERVIEWER SCRIPT - continued

9. **Segments of the Day: “I am going to ask you about the physical activities you engaged in during three segments of the day, which includes morning, afternoon, and evening. Morning is considered from the time you get up in the morning to the time you have lunch; afternoon is from lunch to dinner; and evening is from dinner until the time you go to bed.”**

{If a meal is skipped, it is appropriate to define morning from the time a person wakes up until 12 noon, afternoon from 12-6 PM, and evening from 6 PM to bed. Always spend some time setting the stage for each day to help people remember their activities. Physical activity can be performed intermittently or continuously}

10. **“Today is (Monday), so yesterday was (Sunday). Think about what you did (Sunday) morning. Where were you? Think about what you usually do. Did you do anything unusual? Did you do any physical activity (Sunday morning)? How long did you do that activity? How much of that time was spent standing still or taking breaks?”**

{Do not record time spent on breaks, rest periods, and meals. Be sure that the time reported for an activity was actually spent doing the activity. Being at the swimming pool for 2 h but only swimming for 15 min should be recorded as 15 min, not 2 h. Working in the garden all day Saturday (8 h) should mean actually working for 8 h. Query participants to be sure they are reporting these activities accurately. Start with yesterday and work backward throughout the week. Differentiate work-related activities with an asterisk or star. The asterisk should be placed to the right of the duration corresponding to the work-related activity; e.g. .75 h}.*

11. **Intensity: “Did that activity feel similar to how you feel when you are walking or running or is it somewhere in between?” {Always refer to intensity guidelines}. “Keep in mind that a moderate intensity activity feels similar to walking at a normal-to-brisk pace, and very hard feels similar to running.”**

{The interviewer should not guess what intensity an activity is. The subject is responsible for classifying his or her physical activities into intensity categories.}

12. **At the End of Each Day Ask: “Are there any physical activities that you might have forgotten? Did you do any physical activity at work? How do you get to and from work? Are there any other recreational or sport activities? Did you participate in any sports or any vigorous family activities? How about any housework that made you feel similar to brisk walking? Or gardening? Were there any other walks that you might have taken?”**

13. **On the Last Day of Recall: “Take a moment to think back over the course of the week and think of any activities that you may have forgotten. Did you want to add any other household, occupational, or sports activities that you participated in during the past week that you may have overlooked? Did you take any walks you did not tell me about? Are there any activities that you are unsure about?”**

14. **Last Question: “The last question I am going to ask you is, Compared to your physical activity over the past 3 mo, was last week's physical activity more, less, or about the same?”**

{Record answer on page 2 of worksheet}

15. **“Thank You”:** *{Thank the participant for his/her time and participation}*

PAR REFERENCES & ADAPTATIONS

References:

- 1) Seven-day physical activity recall. *Med. Sci. Sports Exerc.*, 29(6)Suppl:S89-S103, 1997.
- 2) Sallis JF, WL Haskell, PD Wood, SP Fortmann, T Rogers, SN Blair, RS Paffenbarger, Jr. Physical activity assessment methodology in the Five-City Project. *Am. J. Epidemiol.* 121(1):91-106, 1985.
- 3) Wilson PWF, RS Paffenbarger, Jr, JN Morris, RJ Havlik. Assessment methods for physical activity and physical fitness in population studies: report of a NHLBI workshop. *Am. Heart. J.* 111:1177-1192, 1986.

Adaptation for Discussion with Consultant at Training:

The protocol for administering and scoring the PAR has been adapted for use in various different studies.

The following modifications have been made for use in the CALERIE Study.

- 1) The original version of the PAR List of Activities categorized “softball” and “bowling” as light activities, and therefore did not count them. Because the intensity of these activities is variable, the instructions for the CALERIE study will consider them like all other activities, with the participant in consultation with the interviewer responsible for determining the intensity category.
- 2) Data from the PAR is expressed in METs, from which energy expenditure can be calculated. The formula to calculate energy expenditure from METs is based upon the estimate that 1 MET = 1 kcal/kg/hour. This formula is appropriate for normal-weight individuals, but often results in an overestimate of energy expenditure in overweight individuals. Therefore, the CALERIE study will use a modified formula to calculate energy expenditure from METs; this formula uses each participant’s measured resting metabolic rate to determine the energy cost of 1 MET, and is to be used in place of body weight.

Additional QC items:

The interviewer (study coordinator and backup person) will receive training, and will practice three times before first real study interview is performed.

The CC will evaluate the info on worksheets and tally by site:

1. Number of interviews with incomplete data
2. Number of problem interviews (“yes” to item #5)
3. Number of invalid interviews (“No” to item #6)

To be reviewed by QC committee quarterly for first year and then every six months thereafter.

9.8 Oral Glucose Tolerance Test

The oral glucose tolerance test (OGTT) is used in CALERIE Phase 2 to assess (a) glucose tolerance, (b) insulin action on glycemic control, and (c) the insulin secretory response to glucose ingestion. No details regarding blood draw procedures, volumes, or conditions (collection tube additives, etc.), or about sample handling after collection are provided in this section of the MOP; rather, these details are included in the “Blood Collection for Central Biochemistry Analysis” section of the MOP (section 13).

Scheduling

- The OGTTs are performed at baseline and at the 12- and 24-month time points during the study.
- OGTTs are scheduled for the morning following the first overnight stay for each time point. The OGTT should not be scheduled to occur within 96 hours (4 days) after the maximal treadmill exercise test.
- All OGTTs are scheduled to start between 6:30 and 9:30 am and after an overnight fast of approximately 12 hours.
- At the time of scheduling the OGTT, a study team member is scheduled to contact the participant 5-7 days before the OGTT appointment to verbally remind the participant to (a) refrain from structured exercise and/or unusual amounts of other physical activity during the 4 days before the test, (b) continue their normal medication and supplements regimen during the 3 days prior to the tests, and (c) to query the participant to determine if habitual carbohydrate consumption is at least 150g/day and if it is not, to advise the participant to increase carbohydrate consumption to at least 150g/day for 3 days prior to the test by eating more carbohydrate-rich foods such as bread, pasta, potatoes, fruit, and fruit juice each day.

Materials

- OGTT glucose tolerance test kit as provided by the University of Vermont laboratory
- Ice bucket with ice
- Post-test snack or meal

Procedure

Evening check-in for the overnight stay:

A study dietitian, coordinator, or GCRC nurse will meet with the participant to remind him/her to refrain from taking all medications the next morning and to assess, based on the subject’s recall, if carbohydrate intake was adequate (150g/day) for the 3 days prior to the test. If pre-test carbohydrate intake was deemed adequate, the “dietary CHO appears adequate” box is checked on the OGTT Worksheet. If carbohydrate intake was inadequate, “dietary CHO appears inadequate” box is checked and the OGTT is rescheduled.

Test:

1. Query participant about the last time they consumed anything other than water, when they last performed structured exercise or an unusually large amount of other

physical activity, and if they have current or recent (within past 3 days) symptoms of a systemic infection such as fever, swollen glands, persistent cough, etc., and whether medications and supplements were taken as usual over the past 3 days. Record details on the OGTT Worksheet. If the participant has performed structured exercise or unusual amounts of physical activity in the past 4 days, has been ill, or has not complied with the medication use guidelines as described above, the test must be rescheduled.

2. Measure oral temperature and record on the OGTT Worksheet.
3. Based on information in steps 1 and 2, if there are no current or recent symptoms of infection and oral temperature is $<38.0^{\circ}$ Celsius, check the “infection unlikely” box on the OGTT worksheet and proceed with the test. If there have been recent symptoms or there are current symptoms, or if oral temperature is $> 38.0^{\circ}$ Celsius, a physician will perform a further evaluation (including lymph node check) for signs of systemic infection. If the physician determines that an infection is likely present, the “infection likely” box will be checked on the OGTT Worksheet and the test will be rescheduled for another day.
4. Confirm that the subject did not take any medications on the morning of the test. If confirmed, check the box to indicate “participant did not take medications on morning of test” on the OGTT Worksheet. If medication was taken, test must be rescheduled.
5. Insert intravenous (IV) catheter and draw **XX** mL blood as the fasting sample and record the time of the draw on the OGTT Worksheet (see “Blood Acquisition and Handling” section of MOP for details on IV catheter insertion and care, blood acquisition, specific tube types and tube additives, draw volumes, draw order, and post-collection handling).
6. Give the participant a blanket if necessary to keep him/her warm (for blood flow and comfort purposes).
7. Administer glucose drink. Start the test timer and record the time of day on the OGTT Worksheet when the participant starts drinking the glucose beverage. The whole bottle must be consumed in < 5 minutes (ideally < 2 minutes). Record on the OGTT Worksheet if the whole 10 fl. oz. beverage was consumed or if less than 10 fl. oz was consumed (if less, also record how much was estimated to have been consumed).
8. A water “chaser” should not be provided within 30 minutes of glucose ingestion since this may dilute the glucose solution in the stomach and alter the rate of absorption.
9. At 30, 60, 90, and 120 minutes post-glucose ingestion, draw **XX** mL of blood (details provided in “Blood Acquisition and Handling” section of MOP). Record the time of day for each blood draw on the OGTT Worksheet.

Test End:

1. After the last blood sample has been drawn, discontinue IV as described in the Blood Acquisition and Handling section (section 13) of the MOP.
2. Feed the participant a snack or meal before they leave the laboratory.
3. Instruct to the participants about symptoms of hypoglycemia, what to do if they experience these symptoms, and what to do if bleeding occurs at the IV site.
 - Symptoms of hypoglycemia: sweating, shakiness, dizziness, hunger, vision disturbances, unsteadiness, tingling hands or lips, headache, and trouble with speech.
 - If symptoms of hypoglycemia occur: The participant is instructed to alert the study staff about these symptoms and to request a sugar-containing snack. If the

- notified staff member is not medically trained, he/she will contact medically trained personnel for assistance, further monitoring, and treatment.
- If bleeding at the IV site occurs: The participant is instructed to notify the study staff and apply direct pressure to the site and elevate the affected limb.

Processing of blood samples:

See “Blood Collection for Central Biochemistry Analysis” section of MOP (section 13).

Calculations

While the test-time specific values (i.e. fasting, 30”, 60”, etc.) for glucose, insulin, C-peptide, and free-fatty acids are examined individually, several calculated outcomes are also examined. The calculations for these outcomes are as follows and are performed by the Coordinating Center:

Total areas under the glucose, insulin, and C-peptide curves are calculated as follows:

$$AUC_x = 15(X_0) + 30(X_{30}) + 30(X_{60}) + 30(X_{90}) + 15(X_{120})$$

Where: AUC_x is the area under the curve for the analyte of interest (i.e. glucose, insulin, or C-peptide) in concentration units per minute and X_0 , X_{30} , X_{60} , X_{90} , and X_{120} are the concentrations of the analyte of interest at the 0-, 30-, 60-, 90-, and 120-minute OGTT time points, respectively.

An index of insulin action on glycemic control (ISI) will be calculated according to the method of Matsuda and DeFronzo (*Diabetes Care*. 1999 Sep;22(9):1462-70) as follows:

$$ISI = 10,000/\text{square root of } [\text{fasting glucose} \times \text{fasting insulin}] \times [(\text{mean of 0-, 30-, 60-, 90-, and 120-min glucose values}) \times (\text{mean of 0-, 30-, 60-, 90-, and 120-min insulin values})]$$

Quality Control

Quality control for the glucose tolerance test falls into three domains, test performance, quality control for analytic variability and quality control for biological variability. Quality control for analytic variability (for example, the degree of agreement between insulin values as measured on the same sample in different assay batches) is beyond the scope of this OGTT procedure description. For details on analytic quality control, see the MOP for the clinical laboratory analyses (MOP section 13).

Quality Control for test performance (i.e. to be sure the OGTT was properly administered) is performed by evaluating the information on the OGTT Worksheet. Specifically, the frequency of tests in which the whole glucose beverage was not consumed is tabulated every 6 months during the study and reviewed by the QC Committee. Furthermore, the frequency of blood draws that are performed more than 5 minutes early or late according to the draw schedule will be tabulated and reviewed by the QC Committee every 6 months.

Quality control for biological variability in OGTT-related outcomes is addressed by assessing and/or controlling for factors that are known to affect glucose tolerance, insulin action, and the insulin secretory response to oral glucose ingestion. The main factors of concern in this context are (a) the timing between exercise and the OGTT, (b) the presence of systemic infections, (c) the adequacy of carbohydrate intake during the days prior to the OGTT, and (d) the use of medications that affect glucoregulatory function. Each of these factors is addressed and evaluated as follows.

(a) Timing between exercise and the OGTT:

From a procedural perspective, participants are advised to refrain from structured exercise and from unusual amounts of other activities during the 4 days prior to the OGTT. On the morning of the OGTT, the participants are asked when they last performed structured exercise or unusual amounts of other activity and the responses are recorded on the data form for entry into the common CALERIE database. Allowable answers are either "> 4 days ago", or a specific number of days ago (estimated to the nearest ½ day). For reporting purposes, a report of the frequency of tests performed with < 4 days of exercise/unusual activity abstinence will be generated and reviewed.

(b) Presence of systemic infections:

Based on the procedures described above, OGTTs will only be performed if an infection is not likely present. If appropriate screening for infection has been performed and an infection does not appear to be present, the "infection unlikely" box on the OGTT Worksheet is checked. Therefore, the number of OGTTs that are performed without the "infection unlikely" box checked is tabulated and reviewed as a QC procedure.

(c) Adequacy of carbohydrate intake:

As described above, OGTTs will only be performed if carbohydrate intake for the 3 days before the OGTT was estimated to be $\Delta 150\text{g/day}$. When this was evaluated and carbohydrate intake was deemed sufficient, the "dietary CHO appears adequate" box is checked on the OGTT Worksheet. Therefore, the number of OGTTs that are performed without the "dietary CHO appears adequate" box checked on the OGTT form is tabulated and reviewed as a QC procedure.

(d) Medications that affect glucoregulatory function:

From a procedural perspective, the participants are asked to refrain from taking all medications on the morning of the OGTT until after the OGTT is complete. If the study staff confirmed this with the participant immediately prior to the start of the OGTT, the appropriate box is checked on the OGTT Worksheet. Therefore, the number of OGTTs that are performed without confirmation that no medications were taken can be tabulated and reviewed as a QC procedure.

9.9 Immune Function

9.9.1 DTH Test

Delayed-type hypersensitivity (DTH) test is conducted using the Mantoux method. Three skin test antigens including candida, trichophyton, and tetanus toxoid (plain), and a negative control (normal saline solution) is injected in a standard volume of 0.1 ml except for tetanus toxoid which is injected in a volume of 0.025 ml (0.2 LF unites per dose). All antigens are to be injected intradermally at separate sites on the volar surface of the forearm (the same side as the palm of the hand) in a clean area free of hair or acneiform. The skin on the subjects' arms is examined to measure the diameter of skin induration after 24 and 48 hours.

Exclusions

Individuals who present with any of the following conditions must be excluded from administration of the DTH test:

1. Acute or Serious Chronic diseases or any disorders associated with the immune system such as infectious diseases, asthma or active neoplastic disease.
2. Using Non-Steroids Anti-Inflammatory Drugs (NSAIDs) on a regular basis or within last 72 hours.
3. Influenza vaccination within last 3 weeks or other vaccination within last 6 weeks
4. Taken antibiotics within last 2 weeks.
5. Taking steroids greater than 10 mg/day.
6. Vaccinated with Tetanus within the last 6 weeks must not be administered Tetanus antigen.

Risks and Side Effects

Allergic reactions to these antigens resulting in severe tissue damage have not been observed in clinical studies but they are theoretically possible and might occur in persons with exquisite cellular allergy (hypersensitivity) to the specific antigen. Systemic allergic reaction may occur in some people. The symptoms of a systemic allergic reaction could include a change in the vital signs, difficulty in breathing, loss of consciousness, hives, and/or major flushing. If such reactions occur, epinephrine must be administered by the medical staff. Epinephrine might cause temporary sweating, headache, or shaking. In case of a severe allergic reaction, the study physician must be notified immediately and no subsequent test is to be administered.

In rare occasions, there is a chance of a faded scar mark left on the skin after the test. If the reaction is greater than 45 mm at any one antigen site and/or evidence of skin blisters or necrosis is present, the particular antigen are not to be planted at subsequent time points.

Precautions and emergency procedures

- If volunteer has a known systemic reaction to any of the antigens, they must not be administered the test (DTH questionnaire Q.1 D)
- The participant must stay under the observation of a medical professional for 20 minutes after the injections for signs of any allergic reactions. The study physician must be immediately notified and proper procedures need to be followed according to the physician's directions.

- Epinephrine must be available in case of a systemic allergic reaction. Administer epinephrine 1:1000, at 0.3 MG IM for severe reaction, repeat x 1.

Test Administration and Reading

Antigens must be administered and results read by a nurse practitioner or a registered nurse. For each participant, every effort should be made to have the test administered by the same nurse. Evaluation/reading of the results will be performed by the Study Manager or a back-up staff member who has the reading closest to that of the Study Manager. Please see section Training of a Back-up Staff Member below. Regardless, for every participant, the names of the person who administered the test and the person who evaluated the test results must be recorded.

1. Prior to administering the test, complete the DTH Test Questionnaire (Appendix 1).
2. On day 1, inject the following intradermally on volar surface of the arm:
 - Control: Normal Saline, 0.1 ML # 1
 - Tetanus Toxoid: 0.025 ML # 2
 - Candida: 0.1 ML # 3
 - Trichophyton: 0.1 ML # 4
3. Administer all 4 injections on the same arm in the order shown on the DTH Results Sheet (Appendix 2). Space each injection 2 inches apart and mark them with indelible ink.
4. Remind a participant not to scratch, rub or scrub area or apply anything to the test area. Exposures to water, such as showers are allowed. Also remind participants that no immunizations are allowed until the 48 hour reading (within 2 days after injections).
5. On days 2 and 3, at 24 and 48 hours after the test administration, measure any reaction for each antigen and control (normal saline) twice using the metric calipers.
6. Take an average of two measurements for each antigen. The average represents the score for that time point and that antigen and must be recorded on the DTH Results Sheet. **A positive reaction is identified by a raised, reddened circular area around the test site (induration) that exceeds 5 mm in diameter.**
7. If there is any reaction for the negative control (normal saline), take the average of two measurements. Subtract the diameter of the negative control from result for the test antigen. A skin test is positive if a reaction for the antigen is 5 mm greater than a reaction for the negative control.
8. The test area may be slightly tender, itchy or warm to the touch for 2-3 days. **Immediately notify the study physician about any breaks, bleeding, severe pain, fever or blistering.**

Quality Control Procedures

- All antigens must be held at 4 degrees Celsius. After being opened, each antigen vial could be used for a period of one month only and must be discarded after that. Each antigen usually expires within 18 months from the date of purchase. **Always check the expiration date prior to administer the antigen!**
- Since the length of study for each subject volunteer is 24 months, it is not possible to use the same antigen lot for the entire study for each participant. However, both

manufacturers of the specified antigens have indicated that there are no variations between the lots. Therefore, the antigens need to be purchased at the beginning of the study and the second lot about 18 months after the study start.

Training of a Back-up Staff Member

At study start, each site's Study Manager must identify and train a staff member who has the reading closest to that of the Study Manager by screening several available individuals. This will be achieved by following the procedures described below:

- Perform reading of the test results. Do not say the results aloud!
- Have a staff member read the results immediately after the reading was performed by you. **Please note** that diameter of the induration may increase if too many readings performed sequentially within a short period of time on the same participant. Thus, not more than one reading by one staff member in addition to that made by you could be performed on the same participant! Have as many staff members as possible going through this process on as many participants as necessary till a person who reads within $\pm 0.5 - 1.0$ mm of your reading is identified.
- Have this person perform readings on at least additional five participants. Record results of the readings. If readings by the staff member are still within $\pm 0.5 - 1.0$ mm of your readings, add this person to the Delegation of Responsibilities Log (if not already listed) or add the "DTH Reading" to list of responsibilities assigned to this staff member.
- Document the trainee's reading results at 24 and 48 hours on at least five participants on a separate copy of the DTH Results sheet and sent these sheets to the CC. The CC will review and compare the trainees reading results with those done by the Study Manager and documented on the CRFs and will grant certification to the trainee.
- Once the CC has confirmed trainee's certification, their name must be added to the Delegation of Responsibilities Log. The sites need to provide a copy of the updated Delegation of Responsibilities Log to the CC.

9.9.1.1 Appendix 1 – DTH Test Questionnaire

DTH TEST QUESTIONNAIRE

DATE: _____ Day of Study _____ DTH # 1 2 3

Vital Signs: pulse rate _____ Blood Pressure _____ Temp. _____
(Do not administer if vital signs are not normal for the individual. Temp. higher than 100 is considered fever. Pulse rate is too high if greater than 90. If vital signs are not within normal range, it would be up to the physician to determine if they can proceed with the test.)

MEDICATIONS: _____ SUPPLEMENTS: _____

If yes to #2 3, 4, 5, 6, 7, or 8..... <VOLUNTEER NOT ELIGIBLE FOR SKIN TESTING
If yes to #9, #10..... <Do not administer Tetanus or the specific antigen

ALLERGIES: _____ (ALLERGY TO EGGS, MERCURY, THIMEROSAL, LATEX CANNOT Receive DTH).

1. HAVE YOU EVER HAD A SKIN TEST IN THE PAST? YES ___ NO
A. If Yes, When _____ Why
B. If Yes, Please List Positive Results:
C. If Yes, Site Planted
D. If yes, any allergic reactions? YES _____ NO _____

Note: Do not administer test in case of past allergic reactions.

2. HAVE YOU HAD A FEBRILE ILLNESS AND/OR INFECTION WITHIN THE PAST 2 WEEKS?

A. If Yes, Please Indicate

3. HAVE YOU TAKEN ANY STEROIDS (oral or parenteral) 10mg/DAY WITHIN THE PAST MONTH?

(Topical and inhaled OK) YES ___ NO
A. If Yes, Please List

4. ANY ANTIBIOTICS IN LAST THREE WEEKS YES ___ NO

5. ANY ASA/NSAID=s/ANTIHISTAMINES IN LAST 72 HOURS: YES ___ NO

6. ANY HISTORY DM, CAD, HEART DISEASE, AIDS, CA, SUBSTANTIAL RECENT UNEXPLAINED WEIGHT LOSS YES ___ NO

7. HISTORY OF ANAPHYLAXIS WITH UNKNOWN CAUSE, SEVERE ALLERGIES, ASTHMA YES ___ NO

8. ANY IMMUNIZATION WITHIN LAST 6 WKS/FLUSHOT WITHIN 3 WKS? YES ___ NO

Note: Tetanus test will not be administered if vaccinated within 6 weeks from DTH test date.

9. ADVERSE REACTION TO TETANUS VACCINE? YES ___ NO

10. SPECIFIC ANTIGEN ALLERGY YES ___ NO
If yes, ID _____ and DO NOT PLANT.

COMMENTS:

RN Signature _____ Date

9.9.1.2 Appendix 2 – DTH Results Sheet

DTH Results Sheet: Calorie Restriction Study

Subject name:

Subject ID #:

Age:

Sex:

Antigens	Test 1							Test 2							Test 3									
	Injection Date / /	24 hr			48 hr			Injection Date / /	24 hr			48 hr			Injection Date / /	24 hr			48 hr					
	Injection By:	Diameters (mm)							Injection By:	Diameters (mm)							Injection By:	Diameters (mm)						
	Read By:	A	B	Ave	A	B	Ave	Read By:	A	B	Ave	A	B	Ave	Read By:	A	B	Ave	A	B	Ave			
1. Control																								
2. TT																								
3. Candida																								
4. Trichoph																								
Scoring: No. of positive Antigens Sum of Average																								

Arm (please circle): R L

Med Lat	1	4
	2	
	3	
	proximal	

Arm (please circle): R L

Med Lat	1	4
	2	
	3	
	proximal	

Arm (please circle): R L

Med Lat	1	4
	2	
	3	
	proximal	

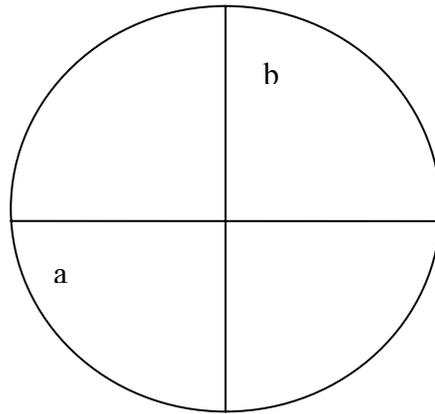
Notes:

For each reaction, measure two diameters in mm and take the average. The first diameter is called the maximum diameter because the induration may not be in the shape of a circle. If the induration is an oval shape, first measure the long diameter (a) and then the diameter perpendicular to it (b). Do not measure erythema.

Reaction is considered positive if the average diameter is equal to or greater than 5 mm.

a = Largest diameter

b= second diameter perpendicular to a



9.9.2 Antibody Response to Vaccines

9.9.2.1 Hepatitis A Vaccination

The hepatitis A vaccination (HAVRIX® or VAQTA®) is performed at month 17. The first vaccine injection is followed by one booster shot at month 23. The vaccine must be administered intramuscularly, preferably in the deltoid muscle.

Exclusions

- Persons with anaphylactic reaction to a previous dose or to neomycin are to be excluded from receiving the vaccine and/or the boosters.
- Any acute or serious chronic diseases or any disorders associated with the immune system such as infectious diseases, asthma or active neoplastic disease.
- Do not administer to persons at risk of hemorrhage caused by intramuscular injection (in this case, consult study physician for possibility of subcutaneous administration).

Precautions and emergency procedures

- Do not administer IV or intradermally.
- Store vaccines in refrigerator (2 to 8 degrees C). Do not freeze.
- Do not use vaccine past expiration date.
- The participant must stay under the observation of a medical professional for 20 minutes after the injections for signs of any allergic reactions. The study physician must be immediately notified and proper procedures need to be followed according to the physician's directions.
- Epinephrine must be available in case of a systemic allergic reaction. Administer epinephrine 1:1000, at 0.3 MG IM for severe reaction, repeat x 1.

Procedure

Vaccination is to be performed by a nurse practitioner or a registered nurse.

1. Administer 1 ml single-dose vial hepatitis A vaccine provided by the study (1 ml single-dose vial of HAVRIX containing 1440 EI.U or 1 ml single dose vial of VAQTA containing 50 U).
2. Verify that vaccination questionnaire has been filled before vaccine administration (Appendix 1).
3. Shake vaccine vial before using.
4. Administer vaccine into upper arm muscle, preferably in the deltoid muscle.
5. Make sure that the needle does not enter blood vessel.
6. Record vaccine and administrator information in the Vaccination Data Sheet (form attached)

Safety

The Hepatitis A vaccine has been used by the medical and public health communities as a safe and effective way to prevent the Hepatitis A disease. As with any medicine, there are small risks associated with the Hepatitis A vaccine as explained in the Risks/Side Effects section for all vaccines.

9.9.2.2 Tetanus/Diphtheria (TD) Vaccination

Tetanus/diphtheria DECAVAC (Aventis Pasteur) vaccine is to be administered at month 17. The vaccine must be administered intramuscularly.

Exclusions

- Persons who experienced allergic reaction or temperature greater than
- 39.4° C (103° F) to a previous dose of the TD vaccination
- Persons who are allergic to latex rubber
- Persons with bleeding disorders such as hemophilia (in this case, consult study physician for possibility of subcutaneous administration).
- Persons with previous adverse or allergic reaction after the administration of either vaccine

Precautions and emergency procedures

- The vaccine should not be injected into the gluteal area or areas where there may be a major nerve trunk.
- Store vaccines in refrigerator (2 to 8 degrees C). Do not freeze.
- Do not use vaccine past expiration date.
- The participant must stay under the observation of a medical professional for 20 minutes after the injections for signs of any allergic reactions. The study physician must be immediately notified and proper procedures need to be followed according to the physician's directions.
- Epinephrine must be available in case of a systemic allergic reaction. Administer epinephrine 1:1000, at 0.3 MG IM for severe reaction, repeat x 1.

Procedure

Vaccination is to be performed by a nurse practitioner or a registered nurse.

1. Verify that vaccination questionnaire has been filled before vaccine administration (Appendix 1)
2. Shake the vial well for uniform distribution of the suspension before withdrawing for vaccine administration
3. Inject 0.5 mL intramuscularly in the area of the vastus lateralis (mid-thigh laterally) or deltoid muscle.
4. Make sure that the needle does not enter blood vessel
5. Record vaccine and administrator information in the Vaccination Data Sheet (form attached)

Safety

The TD vaccine has been used by the medical and public health communities as a safe and effective way to protect against tetanus and diphtheria. As with any medicine, there are small risks associated with the TD vaccine as explained in the Risks/Side Effects section for all vaccines.

9.9.2.3 Pneumococcal Vaccine

A standard dose of the pneumococcal vaccine PNU-Immune® 23, polyvalent (23-valent) is to be administered at month 17 (single 0.5 ml dose). The vaccine is to be administered intramuscularly, preferably in the deltoid muscle.

Exclusions

- Persons who have received previous vaccination with any polyvalent pneumococcal vaccine
- Persons with bleeding disorders such as hemophilia (in this case, consult study physician for possibility of subcutaneous administration).
- Persons with previous adverse or allergic reaction to the vaccine or any component of the vaccine including thimerosal, a mercury derivative

Precautions and emergency procedures

- Do not administer vaccine IV or intradermally.
- Store vaccines in refrigerator (2 to 8 degrees C). Do not freeze.
- Do not use vaccine past expiration date.
- The participant must stay under the observation of a medical professional for 20 minutes after the injections for signs of any allergic reactions. The study physician must be immediately notified and proper procedures need to be followed according to the physician's directions.
- Epinephrine must be available in case of a systemic allergic reaction. Administer epinephrine 1:1000, at 0.3 MG IM for severe reaction, repeat x 1.

Procedure

Vaccination is to be performed by a nurse practitioner or a registered nurse.

1. Verify that vaccination questionnaire has been filled before vaccine administration (Appendix 1)
2. Shake the vial well before withdrawing suspension
3. Use standard dose for the pneumococcal vaccine per package insert
4. Injection is administered into upper arm muscle, preferably in the deltoid muscle.
5. Special care should be taken to prevent injection into a blood vessel.
6. Record vaccine and administrator information in the Vaccination Data Sheet (Appendix 2).

Safety

The pneumococcal valent-23 vaccine has been used by the medical and public health communities to reduce the risk of pneumococcal disease. As with any medicine, there are small risks associated with this vaccine as explained in the Risks/Side Effects section for all vaccines.

9.9.2.4 Important Information for All Study Vaccines

General Exclusions

Persons with the following conditions will be excluded from receiving vaccinations:

- Persons with a history of allergic reaction to a previous administration of the vaccines or their components
- Persons with a moderate or severe acute illness
- Serious chronic diseases or any disorders associated with the immune system such as infectious diseases, asthma or active neoplastic disease.
- Using Non-Steroids Anti-Inflammatory Drugs (NSAIDs) on a regular basis or within last 72 hours
- Persons with any vaccinations within last 6 weeks
- Taken antibiotics within last 2 weeks
- Presently taking steroids greater than 10 mg/day
- Presently taking any type of immunosuppressive medication
- Persons with history of vaccine sensitivity, previous vaccination-related adverse reaction
- Persons with bleeding or coagulation disorders cannot receive the intramuscular injections for the vaccines

Risks/Side Effects

The injections can result in localized soreness, redness, swelling, pain, or warmth. Other temporary side effects may include fever, fatigue, myalgia, malaise, anorexia, nausea, rash, weakness, headache, sore throat, or general body discomfort. Mild effects on the digestive system such as nausea and diarrhea have been reported. If the symptoms last or become worse, the study physician must be contacted. Anaphylactic reactions to all three vaccines are rare but possible. A systemic allergic reaction can result in drop in blood pressure, hives, itching, reddening of the skin, difficulty in breathing, sudden and severe weakness, and/or swelling. If such reactions occur, epinephrine (1:1000) will be administered by the medical staff. Epinephrine might cause temporary sweating, headache, or shaking. In case of a severe allergic reaction, the study physician and PI will be notified immediately and no subsequent test will be administered.

Quality Control Procedures

All vaccines must be stored at 4 degrees Celsius. The vaccines do not contain preservatives, therefore, after being opened, each vaccine vial will be used promptly and will be discarded after that. Vaccines are to be ordered close to the 21 months time point, in order to make sure that they can be used before the expiration dates. All vaccine information such as lot number, manufacturer, and relevant dates must be recorded in each participant's file.

9.9.2.5 Appendix 1 – Vaccination Questionnaire

PROTOCOL # _____
VACCINATION QUESTIONNAIRE

DATE: _____ Day of Study _____ Subject ID _____ Subject Name _____

Vital Signs: pulse rate _____ Blood Pressure _____ Temp. _____
(Do not administer if vital signs are not normal for the individual. Temp. higher than 100 is considered fever. Pulse rate is too high if greater than 90. If vital signs are not within normal range, it would be up to the physician to determine if they can proceed with the vaccination.)

MEDICATIONS: _____ SUPPLEMENTS: _____

ALLERGIES: _____ (ALLERGY TO YEAST
CANNOT RECEIVE HA VACCINE)

If yes to #1,2 3, 4, 5, 6..... <VOLUNTEER NOT ELIGIBLE FOR VACCINATION

If yes to #7..... <If previously vaccinated for Hepatitis A and/or Pneumococcal vaccine, do not administer those vaccines>

If yes to #8, 9, 10..... <Do not administer the specific allergy-causing vaccines>

1. HAVE YOU HAD A FEBRILE ILLNESS AND/OR INFECTION WITHIN THE PAST 2 WEEKS?

A. If Yes, Please Indicate

2. HAVE YOU TAKEN ANY STEROIDS (oral or parenteral) 10 mg/DAY WITHIN THE PAST MONTH?

(Topical and inhaled OK)

YES ___ NO

A. If Yes, Please List

3. ANY ANTIBIOTICS IN LAST THREE WEEKS YES ___ NO

4. ANY ASA/NSAIDs/ANTIHISTAMINES IN LAST 72 HOURS: YES ___ NO

5. ANY HISTORY DM, CAD, HEART DISEASE, AIDS, CA, SUBSTANTIAL RECENT UNEXPLAINED WEIGHT LOSS YES ___ NO

6. HISTORY OF ANAPHYLAXIS WITH UNKNOWN CAUSE, SEVERE ALLERGIES, ASTHMA YES ___ NO

7. ANY IMMUNIZATION WITHIN LAST 6 WKS? YES ___ NO

A. If Yes, Please List

8. ADVERSE REACTION TO DIPHTHERIA/TETANUS VACCINE? YES ___ NO

9. ADVERSE REACTION TO HEPATITIS A VACCINE? YES ___ NO

10. ADVERSE REACTION TO PNEUMOCOCCAL VACCINE? YES ___ NO

RN Signature _____ Date _____

9.9.2.6 Appendix 2 – Vaccination Sheet Source

CALERIE PHASE II
VACCINATION DATA SHEET

Date _____ Day of Study _____

Subject Name _____ Subject ID _____

Note: Check vaccination questionnaire and protocol before administering vaccines

I. 1.0 ml Hepatitis A (Recombivax HB)

_____ # 1 Lot # _____ Expiration Date _____
Date

Administered by _____

_____ # 2 Lot # _____ Expiration Date _____
Date

Administered by _____

_____ # 3 Lot # _____ Expiration Date _____
Date

Administered by _____

II. Tetanus/Diphtheria (TD) Lot # _____ Expiration Date _____

_____ Administered by _____
Date

III. Pneumococcal Vaccine, polyvalent

Lot# _____ Expiration Date _____

_____ Administered by _____
Date

9.10 Quality of Life and Psychological Assessments

This MOP section describes procedures that the study staff members need to follow to administer quality of life and psychological tests. These tests should be administered in the order presented in this MOP section. The two batteries of tests should be administered in two sessions. Each session should be approximately 1.5 hours. This schedule of administration is designed to prevent fatigue. These two sessions do not have to be administered on the same day but if they are they should be separated by at least a 30 minute break. These measures should not be administered on days with other procedures that may interfere with the outcome of these measures, e.g. measures that induce pain or fatigue (biopsies, VO2 max). Measurements should be made in the postprandial state, 0.5 to 3 hours after the last meal for consistency and out of concern that fluctuating hunger may influence some of the craving and mood questions. There is no specific time in which these measures should be given; however, they should be given at the same time each measurement period to maintain consistency between assessment periods.

9.10.1 Quality of Life Measures (Battery 1)

Quality of life assessment procedures are completed at Baseline, Months 6, 12, and 24. The site measurement technician(s) will administer the questionnaires.

Tests to be Performed

- Rand SF-36
- Profile of Moods State
- Perceived Stress Scale

Conditions for Tests Administration

- A quiet, comfortable room without distracting stimuli.
- An adequate writing surface.
- Assessment should not be administered during a fasting state and they should not be administered following invasive measurement procedures or procedures that might have induced physical pain.

Instructions for the Participant

- Use the pencil provided by the technician.
- Answer all questions in the order in which they appear on the questionnaire.
- If you need to make a correction, cross the wrong answer, put your initial and date next to the line, and then mark the correct answer.
- If you have any questions, please do not hesitate to ask them.
- Initial and date each page of the questionnaire that you have completed.
- Please let the measurement technician know if you need a break to visit the restroom or get a drink of water during testing, but try to do your best to complete the measure in its entirety before taking a break.

- All the questionnaires for the battery should be completed prior to going to the other battery. Participants should not complete questionnaires from different batteries interchangeably.

Roles and Responsibilities

Measurement Technician

- Provide a participant with the questionnaires and a Number 2 pencil.
- Explain how to complete the questionnaires (please see “Instructions for the Participant” above).
- Ask whether a participant has any questions and if yes, answer them.
- Remain available throughout the assessment period to answer any questions that participant may have.
- If a participant has difficulty to understand some particular question, explain the meaning of that question but **do not lead a participant to select a particular answer to a questions.**
- Review each questionnaire for completeness. Have the participant complete any unanswered questions.
- If a participant answers any questions with two responses, the administrator should ask which answer is most accurate.
- Initial and date the last page of each complete questionnaire after you reviewed them.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.

Quality Control Procedures

- Review each questionnaire for completeness.
- Have the participant complete any unanswered questions!
- If the participant has any scratched out answers or multiple answers, please review those questions with the participant.
- Any additions, changes, or deletions should be initialed and dated by the Measurement Technician at the time of the completion of the questionnaire measure.
- Once the measure is checked again for completeness, make a photocopy of the questionnaire.
- Place the original questionnaire in the participant’s chart and the photocopy in the appropriate place to be mailed to the coordinating center.

9.10.1.1 Scoring the Questionnaires

Scoring the questionnaires

The questionnaires will be integrated with the CRF and completed by the participants. The sites will submit completed CRFs to the CC for data entry in accordance with the standard data entry procedures. All scoring will be completed by the CC in SAS using the defined algorithms and subscores specific to the instrument. However, described below are the general scoring procedures for the measures. Further, for the measures

that will be scored on site for safety reasons, e.g., the MAEDS and the BDI-II, more detailed scoring information is presented in this MOP.

Rand SF-36:

The Rand Short Form with 36 items (SF-36) has eight subscales: physical functioning, role limitations due to physical problems, role limitations due to emotional problems, vitality, bodily pain, social functioning, mental health, and general health perceptions. The SF-36 is scored so that higher scores are indicative of better health functioning. The questions and scales are then scored in a series of steps. Step 1: item recoding, for the 10 questions that require recoding. Step 2: scales scored are computed by summing across questions in the same scale (raw scale scores). Step 3: raw scores are then transformed to a 0-100 scale (producing transformed scale scores).

For additional information regarding reliability and validity and for scoring procedures, consult the "SF-36 Health Survey Manual and Interpretation Guide" (Ware, Kosinski, & Gandek, 2002)

Profile of Mood States:

Profile of Mood States (POMS) is an adjective checklist of 65 items rated on a five-point scale that ranges from (1) "not at all" to (5) "extremely". Six subscales are derived from the POMS: anxiety-tension, depression-dejection, anger-hostility, fatigue-inertia, vigor-activity and confusion-bewilderment. The subscales are combined to calculate a total mood disturbance score. Each mood factor receives an individual score by summing the responses for adjectives that define the factor. Throughout the POMS, all items are scored in the same direction with the exception the following: "Relaxed" in the Tension-Anxiety Scale and "Efficient" in the Confusion Scale. These questions are to be weighted negatively when calculating factor scores. To obtain a Total Mood Disturbance Score, sum the scores (weighting "Vigor" negatively) on the six primary mood factors. Hence, after adding together the five scores received for Tension, Depression, Anxiety, Fatigue, and Depression, the score received for vigor is subtracted. For validity and reliability information and additional scoring criteria, reference the manual "Profile of Mood States" (McNair & Heuchert, 2003).

Perceived Stress Scale:

The Perceived Stress Scale (PSS), a four-item questionnaire that is administered to assess perceived changes in stress during a period of prolonged caloric restriction. To calculate PSS scores, one must first calculate reverse responses (e.g. 0=4, 1=3, 2=2, 3=1, & 4=0) to the four positively stated questions (items # 4, 5, 7, & 8). The items are then added across all questions. If desired, a short 4 item scale can be obtained from questions 2, 4, 5, and 10 of the 10 item questionnaire. For validity and reliability information and additional scoring criteria, reference Cohen, Kamarck, & Mermelstein, 1983.

Data for the Questionnaires

At baseline and following visits, the research centers will make a copy of a printout of the questionnaire data, retain the original, and send the copy to the coordinating center. The coordinating center will then enter the data into the study database at the CC.

9.10.2 Psychological Assessments (Battery 2)

Psychological assessment procedures are completed at Baseline, Months 6, 12, and 24. The site measurement technician(s) will perform the assessments.

Tests to be Performed

- Pittsburgh Sleep Quality Index
- Derogatis for Sexual Functioning-Self Report
- Food Craving Questionnaire
- Food Craving Inventory
- Eating Inventory/Three Factor Eating Questionnaire
- Weight Efficacy Lifestyle Questionnaire
- Multiaxial Assessment of Eating Disorder Symptoms
- Body Shape Questionnaire

Conditions for Tests Administration

- A quiet, comfortable room without distracting stimuli.
- An adequate writing surface.
- Assessment should not be administered during a fasting state and they should not be administered following invasive measurement procedures or procedures that might have induced physical pain.

Instructions for the Participant

- Use the pencil provided by the technician.
- Answer all questions in the order in which they appear on the questionnaire.
- If you need to make a correction, cross the wrong answer, put your initial and date next to the line, and then mark the correct answer.
- If you have any questions, please do not hesitate to ask them.
- Initial and date each page of the questionnaire that you have completed.
- Please let the measurement technician know if you need a break to visit the restroom or get a drink of water during testing, but try to do your best to complete the measure in its entirety before taking a break.
- All the questionnaires for the battery should be completed prior to going to the other battery. Participants should not complete questionnaires from different batteries interchangeably.

Roles and Responsibilities

Measurement Technician

- Provide a participant with the questionnaires and a Number 2 pencil.
- Explain how to complete the questionnaires (please see “Instructions for the Participant” above).
- Ask whether a participant has any questions and if yes, answer them.
- Remain available throughout the assessment period to answer any questions that participant may have.

- If a participant has difficulty to understand some particular question, explain the meaning of that question but **do not lead a participant to select a particular answer to a questions.**
- Review each questionnaire for completeness. Have the participant complete any unanswered questions.
- If a participant answers any questions with two responses, the administrator should ask which answer is most accurate.
- Initial and date the last page of each complete questionnaire after you reviewed them.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.

Quality Control Procedures

- Review each questionnaire for completeness.
- Have the participant complete any unanswered questions!
- If the participant has any scratched out answers or multiple answers, please review those questions with the participant.
- Any additions, changes, or deletions should be initialed and dated by the Measurement Technician at the time of the completion of the questionnaire measure.
- Once the measure is checked again for completeness, make a photocopy of the questionnaire.
- Score the MAEDS. Follow directions in safety MOP sections if safety is indicated. Place the original questionnaire in the participant's chart and the photocopy in the appropriate place to be mailed to the coordinating center.
- Place the original other questionnaires in the participant's chart and the photocopies in the appropriate place to be mailed to the coordinating center.

9.10.2.1 Scoring the Questionnaires

The questionnaires will be integrated with the CRF and completed by the participants. The sites will submit completed CRFs to the CC for data entry in accordance with the standard data entry procedures. All scoring will be completed by the CC in SAS using the defined algorithms and subscores specific to the instrument. However, described below are the general scoring procedures for the measures. Further, for the measures that will be scored on site for safety reasons, i.e. the MAEDS and BDI-II, more detailed scoring information is presented in this MOP.

Pittsburgh Sleep Quality Index (PSQI):

The Pittsburgh Sleep Quality Index (PSQI) is a nineteen- item questionnaire that yields seven subscale scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction) and one total score. Only self-rated questions are included in the scoring. The 19 self-rated items are combined to form seven "component" scores, each of which has a range of 0-3 points. In all cases, a score of "0" indicates no difficulty, while a score of "3" indicates severe difficulty. The seven component scores are then added to yield one "global" score, with a range of 0-21 points, "0" indicating no difficulty and "21" indicating severe difficulties in all areas.

Derogatis Interview for Sexual Functioning Self-Report:

The Derogatis Interview for Sexual Functioning-Self Report (DISF-SR) is a reliable and valid measure of sexual functioning for men and women with different parallel forms for each gender. The DISF-SR has five subscales (sexual cognition and fantasy, sexual arousal, sexual behavior and experience, orgasm, sexual drive and relationship) and a total score is derived.

Food Craving Questionnaire:

The Food Craving Questionnaire (FCQ) was developed to measure trait (generalized) and state (at the moment) craving for food. The 39-item Trait FCQ measures a general susceptibility to craving foods and is administered only at baseline. The 15-item State FCQ measures the strength of food cravings at the moment of administration and is administered at baseline and every six months during the study. Scoring is based on a 5 point Likert-scale that assesses the level of self-reported food craving. For additional information, consult Cepeda-Benito, Gleaves, Williams, & Erath, 2000.

Food Craving Inventory:

The Food Craving Inventory is a 28-item self-administered measure designed to assess the subjective experience of specific food craving across 28 different foods. The measure consists of 4 scales: high fats, sweets, carbohydrates/starches, and fast food fats. The FCI is scaled in a frequency format assessing the frequency of an individual experiencing a craving for a particular food. All items are scored as: Never = 1, Rarely = 2, Sometimes = 3, Often = 4, Always = 5. A total score is derived for each of the four scales. For additional information regarding validity and reliability and scoring procedures, reference White, Whisenhunt, Williamson, Greenway, & Netemeyer, 2002.

Eating Inventory or Three Factor Eating Questionnaire:

The Three Factor Eating Questionnaire (more recently called the Eating Inventory) assesses dietary restraint, disinhibition, and perceived hunger. The questionnaire produces three scores for the three subscales: Dietary Restraint, Disinhibition, and Perceived Hunger. A total score is not computed. For all three subscales, the higher number indicates the greater levels of restraint, disinhibition, and/or perceived hunger. Scoring will result in three factor scales of the Eating Inventory (1) cognitive restraint of eating, (2) disinhibition, and (3) hunger. For additional information regarding scoring, refer to the "Eating Inventory Manual" (Stunkard & Messick, 1988).

Weight Efficacy Life-Style Questionnaire

The Weight Efficacy Life-Style Questionnaire is composed of 20 items and is intended to measure categories of efficacy for weight management. The hypothesized categories are the following: availability, negative emotions, physical discomfort, positive activities, and social pressure. Each scale has four items and each is scored utilizing a 10 point Likert-type scoring system. Participants are asked to rate their belief in their ability to resist overeating in 20 situations, with higher scores being representative of greater confidence. The range of possible scores (summed) on each scale is 10 to 40.

Multiaxial Assessment of Eating Disorder Symptoms:

Note: This measure will be scored by hand on site

The Multiaxial Assessment of Eating Disorder Symptoms (MAEDS) is a self-report inventory that measures the six symptom domains related to eating disorders: binge eating, restrictive eating, purgative behavior, fear of fatness, avoidance of forbidden foods, and depression. Additional information can be found in Anderson, Williamson, Duchmann, Gleaves, & Barbin, 1999.

This self-report questionnaire is composed of 56 items that question food and mood related behaviors. For each statement, the participant chooses how much a comment relates to him/her along a seven point scale from “never” to “always”. When scoring the MAEDS, each item corresponds to a particular subscale. After the participant has answered all items, the clinician sums all items and a raw score is obtained; the raw score is then converted to a t-score and evaluated for clinical significance based on a normative population

Following is a detailed scoring method for the MAEDS:

For each response, “never”= 1, “very rarely”= 2, “rarely”=3, “sometimes”=4, “often”=5, “very often”=6, and “always”=7. For reverse scored items, “never”= 7, “very rarely”= 6, “rarely”=5, “sometimes”=4, “often”=3, “very often”=2, and “always”=1.

For the Depression subscale, sum item numbers 2, 11 (reversed), 12 (reversed), 13, 16, 24, 29, 30, 33, 39, and 51

For the Binge Eating subscale, sum item numbers 5, 19, 17, 22, 26, 27, 48, 49, and 54

For the Purgative Behavior subscale, sum item numbers 6, 9, 15, 17, 21, 35, and 37

For the Fear of Fatness subscale, sum item numbers 7, 20, 23 (reversed), 25, 28, 36, 40, 43, 47, 55, and 56 (reversed)

For the Restrictive Eating subscale, sum item numbers 1, 3, 14, 32 (reversed), 42, 44, 45, 50, and 53

For the Avoidance of Fear Foods subscale, sum item numbers 4, 8, 10, 18, 31, 34, 38, 41, 46, and 52

After getting the sums for each subscale, t-scores will be looked up on a table provided for each subscale.

Body Shape Questionnaire:

The Body Shape Questionnaire (BSQ) used in this study is an 8-item shortened form of the BSQ that measures global appearance satisfaction, as well as the experience of “feeling fat.” Questions are presented with a 6-point Likert scale response format ranging from 1 (“never”) to 6 (“always”). Responses are summed, with higher responses being indicative of greater presence of eating disorder symptomology. For additional information, reference Cooper, Taylor, Cooper, & Fairburn, 1987.

Data for the Questionnaires

At screening (this will only include the MAEDS and Eating Inventory), the individual research centers will score the measures and retain the data. At baseline and following visits, the research centers will make a photocopy of a printout of the questionnaire data, retain the original, and send the copy to the coordinating center. The coordinating center will then enter the data into the database at the CC.

References

Anderson, D. A., D. A. Williamson, et al. (1999). "Development and validation of a multifactorial treatment outcome measure for eating disorders." Assessment 6(1): 7-20.

Buysse DJ, Reynolds CF, Monk TH, Merman SR, Kupfer DJ. The Pittsburg Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.

Cepeda-Benito, A., D. H. Gleaves, et al. (2000). "The development and validation of the State and Trait Food-Cravings Questionnaires." Behavior Therapy 31: 151-173.

Cohen, S., T. Kamarck, et al. (1983). "A global measure of perceived stress." J Health Soc Behav 24(4): 385-96.

Cooper, P. J., Taylor, M. J., Cooper, Z., & Fairburn, C. G. (1987). "The development and validation of the Body Shape Questionnaire." International Journal of Eating Disorders 6: 485-494.

McNair, D. M., M. Lorr, et al. (1992). POMS Profile of Mood States: Manual. North Tonawanda, NY.

Stunkard, A. J. and S. Messick (1988). Eating Inventory Manual (The Psychological Corporation). San Antonio, TX, Harcourt Brace & Company.

Ware, J. E., Jr., M. Kosinski, et al. (1993, 2002). SF-36 Health Survey: Manual & Interpretation Guide. Lincoln, RI, QualityMetric Incorporated.

White, M. A., B. L. Whisenhunt, et al. (2002). "Development and validation of the food-craving inventory." Obes Res 10(2): 107-14.

9.10.3 Tests for Monitoring for Eating Disorders

Eating disorder assessments are performed at Screening, baseline, Months 3, 6, 12, 18 and 24. These assessments are study exclusion criteria and on-study safety measures and will thus be scored by the research team at the sites before sending data to the Coordinating Center for data entry into the CALERIE database. The site measurement technician(s) will perform the MAEDS and BAM assessments and site measurement leader or clinical psychologist will conduct the IDED-IV semi-structural interview. **The assessments should be scheduled at the same time of day and in the same conditions at each time point!** This controls for temporal factors such as time of day, hunger, etc.

Note: The IDED-IV is administered only if BAM and / or safety alerts indicate a need for its administration.

Note: The BAM, MAEDS may only be administered by trained measurement technicians so that they can monitor for the appropriate safety alerts. The IDED-IV may only be given by an appropriately trained measurement technician, clinical psychologist, or the site measurement leader.

Tests and Order in which the measures must be Performed

- Body Acceptability Morph (BAM).
- The Multiaxial Assessment of Eating Disorder Symptoms (MAEDS).
- Interview for the Diagnosis of Eating Disorders (IDED-IV) - administered when MAEDS and/or BAM indicates possible eating disorder.

9.10.3.1 BAM

The BAM is a computerized body image measure designed to assess the acceptability of body size estimates. The BAM utilizes a computer “morph” movie of a human body. This measure consists of several morph movies that are distinguished between gender and race (i.e. White female, White male, Black female, Black male). The image of the human body that is utilized with each subject is an image that matches the subject’s race and gender. The BAM measures very small increments of changes in body size estimation. The morph demonstrates the transformation of an exceptionally thin body into an obese body.

Phase I: Phase I of the test asks the participant to select their perceptions of their current and ideal body sizes in a random order. One trial for each selection starts thin and one will begin overweight. This part of the assessment also assesses the current/ideal discrepancy, indicating body size dissatisfaction.

Phase II: Phase II of the test includes acceptability ratings for several different body sizes. Part 1 includes acceptability ratings for a normal body size. Part 2 includes acceptability ratings for the participant’s individual predicted body size after weight loss at 6 months and 1 year’s time. Part 3 includes acceptability ratings for an extremely low body size.

Conditions for BAM Administration

- A quiet, comfortable room without distracting stimuli.
- A laptop or desktop computer with appropriate software installed.
- Assessment should not be administered during a fasting state and if should not be administered following invasive measurement procedures or procedures that might have induced physical pain.
- Once the software is installed and running properly (see data MOP sections), there is no need for software testing and maintenance actions required by measurement technicians.

Instructions for the Participant

Instructions for the BAM are on board the BAM program. The BAM program is a self-administered program. The measurement technician does not have to read any instructions to the participant.

- Please read all of the instructions on the screen carefully and do your best to follow the instructions carefully.
- Please ask questions if you do not understand any of the instructions given by the computer program.

Roles and Responsibilities

Measurement Technician

- Position a participant in front of a computer screen. Make him/her feel comfortable.
- Begin by double clicking on the desktop icon to start the program.
- Explain how to use the software (please see “Instructions for the Participant” above).
- Ask whether a participant has any questions and if yes, answer them.
- Remain available throughout the assessment period to answer any questions that the participant may have.
- After the participant completes the test, the computer will prompt you to enter the safety password (“ALERT”) to retrieve any safety alerts and/or screening alerts for that participant (please see BAM Screening and Safety Alerts below for alert types) in the event that the participant received any. If a participant receives no alerts, then there will be no prompt.
- If the BAM is indicative of a need for further assessment for an eating disorder, immediately inform the site measurement leader.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.

BAM Screening Alerts

Screening alert for the Barriers Interview: This alert will ONLY occur at screening. After screening, the only alerts possible will be for the IDED-IV (see below). The Barriers Semi-Structured Interview Question #6 will be readministered (if already given) and/or strongly queried (if not already given) to further assess an individual’s acceptability of a potential smaller body size they may obtain in the CALERIE study. The Barriers will be given if a person reports unacceptability in response to the viewed predicted body sizes after weight loss that they are shown on the BAM.

BAM Safety Alerts

Safety alert for the IDED-IV: The IDED-IV will be administered if participants report body image disturbance on the Body Acceptability Morph (BAM), defined as: 1) scoring 2 standard deviations or more above the mean on the Current Body Size scale of the BAM (2 SDs is equal to a t -score of 70, these people view their body as larger than it actually is), and/or 2) scoring two SDs or more below the mean (t -score < 30) on the Ideal Body Size scale (these people desire an ideal body size that is excessively small), and/or 3) confirming acceptability of the extreme ideal body size shown to the participant in the

acceptability phase (phase II) of the measure. If a participant meets any of these criteria on the BAM, the measurement technician will be prompted by the computer program that a safety alert for the IDED-IV is present.

Once the participant has completed the program, the measurement technician is prompted to put in a safety password,("ALERT"), that will retrieve alerts, if any.

Scoring the BAM

A computer program has been written to automatically score the BAM. Data obtained from the BAM includes:

1. Raw and standardized scores (norms) for perceived Current and Ideal body size (CBS, IBS)
2. Discrepancy score for body dissatisfaction: Current- Ideal (CBS-IBS)
3. Acceptability ratings for a derived "Normal" body size
4. Acceptability ratings for derived "Predicted" body sizes at 6 months and 2 years
5. Acceptability ratings for a derived "Extreme Ideal" body size
6. Differences between derived "Normal" and "Predicted" acceptability ratings

Data for the BAM

At screening, the individual research centers will score the BAM and retain the data. At baseline and following visits, the research centers will make a photocopy of a printout of the BAM data, retain the original, and send the copy to the coordinating center. The coordinating center will then enter the data into the study database at the CC.

9.10.3.2 MAEDS

The MAEDS is a self-report inventory that measures the six symptom domains related to eating disorders: binge eating, restrictive eating, purgative behavior, fear of fatness, avoidance of forbidden foods, and depression.

Conditions for MAEDS Administration

- A quiet, comfortable room without distracting stimuli.
- An adequate writing surface.
- Assessment should not be administered during a fasting state and they should not be administered following invasive measurement procedures or procedures that might have induced physical pain.

Instructions for the Participant

- Use the pencil provided by the technician.
- Answer all questions in the order in which they appear on the questionnaire.
- If you need to make a correction, cross the wrong answer, put your initial and date next to the line, and then mark the correct answer.
- If you have any questions, please do not hesitate to ask the measurement technician.

- Initial and date each page of the questionnaire that you have completed.
- Please let the measurement technician know if you need a break to visit the restroom or get a drink of water during testing, but try to do your best to complete the measure in its entirety before taking a break.

Roles and Responsibilities

Measurement Technician

Provide a participant with the questionnaire and a Number 2 pencil.

- Explain how to complete the questionnaire (please see “Instructions for the Participant” above).
- Ask whether a participant has any questions and if yes, answer them.
- Remain available throughout the assessment period to answer any questions that participant may have.
- If a participant has difficulty to understand some particular question, explain the meaning of that question. **Do not lead a participant to select a particular answer to a question!**
- Review each questionnaire for completeness. Have the participant complete any unanswered questions.
- If a participant answers any question with two responses, ask which answer is most accurate. **Do not lead a participant to select a particular answer to a question!**
- Initial and date the last page of the completed questionnaire after you reviewed them.
- Score the MAEDS by hand.
- If MAEDS is indicative of an eating disorder (a t-score of 70 or above on any subscale), immediately inform the site measurement leader that an IDED-IV is needed.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.

Quality Control Procedures

- Review each questionnaire for completeness.
- Have the participant complete any unanswered questions!
- If the participant has any scratched out answers or multiple answers, please review those questions with the participant.
- Any additions, changes, or deletions should be initialed and dated by the Measurement Technician at the time of the completion of the questionnaire measure.
- Once the measure is checked again for completeness, make a photocopy of the questionnaire.
- Place the original questionnaire in the participant’s chart and the photocopy in the appropriate place to be mailed to the coordinating center.

Scoring the MAEDS

Note: This measure will be scored by hand on site

The Multiaxial Assessment of Eating Disorder Symptoms (MAEDS) is a self-report inventory that measures the six symptom domains related to eating disorders: binge eating, restrictive eating, purgative behavior, fear of fatness, avoidance of forbidden foods, and depression. Additional information can be found in Anderson, Williamson, Duchmann, Gleaves, & Barbin, 1999.

This self-report questionnaire is composed of 56 items that question food and mood related behaviors. For each statement, the participant chooses how much a comment relates to him/ her along a seven point scale from “never” to “always”. When scoring the MAEDS, each item corresponds to a particular subscale. After the participant has answered all items, the clinician sums all items and a raw score is obtained; the raw score is then converted to a t-score and evaluated for clinical significance based on a normative population.

The scoring algorithm is provide in Section 11.2 above.

Data for the MAEDS

At screening, the individual research centers will score the MAEDS and retain the data. At baseline and following visits, the research centers will score the MAEDS for safety reasons and retain the data, but will also make a copy of the MAEDS, retain the original, and send the copy to the coordinating center. The coordinating center will then enter the data into a tracking system for the overall study data collection.

9.10.3.3 IDED-IV

Note: This measure will be scored by hand on site

The IDED-IV-IV is a semi-structured interview for the diagnosis of eating disorders. In CALERIE, the IDED-IV-IV is used to diagnose eating disorders, defined by the DSM-IV, including binge eating disorder and eating disorder not otherwise specified. Participants must be administered the IDED-IV and a clinical interview if the intervention staff believe that the participant is exhibiting signs of an eating disorder as determined by MAEDS or shows body image disturbance on the BAM. The IDED-IV-IV should be administered by a trained measurement technician or the site clinical psychologist. This measure takes approximately one hour to administer.

Conditions for IDED-IV Interview

- A quiet, comfortable room without distracting stimuli.
- Interview should not be performed during a fasting state and they should not be administered following invasive measurement procedures or procedures that might have induced physical pain.

Roles and Responsibilities

Site Measurement Leader/Clinical Psychologist

- Position a participant in front (on the left, on the right) of you approximately two to three feet away. Make him/her feel comfortable.

- Begin by introducing yourself to the participant and asking them to describe eating patterns and/ or any issues that may be a cause of concern in daily life. This will give an opportunity to begin to establish rapport as well as provide background information for the semi-structured interview.
- Many questions will require more than a simple yes/ no answer and the participant must be encouraged to expand upon the given answer in order to ascertain if symptomology is present.
- A clinical judgment will be made regarding presence of symptomology (e.g. if a participant denies restrictive eating, yet consumes less than 900 kcal per day, caloric restriction will be noted based on clinical interpretation rather than participant response).
- When possible and/ or deemed necessary, additional sources of information may be pursued (e.g. family, friends) to fully understand the behavior patterns present.

Scoring the IDED-IV

The IDED-IV is a semi- structured interview designed to diagnose the presences of eating disorders (e.g. anorexia nervosa, bulimia nervosa, and binge eating disorder).

This measure must be administered by a clinician who has been thoroughly trained and validated as per IDED-IV protocol! No exceptions. After administration of the semi- structured interview, the clinician transfers information from the interview to the DSM-IV diagnostic checklist and follows a decision tree to determine if symptoms are sufficient to rate diagnosis utilizing DSM-IV criteria. A rating of 3 or more on each of the symptoms for a particular disorder, e.g. anorexia nervosa, bulimia nervosa, binge eating disorder, eating disorder not otherwise specified, is the operational definition for establishing that an individual indicates presence of a particular diagnostic symptom. If IDED-IV ratings are 3 or more on 5 of the 8 combined symptoms for bulimia nervosa and anorexia nervosa, then the participant is experiencing a sub threshold eating disorder. This measure will be utilized to determine if the diagnosis of an eating disorder or subclinical eating disorder is present.

Data for the IDED-IV

Anytime the IDED-IV is given, it will be as the result of a safety issue on the BAM or the MAEDS. This measure will be utilized as a diagnostic tool for the presence of an eating disorder. The research centers will make a copy of the IDED-IV, retain the original, and send the copy to the coordinating center. The coordinating center will then enter the diagnosis data, e.g. “met criteria for Bulimia, binge/purge type”, into a tracking system for the overall study data collection.

9.10.4 Beck Depression Inventory-II (BDI-II)

Note: This measure will be scored by hand on site

The BDI-II is used to assess levels of depressed mood over the period of past two weeks and is administered at screening, baseline, Month 1, 3, 6, 9, 12, 18 and 24 by the measurement technician(s). This is a safety measure and as such will be scored by the sites for immediate review of data prior to transmitting data forms to the Coordinating Center.

Tests to be Performed

- BDI-II

Conditions for BDI-II Administration

- A quiet, comfortable room without distracting stimuli.
- An adequate writing surface.
- Assessment should not be administered during a fasting state and they should not be administered following invasive measurement procedures or procedures that might have induced physical pain.

Instructions for the Participant

- Use the pencil provided by the technician.
- Answer all questions in the order in which they appear on the questionnaire.
- If you need to make a correction, cross the wrong answer, put your initial and date next to the line, and then mark the correct answer.
- If you have any questions, please do not hesitate to ask them.
- Initial and date each page of the questionnaire that you have completed.
- Please let the measurement technician know if you need a break to visit the restroom or get a drink of water during testing, but try to do your best to complete the measure in its entirety before taking a break.

Roles and Responsibilities

Measurement Technician

- Provide a participant with the questionnaire and a Number 2 pencil.
- Explain how to complete the questionnaire (please see “Instructions for the Participant” above).
- Ask whether a participant has any questions and if yes, answer them.
- Remain available throughout the assessment period to answer any questions that participant may have.
- If a participant has difficulty to understand some particular question, explain the meaning of that question. **Do not lead a participant to select a particular answer to a question!**
- Review each questionnaire for completeness. Have the participant complete any unanswered questions.
- If a participant answers any question with two responses, ask which answer is most accurate. **Do not lead a participant to select a particular answer to a question!**
- Initial and date the last page of the completed questionnaire after you reviewed them.
- Score the BDI-II by hand.
- If BDI-II score is ≥ 20 , immediately inform the site measurement leader.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.

Quality Control Procedures

- Review each questionnaire for completeness.
- Have the participant complete any unanswered questions!
- If the participant has any scratched out answers or multiple answers, please review those questions with the participant.
- Any additions, changes, or deletions should be initialed and dated by the Measurement Technician at the time of the completion of the questionnaire measure.
- Once the measure is checked again for completeness, make a photocopy of the questionnaire.
- Place the original questionnaire in the participant's chart and the photocopy in the appropriate place to be mailed to the coordinating center.

Scoring the BDI-II

Note: This measure will be scored on site by hand for safety purposes

The Beck Depression Inventory- II is an assessment of current depressive symptomology composed of 21 groups of statements. The participant reads each group and chooses the one statement from each group that most accurately reflects how they have been feeling for the last two weeks. The statements are each numbered on a 4 point scale (0 to 3).

After completion of the questionnaire, the clinician sums the numerical responses and a total score is assigned. Based on the score, the participant may be rated as one of the following level of depressive symptomology: minimal (0-13), mild (14-19), moderate (20-28), or severe (29-63).

Data for the BDI-II

At screening, the individual research centers will score the BDI-II and retain the data. At baseline and following visits, the research centers will score the measure for safety reasons and retain the data, but will also make a copy of the BDI-II, retain the original, and send the copy to the coordinating center. The coordinating center will then enter the data into a tracking system for the overall study data collection.

References

Anderson, D. A., D. A. Williamson, et al. (1999). "Development and validation of a multifactorial treatment outcome measure for eating disorders." Assessment 6(1): 7-20.

9.11 Cognitive Functioning Assessments

This MOP section describes procedures that the study staff members need to follow to perform cognitive function assessments. The cognitive bias tests, which include an Encoding paradigm, Stroop Color-naming Task, Polysemous Word/Homophone Task, and Word Stem Completion Task are administered via a computer application called "Cognitive Bias Tests or CBT." The cognitive bias tests outlined in this section of the MOP will be administered at baseline and, months 6, 12, and 24 in the afternoon of Day

1 of the inpatient stay. These batteries of tests are computer-based, and it will take no more than one hour to complete the Tests for Information Processing Biases (most people complete the tests in 20 to 40 minutes). These tests should be given at the same time of day at each visit, and they should not be administered when the participant is excessively hungry or full, or has recently undergone invasive/painful procedures. The testing should occur in a quiet comfortable room and the same type of computer (e.g., lap-top vs. desk-top) should be used throughout the study, since participants respond to stimuli on the screen. The Site Measurement Technician(s) will perform the assessments under the supervision of the Site Measurement Leader.

These measures will be completed during the course of the study by all CALERIE participants actively under follow-up at that point.

9.11.1 Tests for Information Processing Biases

Information processing biases are demonstrated when cognitive resources are disproportionately allocated to the processing of certain types of information. For example, depressed people recall more negative or depressive stimuli than non-depressed people.

Tests to be performed

- Encoding Procedure (Word List I)
- Test for Attentional Biases - Stroop Test (Word List II)
- Test for Selective Interpretation (Judgment) Bias – Polysemous Words/Homophones Test (Word List III)
- Memory Test – Word Stem Completion (Word List IV)

To test for cognitive bias, four types of words were generated: 1) control, 2) body-related (i.e., related to body shape or size), 3) food-related, and 4) depressive. For the purpose of summarizing the data, the body-related and food-related words will be: 1) scored separately, and 2) collapsed/combined.

Roles and Responsibilities

Measurement Technician

- Set up for the tests
- Position the participant in front of a computer screen. Make him/ her feel comfortable.
- Explain how to use the software (please see “Administration of the tests” below).
- Ask whether the participant has any questions and if yes, answer them.
- Administer the tests
- Remain available throughout the assessment period to answer any questions that the participant may have.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.
- Score the test immediately following the administration

- Print two data sheets (one is stored in the participant’s medical record and the other is sent to the DCRI for data entry)

Site Measurement Leader

- Supervise the Measurement Technicians who administer the tests.
- Verify that each Measurement Technician is trained and certified.
- Supervise reliability checks of the data (see Section VI)

I. Overview:

A. Encoding Procedure

A semantic encoding paradigm will be used to encode words that will be used later in the Word Stem Completion task (implicit memory test).

B. Test for Attentional Biases - Stroop Test (Word List II)

The Stroop test is used to measure attentional bias. A bias towards a word, such as a word related to body size, may increase the amount of time it takes a participant to accurately recognize the color of the word, thus demonstrating an attentional bias. The computer will show a word on the screen and the text will be in one of 3 colors (red, green, or blue). The computer will record the participant’s reaction time to indicate the color of the word from the instant the word is displayed on the screen. The computer will also record the accuracy of the number of colors correctly identified. Reaction time stops when a color is selected. Thus, the computer will record the following variables: reaction time, accuracy, bias for word type, participant ID, date, and gender. The primary outcome variables for this test are reaction time for each word type, and the proportion of correct identifications of word color.

C. Test for Selective Interpretation (Judgment) Bias – Polysemous Words/Homophones Tests (Word List III)

This phase of testing includes sentence completion. The computer will state each word in a control “voice” at a moderate pace. The participant then types a sentence onto the computer screen after the word is spoken. This procedure is repeated for the next word in the list when the “Enter” key is hit. The outcome variables for this test are reaction time and sentence interpretation, which will be scored by the measurement technician prior to being saved by the computer.

D. Memory Test – Word Stem Completion (Word List IV)

A word stem is 3 or 4 letters followed by a blank that the participant must complete with the first English word that comes to mind. For example, “BEH___” is considered a 3 letter stem that may be completed with the word “BEHIND”. The outcome variables for this task are the completion of target words, reaction time, and bias for word type.

II. Setup

- A. Ensure proper conditions for test administration
 - a. A quiet, comfortable room without distracting stimuli.
 - b. A laptop or desktop computer with appropriate software installed. The participant should always be tested on the same/similar computer. For example, the

- participant should NOT be tested on a laptop at baseline and a desktop at month 6.
- c. Assessment should not be administered during a fasting state and it should not be administered following invasive measurement procedures or procedures that might have induced physical pain.
 - d. Once the software is installed and running properly (see Section V for installation instructions), there is no need for software testing and maintenance by measurement technicians.
- B. Prepare for administration of the tests.
- a. Place appropriate colored dots on keyboard and keypad, keys 1 (green), 2 (blue), 3 (red) for Stroop test.
 - b. Open program appropriately.
 - c. According to the clinic file, enter the subject's information. The following fields will be completed by the examiner and saved on the chosen network drive
 - i. Participant ID
 - ii. Timepoint
 - iii. First name, middle initial, and last name
 - iv. Gender
 - v. Race
 - vi. Date of birth
 - vii. Height (inches or centimeters)
 - viii. Weight (pounds or kilograms).
 - ix. Education level

*Many of these fields will be automatically completed if the participant recently completed the BAM.

III. Administration of the tests:

A. Encoding Procedure (Word List I)

1. The participant will be seated. The following instructions will appear on the screen for the participant to read. In addition, the technician will read these instructions out loud.

"With the following words, we will ask you to relate them to yourself. You will need to estimate when was the last time you experienced something related to that word. After you hear the word, please type in a number on a scale from 1 to 9 with 1 being 'NEVER' and 9 being 'RIGHT NOW'"
2. Six examples will be performed by the subject before the test starts.
 - a. Each word will be played twice with a 2 second delay.
 - b. Words will be pseudo-randomized so that no more than two words in a row are from the same category
 - c. Each example will be a forced choice format
3. Upon completion of the examples, the computer will prompt the participant to confirm that the instruction/ examples are understood before continuing to the actual test words. It is imperative that the examiner confirm that the participant understands the task before the test begins.
4. After the word is presented by the computer, the participant will type in a number. Participant will choose a response 1-9 on the keyboard or keypad.

Reaction time for the Likert response will start after the word is stated the second time.

5. The directions, outlined above (#1, a-c) will be presented with each word; therefore, they will be available to the participant when he/she makes the rating.

B. Test for Attentional Biases - Stroop Test (Word List II)

1. Instructions will appear on the screen for the participant to read. In addition, the technician will read these instructions out loud.
 - a. ***“ In this experiment you should press the key that corresponds to the color of the word that is displayed on each trial as quickly as you can”***
 - b. ***“Press 1 for the color green, press 2 for the color blue, press 3 for the color red”***
 - c. ***“If you notice, there are colored dots on these keys to aid you in finding the keys”***
 - d. ***“You will see a black fixation point, a plus sign, appear on the screen. This is to show you where the word will appear. You will not need to press a key to indicate the color of the fixation point.***
 - e. ***“When you are ready, you will have six examples to practice and then we will get started”***
2. Six examples will be performed by the subject before the test starts.
3. Colors of words will be chosen randomly, however, each word will be presented three times, once in each color.
4. The word list for the Stroop will be randomized so that no more than two words in a row will be from the same category
5. There will be a 1 – 2 second delay, as well as a cross fixation point indicating no word is being displayed before the next word is displayed. The cross is in black. it is important that the participant understand that this is a fixation point to tell them where the word will appear – they are not to indicate the color of the cross.
6. The participant will be instructed to choose the color of the word displayed on the monitor.
7. The color of the word will be chosen by striking 1, 2, or 3 on the keyboard or keypad. Each number will be coded with a colored paper dot
8. Dependent Variables:
 - a. Reaction time- the amount of time it takes a participant to respond to the word on the screen, beginning from the instant the word is displayed to the instant the answer is made. Reaction time stops when a color is selected.
 - b. Accuracy- the number of correctly named colors of all the words
 - c. Bias for word type- this will be determined by analyzing whether the reaction time for categories of words differs. This analysis will occur after the raw data are collected

C. Test for Selective Interpretation (Judgment) Bias – Polysemous Words/Homophones Test (Word List III)

1. Instructions will appear on the screen for the participant to read. In addition, the technician will read these instructions out loud.
 - a. ***“ In the next series of steps, you will hear a word spoken by the computer”***
 - b. ***“The word will be spoken twice”***
 - c. ***“Write a sentence using the word spoken by the computer***

- d. ***“You must wait until after the word is spoken the second time before typing your sentence”***
 - e. ***“There will be a two second delay between words”***
 - f. ***“The next word will sound when the “Enter” key is hit”***
 - g. ***“Please work as quickly and accurately as you possibly can”***
 - h. ***“You will now do six examples before you start this test”***
2. Six examples will be preformed by the participant before beginning the test.
 3. The computer will state the word twice, with a 1 to 2 second delay between presentations. The “voice” on the computer is selected to be gender neutral.
 4. Words are presented in a pseudo-random order with no more than two words in a row being from the same category
 5. The participants will type the sentence into the computer.
 6. Another word will play when the “Enter” key is hit
 7. Dependant Variables are as follows:
 - a. Sentence Interpretation- the sentence completed for the word will be coded (1=body/food related, 0=other) depending on the overall meaning of the sentence (for clarification, see Appendix A). This coding requires a technician to determine the meaning of the sentence. Therefore a procedure has been developed to train raters to interpret the sentences and make judgments prior to data being transferred to a central location. See Section VI and Appendix A.
 - b. Reaction time- the amount of time taken to complete the sentence

D. Memory Tests – Word Stem Completion (Word List IV)

1. Instructions will appear on the screen for the participant to read. In addition, the technician will read these instructions out loud.
 - a. ***“In the next series of steps, you will be presented with 3-4 letters”***
 - b. ***“Please complete the word stem with the first English word that comes to mind as quickly as possible”***
2. Six examples will be performed by the participant before the test starts.
3. Instruction text will say “In the next series of steps, you will be presented with three letters. You will be asked to add additional letters to make a word.”
4. Participants will be presented with the word stems in a pseudo-random order. After the word is presented, the participant will complete the word by typing in the remaining letters to develop a word.
5. 50% of the word stems will be from Word List I and 50% will not.
6. Dependant Variables
 - a. Completion of target words
 - b. Reaction Time- the amount of time it takes for the participant to complete the word
 - c. Bias for word type- this will be measured by the number and type of target words completed as compared to non-target words completed

IV. Scoring for Tests of Information Biases:

A computer program has been written to automatically score the tests for Information Processing Biases. However, there are two tests that require the technician to judge how 1) the sentences were used in the Selective Interpretation (Judgment) Bias - Polysemous Words/Homophones Test, and 2) words generated in the Word-stem Completion Test (see Section V and Appendix A and B).

Raw Data Recorded

The following will be recorded for each test:

- Participant ID
- Timepoint
- First name, middle initial, and last name
- Gender
- Race
- Date of birth
- Height (inches or centimeters)
- Weight (pounds or kilograms)
- Education level

A. Encoding Procedure (Word List I)

1. For the first portion of the testing procedure (the encoding paradigm) scoring is determined by the following procedure:
 - a. Reaction time (in milliseconds) for the Likert response
 - b. Participants' Likert response (on a scale of 1 to 9) to the word
 - c. Actual word

B. Stroop color naming task (Word List II)

1. The Stroop is scored by collecting the following factors:
 - a. Reaction time (in milliseconds)
 - b. Accuracy

C. Polysemous Words/Homophones Test (Word List III)

1. The Polysemous Words/ Homophones Test is scored by collecting the following factors:
 - a. Reaction time (in milliseconds)
 - b. Sentence Completed
2. It is required for a human rater to score the sentences prior to data transmission according to the rating criteria described below:
 - a. Sentence interpretation: (1=body/food related, 0=control)
 - b. Use Appendix A to determine if sentences created by the participant match the criteria for "food/body" or "other" judgment.

D. Word Stem Completion (Word List IV)

1. The Word Stem Completion Task is scored by collecting the following factors:
 - a. Reaction time (in milliseconds)
 - b. Completed Word Stem
2. It is required for a human rater to score the words prior to data transmission according to the rating criteria described below.
 - a. Word interpretation: (1=match, 0=does not match)
 - b. Use Appendix B to determine if words generated by the participant match the criteria for a target word.

V. Data Management:

To protect data from being lost in the case of computer failure, these data will be stored on a networked drive that is backed up regularly. Immediately after the test is complete, the examiner will judge the output from the Selective Interpretation (Judgment) Bias - Polysemous Words/Homophones Test and Word-stem Completion Test and enter these judgments into the computer. Subsequently, two copies of the output will be printed. One copy is sent directly to the DCRI for data entry and the other copy is stored at the study site. Additionally, should the DCRI request electronic data transfer, this can be accommodated. The following data fields will be gathered by the computerized testing program. For an example of the data output that will be sent to DCRI, see *Appendix C*.

A. Encoding Procedure (Word List I)

1. Frequency of Likert responses for each category of words
2. Frequency of Likert responses for the combined category of both food and body shape words
3. Mean reaction time of the Likert response for each category of words
4. Mean reaction time of the Likert response for the combined category of food and body shape words

B. Stroop Test (Word List II)

1. Mean reaction time for Stroop responses for each category of words
2. Mean reaction time for Stroop responses for the combined category of food and body shape words
3. Number and proportion of correct Stroop responses for each category of words
4. Number and proportion of correct Stroop responses for the combined category of food and body shape words

C. Polysemous Words/ Homophone Test (Word List III)

1. Mean reaction time for Sentence Completion responses for body related words and control words
2. Number and proportion of sentences completed for body words and control words

D. Word Stem Completion (Word List IV)

1. Mean reaction time for Word Stem Completion responses for each category of words
2. Mean reaction time for Word Stem Completion responses for the combined category of food and body shape words
3. Number and proportion of target words completed for each category of words
4. Number and proportion of target words completed for the combined category of food and body shape words

Installation Instructions for the Cognitive Bias Software Program

1. Double-click on the install file (CBTSETUP.EXE).
 - a. This will open the Cognitive Bias Testing Setup Wizard.
2. Click "Next" to continue.
3. Select a destination folder for the Cognitive Bias Testing software.
 - a. The default and suggested location is C:\Program Files\Calerie Applications
 - i. The Calerie Application folder is automatically created by the program
4. Click "Install" to install the program.
5. When the installation is complete, click "Finished."

- a. A shortcut for the CBT program will be created on your desktop.
- b. It can also be accessed via the Windows “Start” menu.

First Initialization

1. Double click the shortcut on your desktop or select the program from your “Start” menu.
2. Upon first initialization, you will be prompted to select:
 - a. Your site
 - b. The units in which height and weight will be collected
 - c. A data storage location
 - i. Multiple computers can share the same data storage location as long as each computer has access to the destination folder.
 - ii. Therefore, your data storage folder should be located on a network drive that is backed up regularly to reduce the chances of data loss.

VI: Certification and Quality Control

A. Certification

1. The Site Measurement Leader from each of the three sites will be certified on how to score the data before a participant is tested. This certification will occur at a special training session.
2. The Site Measurement Leader from each site is solely responsible for certifying the Measurement Technicians at each site who cannot attend the special training session. S/he can obtain the paperwork from the PBRC group, but are responsible for certifying the technicians. S/he must provide documentation to the DCRI that all Measurement Technicians are certified.

B. Quality Control (QC)

1. During the certification process, all technicians will receive instruction on the scoring of the Polyseme/Homophone task and the Word Stem Completion Task. This will include ample review of the criteria outlined in Appendix A and B.
2. Once the study starts, the Site Measurement Leader is responsible for QC and assuring that the judgments are being made consistent with the training. To achieve this, the following QC and reliability protocol will be used.
 - a. Once a Measurement Technician has administered the Cognitive Bias testing, s/he will immediately make judgments of the raw data for the Polyseme/Homophone and Word Stem Completion tasks.
 - b. After the raw data is scored by the Measurement Technician, s/he should print out a copy of the scored data and bring it to the Site Measurement Leader.
 - c. The Site Measurement Leader will double score the judgments or assign another Measurement Technician to double score the data prior to the data summary being sent to the DCRI. This will be accomplished within one week of administration.
 - d. If there are no discrepancies between the first and second scorings, two copies of the data summary will be printed (one copy is sent to the DCRI and one copy is placed in the Medical Record). If discrepancies are discovered, follow the data correction steps outlined in Section VII.
 - e. The Site Measurement Leader will resolve all discrepant ratings in a manner that is consistent with the criteria outlined in Appendix A and B.

VII. Data Corrections

Error detection and correction for the Polyseme/Homophone Task and the Word Stem Completion Task judgments.

1. **Errors will be detected during the double scoring procedures outlined in Section VI B.**
2. The Site Measurement Leader or the designated technician will correct any errors in the Cognitive Bias Software using the following procedures. Once the error is corrected, two copies of the data summary will be printed (one copy is sent to the DCRI and one copy is placed in the Medical Record). Two weeks from the date of administration of the Cognitive Bias tests, the data will have been double scored, errors will have been corrected in the database, and the summary scores will have been sent to the DCRI (and one copy will have been placed in the participant's Medical Record).
3. Steps for data correction
 - Select the CBT Data Manager program from the "Start" Menu.
 - You will be shown a list of subjects for whom there is data, along with the data time point, time stamp, and a checkbox indicating whether the data has been analyzed. From this screen, you can also view and print the data. (This screen is shown below).
 - Click on "View" for the participant whose data needs to be scored/rescored.
 - Rescore where needed and click "Save". This will overwrite the data file.
 - Click "Print" and print two copies of the report. Send one copy to the DCRI and store the other in the participant's medical record.
4. The Site Measurement Leader will submit a QC report to the DCRI every 6 months documenting that the QC procedures outlined herein have been followed.

The screenshot shows the CBTDataManager application window. It contains a table with the following columns: Subject ID, Time Point, Time Stamp, Analyzed?, View, and Print. The table lists data for subjects 01-1111, 01-1234, and 01-6666. All 'Analyzed?' checkboxes are checked. The 'View' link for subject 01-1234 is highlighted.

Subject ID	Time Point	Time Stamp	Analyzed?	View	Print
01-1111	Baseline	11/9/2006 4:25 AM	<input checked="" type="checkbox"/>	View	Print
01-1111	Baseline	11/20/2006 11:25 AM	<input checked="" type="checkbox"/>	View	Print
01-1111	Baseline	11/20/2006 11:34 AM	<input checked="" type="checkbox"/>	View	Print
01-1111	Baseline	2/9/2006 4:25 AM	<input checked="" type="checkbox"/>	View	Print
01-1234	Baseline	1/29/2007 11:34 AM	<input checked="" type="checkbox"/>	View	Print
01-1234	Baseline	1/29/2007 12:01 PM	<input checked="" type="checkbox"/>	View	Print
01-1234	Baseline	1/29/2007 12:30 PM	<input checked="" type="checkbox"/>	View	Print
01-1234	Baseline	1/29/2007 1:25 PM	<input checked="" type="checkbox"/>	View	Print
01-6666	Baseline	2/2/2007 11:38 AM	<input checked="" type="checkbox"/>	View	Print

Appendix A
Instructions for Judging the Raw Data from the Polyseme/Homophone Task

The measurement technician judging the sentences generated by the participant will follow the criteria below. Recording of the judgment occurs within the Cognitive Bias Software. Immediately after the tasks are administered, the scoring screens appear for the Measurement Technician to make his/her judgments.

The sentences generated by the participant are judged as either “body shape/food-related” or “other” using the criteria below. Examples are provided in Table 1.

Note that the participant can easily hear the word incorrectly and still generate a body shape/food related sentence. For example, the word “plump” can be presented to the participant, but s/he might interpret the word as “lump” and write the following sentence: “When I go to the gym, I feel lumpy and lazy because everyone else is in such good shape.” In this case, s/he failed to use the presented word in a sentence, but the sentence is nonetheless body related; therefore, it is coded as such. Additionally, the participant can change the base word’s tense, make the word plural, or use the word as an adjective or adverb, and this will not affect the judgments. The judge is simply determining if the sentence is body or food related, as outlined below.

Criteria

The sentence generated by the participant must be judged to be either food or body-related using either criteria a or b:

- a. The sentence refers to body shape, a part of the body (e.g., chest, lips), body size, body weight, body/physical appearance, or exercise
 - i. Based on clinical judgment, sentences referring to the following are considered body-related if a direct connection can be made to the above criteria (examples are provided in Table 2).
 - a. Apparel (clothes, fashion accessories, make-up)
 - b. Sports/Sports equipment
- b. A food-related activity, a specific type of food or drink, dining locations, dieting, or eating behavior.

Table 1. Example judgments for the Polyseme/Homophone Task.

Sentence	Rating
These pants don't fit my <u>waist</u> .	Food/Body
My <u>waste</u> is expanding. <i>(note misspelling)</i>	Food/Body
I won't <u>waste</u> your time.	Other
My vacation went to <u>waist</u> . <i>(note misspelling)</i>	Other
I wish my <u>butt</u> weren't so big.	Food/Body
I don't like the way my <u>but</u> looks in these jeans. <i>(note misspelling)</i>	Food/Body
I was going to go, <u>but</u> I didn't.	Other
I told him to <u>butt</u> out of the conversation.	Other
I have a picture in a <u>frame</u> .	Other
In a <u>frame</u> , I have a picture of myself from when I was fat.	Food/Body
We need to <u>band</u> together to overcome adversity.	Other
We need to <u>band</u> together to overcome adversity against obese people.	Food/Body

I am a <u>grown</u> man, but I still act like a child.	Other
My niece is all <u>grown</u> up.	Other
My niece has <u>grown</u> to be six feet tall.	Food/Body
He was so vain, he had to have a Lexus to make him feel good.	Other
As a teenager, I was very <u>vain</u>	Food/ Body
I <u>trimmed</u> the hedge	Other
When I <u>get</u> a haircut, I usually just get a <u>trim</u> .	Food/ Body
I am feeling <u>weak</u> .	Other
I felt <u>weak</u> after my afternoon jog.	Food/Body
I am a <u>grown</u> man, but I still have the musculature of a child.	Food/Body

Table 2.

Sentence	Rating
I threw the ball at <u>night</u> .	Other
I threw the ball during last <u>night's</u> championship soccer game.	Food/Body
My ring is on the <u>chest</u> .	Other
My ring is on the <u>chest</u> because it no longer fits on my finger.	Food/Body
My clothes are <u>stacked</u> on the shelf.	Other
My clothes from when I was pregnant are <u>stacked</u> on the shelf.	Food/Body
Oftentimes, my clothes are <u>plain</u> .	Other
I look <u>plain</u> in my clothes.	Food/Body
I ran a <u>figure</u> eight last night to amuse my roommates.	Other

Appendix B
Instructions for Judging the Raw Data from the Word Stem Completion Task

The measurement technician judging the word generated by the participant will follow the criteria below. Recording of the judgment occurs within the Cognitive Bias Software. Immediately after the tasks are administered, the scoring screens appear for the Measurement Technician to make his/her judgments.

The words generated by the participant in response to the word stems are judged as either “matching” the target word or “not matching” the target word. The computer application displays the target word (labeled “Word”) and the word produced by the participant (labeled “WordEntered”). The judge makes his/her judgments using the criteria outlined below.

If the word entered by the participant is identical, including spelling, to the target word, the computer application will automatically judge the word as a “match” and enter this into the computer application. Therefore, the Examiner need not judge these words. If the word entered by the participant does not match precisely the target word, then the Examiner is asked to judge if the WordEntered matches the target word using the criteria below.

Examples are provided in Table 2.

Either Criterion 1 or 2 must be met for the word entered by the participant to match the target word.

Criterion 1

If the word entered by the participant is phonetically similar to the target word, it is judged as a “match”. This criterion allows the Examiner to ignore most spelling errors, as outlined in Table 2. Additionally, it is acceptable for the participant to change the tense, pluralize the word, add a ‘y’ to the word, or use the word as an adjective or adverb (i.e., “-ed,” “-s,” “-ly,” etc.).

Criterion 2

If the participant entered a word that is part of the target word, it is not considered a “match” if the word entered is an actual word with a *different definition* than the target word. For example, if the target word is “belly” and the participant entered “bell”, then the judge considers this “not a match.”

Table 2. Word List IV – Examples of Possible “Correct” Phonetically Similar Misspellings

Target Word (control)	Target Stem	Accepted Spelling Examples
Trend	Tre	Trennd, Trendd,
Label	Lab	Lable, Labell, Lable
Spare	Spa	Sparre, Sparee
Border	Bor	Bordur, Bordar
Shower	Sho	Showur, Showere
Piano	Pia	Pianoe, Pianoh
Climate	Cli	Climat, Climete

Luggage	Lug	Lugguge, Lugage
----------------	-----	-----------------

Target Word (depressive)	Target Stem	Accepted Spelling Examples
Fault	Fau	Faultt, Faultt, Faulty
Crime	Cri	Crim, Crimme, Crimee, Crimes
Despair	Des	Despayer, Despaire, Desppair, Despayr, Despare, Despaired
Guilt	Gui	Guilt, Guiltt
Agony	Ago	Agonny, Agoni
False	Fal	Fals, Falss, Falsee, Falssee
Blame	Bla	Blamme, Blamee, Blayme, Blaim
Coffin	Cof	Cofin, Cofiin, Cofinn, Coffinn, Coffiin, Coffiinn

Target Word (food)	Target Stem	Accepted Spelling Examples
Candy	Can	Canddy, Candyy, Candi, Candie, Cande, Candies
Honey	Hon	Honi, Honie
Cereal	Cer	Cerieal, Ceryeal, Cerial
Bread	Bre	Breadd, Breaad
Picnic	Pic	Picnick, Picinic, Picinick
Potato	Pot	Potatoe, Potayto, Potatoh, Potaytoh, Potaeto
Grain	Gra	Grayn, Grayne, Graine
Mustard	Mus	Musterd, Mustayrd

Target Word (body shape)	Target Stem	Accepted Spelling Examples
Balance	Bal	Balance, Balense,
Cheeks	Che	Cheaks, Cheek
Thighs	Thi	Thiys, Thigh
Belly	Bel	Belli, Beli
Waist	Wai	Waiste
Monstrous	Mon	Monstrus, Monstros
Hips	Hip	Hipps
Bulky	Bul	Bulkie, Bulki, Bulkee, Bulkey

Appendix C

CBT Data Report

CALERIE ID 01-1234
 Date of Birth 09/24/1958
 Time Point Baseline
 Record Date 01/29/2007 15:34:56

Encoding

Category	F1	F2	F3	F4	F5	F6	F7	F8	F9	MeanTime (ms)
Control	1	1	0	1	3	0	0	1	1	511
Depressive	1	2	1	3	0	1	0	0	0	816
Food	0	2	2	0	2	1	0	1	0	845
Body Shape	1	1	1	1	1	2	1	0	0	683
Food + Body	1	3	3	1	3	3	1	1	0	764

Stroop

Category	Mean Time (ms)	# Correct	% Correct
Control	849	24	100
Depressive	841	24	100
Food	779	24	100
Body Size	724	24	100
Food + Body	751	48	100

Polyseme

Category	Mean Time (ms)	# BS/F	% BS/F
Body/Food Related	2809	9	45
Other	3947	10	50

Word Stem

Category	Mean Time	# Match	% Match
Control	2521	4	50
Depressive	2566	4	50
Food	2691	7	87.5
Body Shape	2709	4	50
Food + Body	2580	11	68.8

Printed on: 2/15/2007 3:37 PM
 Shape/Food

F = Frequency, BS/F = Body

9.11.2 Tests for Neuropsychological Functioning

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computerized cognitive assessment battery used to measure reaction time, processing speed, attention, concentration, executive function, short-term memory, and delayed memory. The CANTAB has been extensively evaluated and validated in healthy adults. The battery of tests included in the CANTAB is normed for a wide range of ages (4-90 years) and is suitable for longitudinal studies and repeated testing. The tests are predominantly non-verbal and non-cultural, making them highly suitable for use in diverse populations. Since the tests are computerized, administration and scoring are simple and reliable. The CANTAB uses a touch screen to make it easier for the subject to follow instructions, and the tasks have a game-like quality and objective feedback, which encourage motivation and high subject compliance. The program scores the tests and exports the data into statistical analysis packages or spreadsheet packages. For the present study, we have chosen CANTAB modules to assess for attention, vigilance, executive function, and memory that will be administered at baseline, months 6, 12, and 24.

CALERIE is using the CANTABeclipse version 3.0. All references to CANTABeclipse manuals are for the 3.0 version.

9.11.2.1 Roles and Responsibilities

Measurement Technician

- Position a participant in front of a computer screen. Make him feel comfortable.
- Explain how to use the software (please see “Instructions for the Participant” above).
- Ask whether a participant has any questions and if yes, answer them.
- Remain available throughout the assessment period to answer any questions that participant may have.
- Direct the participant back to the study coordinator or appropriate personnel for completion of any remaining visit requirements.

9.11.2.2 Test Descriptions

Tests to be Performed (In Correct Order)

- Motor Screening (**MOT**)
- Reaction Time (**RTI**)
- Verbal Recognition Memory – Immediate (**VRM – Immediate**)
- Delayed Matching to Sample (**DMS**)
- Spatial Working Memory (**SWM**)
- Verbal Recognition Memory – Delayed (**VRM – Delayed**)
- Rapid Visual Information Processing (**RVP**)
- ID/ED Shift (**IED**)

Motor Screening module is a simple test that screens for visual, movement and comprehension difficulties. The module acclimates the subject to using the touch screen.

Reaction Time module has three purposes, (a) it trains the subject in holding down the press-pad and touching the screen, (b) it provides a screen for the ability to acquire and perform this motor skill and (c) it acts as a simple single and multiple choice reaction time tasks. Its five stages require increasingly complex chains of responses. In each case, the subject must react as soon as a yellow dot appears. In some stages it may appear in one of five locations, and the subject sometimes responds by using the press-pad, sometimes by touching the screen, and sometimes both.

Verbal Recognition Memory module is used to measure immediate free recall and delayed recognition memory.

Delayed Matching to Sample module is a memory test that presents the subject with a complex visual pattern (the sample) and then, after a brief delay, four patterns between which she or he must choose. Each pattern is made up of four sub-elements, each of a different color. One of the choice patterns is identical to the sample, one is a novel distracter pattern, one has the shape of the sample and the colors of the distracter, and the fourth has the colors of the sample and the shape of the distracter. To discourage strategies based on encoding single quadrants, all four choice patterns have a quadrant in common with the sample.

Spatial Working Memory module is a test of spatial working memory and strategy performance. The aim of the test is that the subject should find a blue 'token' in each of the boxes displayed and use them to fill up an empty column on the right hand side of the screen, while not returning to boxes where a blue token has previously been found. The color and position of the boxes used are changed from trial to trial to discourage the use of stereotyped search strategies.

Rapid Visual Information Processing module is a test of sustained attention with a small working memory component. A white box appears in the center of the computer screen, inside which digits, from 2 to 9, appear in a pseudo-random order, at the rate of 100 digits per minute. Subjects are requested to detect consecutive odd or even sequences of digits (e.g. 2-4-6, 3-5-7, 4-6-8, 5-7-9, etc.) and to register responses using the press-pad. Initially, the computer prompts the subject when sequences appear and gives feedback when the pad is pressed. As the practice part of the test progresses, these cues are gradually phased out, and in the assessment part, no cues or feedback are given.

ID/ED Shift module is a test of the subject's ability to attend to the specific attributes of compound stimuli, and to shift that attention when required. Two artificial dimensions are used, color-filled shapes and white lines. Two stimuli (one correct, one incorrect) are displayed, initially each of only one dimension, then each of both dimensions (first adjacent, then overlapping as illustrated). Feedback teaches the subject which stimulus is correct, and after six correct responses, the stimuli and/or rules are changed. These shifts are initially intra-dimensional (e.g. color filled shapes remain the only relevant dimension), then later extra-dimensional (white lines become the only relevant dimension).

9.11.2.3 Conditions for Tests Administration

- The CANTAB is NOT self-administered; it MUST be administered under the supervision of a tester.
- The computer must be in a quiet, comfortable room without distracting stimuli, and with the door closed.
- Assessment should not be administered during a fasting state and they should not be administered following invasive measurement procedures or procedures that might have induced physical pain.
- Subject should be seated upright, directly in front of the computer monitor, about 30-50 cm away.
- When using the press pad, the pad should be positioned such that the key farthest from the cable is in front of the subject and 15 cm away from the touch screen (please see the picture on page 70 of the CANTABeclipse Software User Guide).
- Subject should use dominant hand to touch computer screen – and RIGHT press-pad button.
- The keyboard and mouse should be situated to the side of the computer, in front of the tester.
- Please see the CANTABeclipse Software User Guide pages 67-70 for more details regarding test environment.

9.11.2.4 System Requirements

Please see Chapter 7 (starts on page 137) of the CANTABeclipse Software User Guide. Microsoft Excel is also required for generating data reports. The computer should be used for CALERIE computer assessments only.

9.11.2.5 Software Installation and Set-up

Please see Chapter 2 (starts on page 17) of the CANTABeclipse Software User Guide.

9.11.2.6 Touch Screen Installation and Setup

Please refer to the touch screen manual and Chapter 2 (starting on page 21) of the CANTABeclipse Software User Guide. Please remember that the touch screen drivers need to be set such that:

- Each touch, NOT RELEASE, must immediately register at the location touched (“click on touch”).
- The touch screen driver must NOT implement special behavior for double clicks, drags, or other modifiers.
- The touch screen driver must NOT make any sounds when the screen is touch. Any option such as “click sound on touches” should be unchecked.

9.11.2.7 Press Pad Installation

Please refer to the instructions supplied with the press pad for information.

9.11.2.8 Starting CANTABeclipse

Please see Chapter 3 (starts page 25) of the CANTABeclipse Software User Guide.

Start the software by either double-clicking on the Windows shortcut, or through the programs list in the Windows Start menu. The software will always start up with the **Control Centre** window displayed, with no subject selected.

The **Control Centre** window contains three “tabs”:

- Subject Tab
- Session Tab (you must choose to display this through the “Options” button on the lower right hand of the Control Centre screen)
- Battery Tab

9.11.2.9 Creating the Testing Battery

Please see Chapter 3 (section starting on page 47) of the CANTABclipse Software User Guide.

Since we will be administering the same set of tests to multiple subjects, it is important to initially set up a test “battery” that can be used over and over again. By creating the battery, we specify which tests are run and the order in which they are run. Different batteries will be created for each of the testing time points (i.e. baseline, 6 mos., 12 mos., and 24 mos.). The same tests will be used for each battery, but different versions of selected tests will be used for the purposes of repeated measurement.

To create a battery, click on the “**Battery**” tab. Use the drop down boxes to select the tests and modes that will be used. The buttons in the upper right of the screen are used to add, delete, and change the order of the tests. Once the battery is correctly configured, choose “save as” (in upper right of screen) and label it appropriately. **Be sure to label the battery appropriately so that it will be consistent with the other study CRFs (i.e. CALERIE Baseline 2, CALERIE Month 6, CALERIE Month 12, CALERIE Month 24).**

The Battery tab

Use this to select desired battery (i.e. CALERIE Baseline 2, CALERIE Month 6., etc.)

These are drop down boxes; use them when creating a “battery”

#	Test	Mode
1	(MOT) Motor Screening	clinical
2	(PRM) Pattern Recognition Memory	clinical
3	(SRM) Spatial Recognition Memory	clinical
4	(DMS) Delayed Matching to Sample	clinical
5	(PAL) Paired Associates Learning	clinical
6	(OSP) Spatial Span	clinical
7	(SWM) Spatial Working Memory	clinical
8	(SOC) Stockings of Cambridge	clinical
9	(BLC) Big / Little Circle	clinical
10	(JED) Intra / Extradimensional Shift	clinical
11	(RT) Reaction Time	clinical
12	(MVS) Match to Sample Visual Search	clinical
13	(RVP) Rapid Visual Information Processing	clinical

Figure 3-16 The Battery tab showing the clinical battery

The following are the tests, order, and modes for the 4 testing batteries:

“CALERIE Baseline 2” Battery

Test	Mode
MOT	Clinical
RTI	Parallel
VRM	Parallel 1 – Immediate
DMS	Parallel 1
SWM	Clinical
VRM	Parallel 1 – Delayed
RVP	Clinical
IED	Parallel 1

“CALERIE Month 6” Battery

Test	Mode
MOT	Clinical
RTI	Parallel
VRM	Parallel 2 – Immediate
DMS	Parallel 2
SWM	Clinical
VRM	Parallel 2 – Delayed
RVP	Clinical
IED	Parallel 2

“CALERIE Month 12” Battery

Test	Mode
MOT	Clinical
RTI	Parallel
VRM	Parallel 3 – Immediate
DMS	Parallel 3
SWM	Clinical
VRM	Parallel 3 – Delayed
RVP	Clinical
IED	Parallel 3

“CALERIE Month 24” Battery

Test	Mode
MOT	Clinical
RTI	Parallel
VRM	Parallel 4 – Immediate
DMS	Parallel 4
SWM	Clinical
VRM	Parallel 4 – Delayed
RVP	Clinical
IED	Parallel 4

9.11.2.10 Set-Up and Test Administration

A. At the start of the day:

- Connect the **software key** to a USB port.
- Connect the **press pad** to a USB port
- Make sure that the **touch screen** is **connected** and **calibrated** (run the **Touch USB** software that is supplied by the touch screen manufacturer). Please see refer to Magic Touch Screen User Manual – 6.1 for Windows or 6.2 for Macintosh.)
- Conduct a **sound check** and **calibration double-check** by having a test run of the **Motor Screening Test** (test can be aborted and results deleted once you determine that everything is working).

B. Prior to the arrival of the subject:

1. Go to the “**Subject Tab**”. Enter Subject ID and date of birth (DOB). Delete other fields.

Creating new subjects and retrieving existing subjects:

Only use “subject ID” and “date of birth” fields. Delete the other fields (NART and Gender).

Choose “new subject” only for a new subject. Use “find subject” when administering follow-up tests.

These buttons can be used to add, delete and move fields.

Insert notes about subject here

Field	Value
Subject ID	
Subject NART	
Date of birth	
Gender	

Figure 3-1 CANTABclipse Control Centre showing the Subject tab

2. For a **NEW** Subject (i.e. at the baseline time point)
 - Press “New Subject”
 - Enter the Subject ID
 - Enter Date of Birth
 - Delete other fields
3. For an **Existing** Subject (all other time points)
 - Press “Find a Subject”
 - Either type in the ID, or use the scroll bar
 - Click on the subject ID you wish to select.
4. Go to the “**Session Tab**”. The “Session Tab” is not automatically displayed. You must press the “Options” button (lower right corner of Control Centre screen) in order to display it.

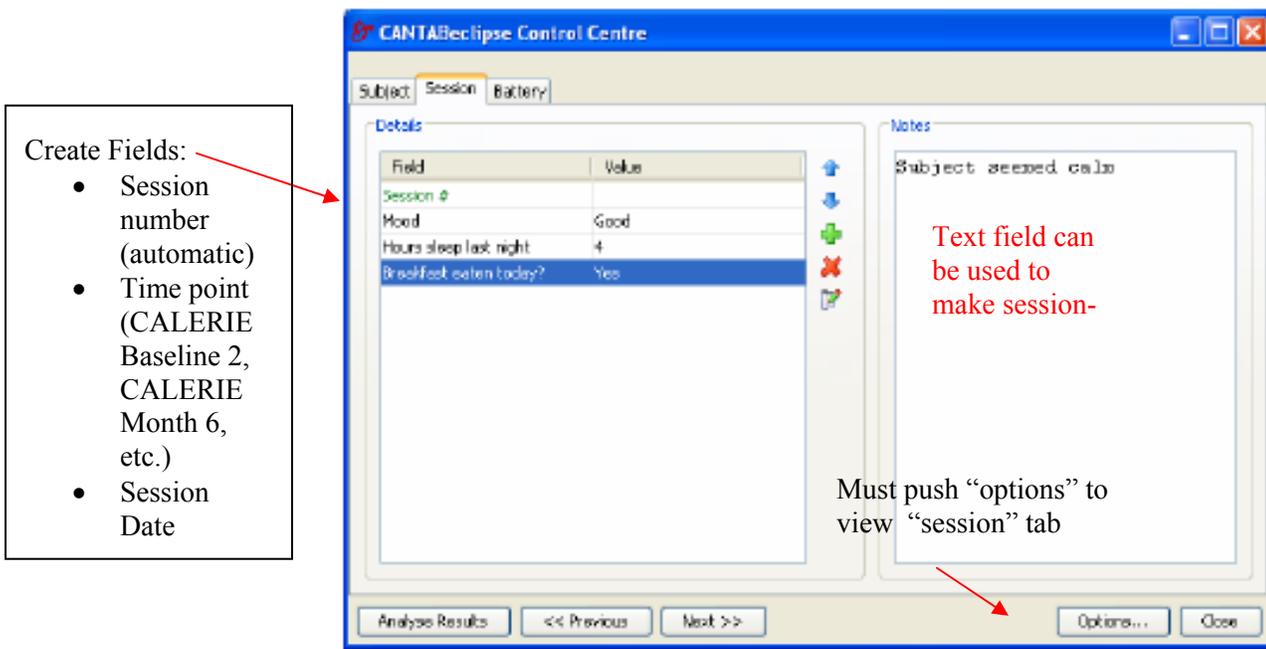


Figure 3-15 The Session tab showing additional session details fields and notes

- Type in the Session # (1 – 4) (this is an automatic field and is required by the software).
- Type in the Date
- Type in the Time point (CALERIE Baseline 2, CALERIE Month 6, CALERIE Month 12, CALERIE Month 24)
- Delete all other variables
- Text field can be used to create notes about the session (e.g. subject is fatigued, anxious, etc). (this won't be included in the data sent to the Data Center).

C. To Run the Battery:

- Go to the Battery Tab
- Select the battery that was created for the particular time point you wish to run
- Press “Run Battery
- See page 78 of the CANTABclipse Software User Guide.

D. General Test Administration Instructions:

- The instructions for each test are SCRIPTED.
- The scripts are located in the CANTAB manual, under each test’s administration subsection.
- Please read the scripts to the subject word-for-word and follow the directions precisely.
- Following the directions will ensure standard administration for each test and will greatly contribute to the reliability of the data.
- The test administrator has the ability to pause the computer between tests. Please do so only for urgent matters. Timing is calculated into the standardization of the tests. For example, there should be about a 20-minute interval between the end of the administration of the Verbal Recognition Memory – Immediate and the start of the administration of the VRM – Delayed. The battery testing order is designed to take into account this interval.
- **Please remember that since some of the tests were designed as repeated measures (and thus have different versions with slightly different stimuli to attenuate any learning effects), it is important that you administer the CORRECT TESTING BATTERY for the CORRECT TIME POINT (i.e. CALERIE Baseline 2, CALERIE Month 6, CALERIE Month 12, CALERIE Month 24)**

E. Instructions for Individual Tests:

1. MOT:

Overview: This simple test screens for visual, movement and comprehension difficulties and acclimates the subject to using the touch screen.

Administration: of this test should take approximately 3 minutes.

Task: Subjects must touch the flashing cross which is shown in different locations on the screen.

Instructions: Please follow instructions (and script) for administering the CLINICAL mode in the Test Administration Guide pages 33-36.

2. RTI:

Overview: The test is a simple single choice and multiple choice reaction time task.

Administration time: Around 5 minutes, depending on level of impairment.

Task: The task is divided into five stages, which require increasingly complex chains of responses. In each case, the subject must react as soon as a yellow dot appears. In some stages the dot may appear in one of five locations, and the subject must sometimes respond by using the press-pad, sometimes by touching the screen, and sometimes both.

Instructions: Please follow instructions (and script) for administering the PARALLEL mode in the Test Administration manual pages 131-141.

3. VRM:

Overview: The VRM test assesses immediate and delayed memory of verbal information under free recall and forced choice recognition conditions.

Administration time: 20 minutes in total for immediate and delayed modes combined. Delayed mode should always be administered 20 minutes after the immediate mode.

Task: The subject is shown a list of 12 words, one at a time, and then asked to:

- Produce as many of the words as possible immediately following the presentation
- Recognize the words they have seen before from a list of 24 words containing the original 12 words and 12 distractors.
- Following a delay of 20 minutes, recognize the words they have seen before from another list of 24 words containing the original list and 12 new distractors.

Instructions: Please follow instructions (and script) for administering the PARALLEL mode in the Test Administration Guide pages 201-208. **Remember – the subject should not be facing the computer screen during the Free Recall block!**

4. DMS:

Overview: This is a test of simultaneous and delayed matching to sample. This test is primarily sensitive to damage in the medial temporal lobe area, with some input from the frontal lobes.

Administration time: around 10 minutes.

Task: The subject is shown a complex visual pattern (the sample) and then, after a brief delay, four similar patterns. The subject must touch the pattern which exactly matches the sample.

Instructions: Please follow instructions (and script) for administering the PARALLEL mode in the Test Administration Guide pages 65-70.

5. SWM:

Overview: SWM is a test of the subject's ability to retain spatial information and to manipulate remembered items in working memory. It is a self-ordered task, which also assesses heuristic strategy. This test is a sensitive measure of frontal lobe and 'executive' dysfunction.

Administration time: Around 8 minutes, depending on level of impairment

Task: The test begins with a number of colored squares (boxes) being shown on the screen. The aim of this test is that, by touching the boxes and using a process of elimination, the subject should find one blue 'token' in each of a number of boxes and use them to fill up an empty column on the right hand side of the screen. The number of boxes is gradually increased, until it is necessary to search a total of eight boxes. The color and position of the boxes used are changed from trial to trial to discourage the use of stereotyped search strategies.

Instructions: Please follow instructions (and script) for administering the CLINICAL mode in the Test Administration Guide pages 193-200.

6. RVP:

Overview: RVP is a test of visual sustained attention. It is sensitive to dysfunction in the parietal and frontal lobe areas of the brain and is also a sensitive measure of general performance.

Administration time: Around 7 minutes.

Task: A white box appears in the centre of the computer screen, inside which digits, from 2 to 9, appear in a pseudo-random order, at the rate of 100 digits per minute. Subjects are requested to detect target sequences of digits (for example, 2-4-6, 3-5-7, 4-6-8) and to register responses using the press pad.

Instructions: Please follow instructions (and script) for administering the CLINICAL mode in the Test Administration Guide pages 147-156.

7. IED:

Overview: IED is a test of rule acquisition and reversal. It features:

- visual discrimination and attentional set formation
- maintenance, shifting and flexibility of attention

This test is primarily sensitive to changes to the fronto-striatal areas of the brain.

Administration time: Around 7 minutes, depending on level of impairment.

Task: Two artificial dimensions are used in the test:

- color-filled shapes
- white lines

Simple stimuli are made up of just one of these dimensions, whereas compound stimuli are made up of both, namely white lines overlying color-filled shapes. The subject starts by seeing two simple color-filled shapes, and must learn which one is correct by touching it. Feedback teaches the subject which stimulus is correct, and after six correct responses, the stimuli and/or rules are changed. These shifts are initially intra-dimensional (e.g. color filled shapes remain the only relevant dimension), then later extra-dimensional (white lines become the only relevant dimension). Subjects progress through the test by satisfying a set criterion of learning at each stage (6 consecutive

correct responses). If at any stage the subject fails to reach this criterion after 50 trials, the test terminates.

Instructions: Please follow instructions (and script) for administering the PARALLEL mode in the Test Administration Guide pages 75-80.

9.11.2.11 Results Manager

(Please refer to CANTABeclipse Software Guide starting on page 81)

You can use the Results Manager to:

- Create re-usable reporting templates
- Archive data to a network drive
- Perform a general backups to a network drive
- Generate reports and data sheets

From the Control Centre:

Go to File

Results Manager

A. To create **Data Reporting Templates**

- A template needs to be created for each time point (CALERIE Baseline 2, CALERIE Month 6, CALERIE Month 12, CALERIE Month 24)
- Choose advanced settings

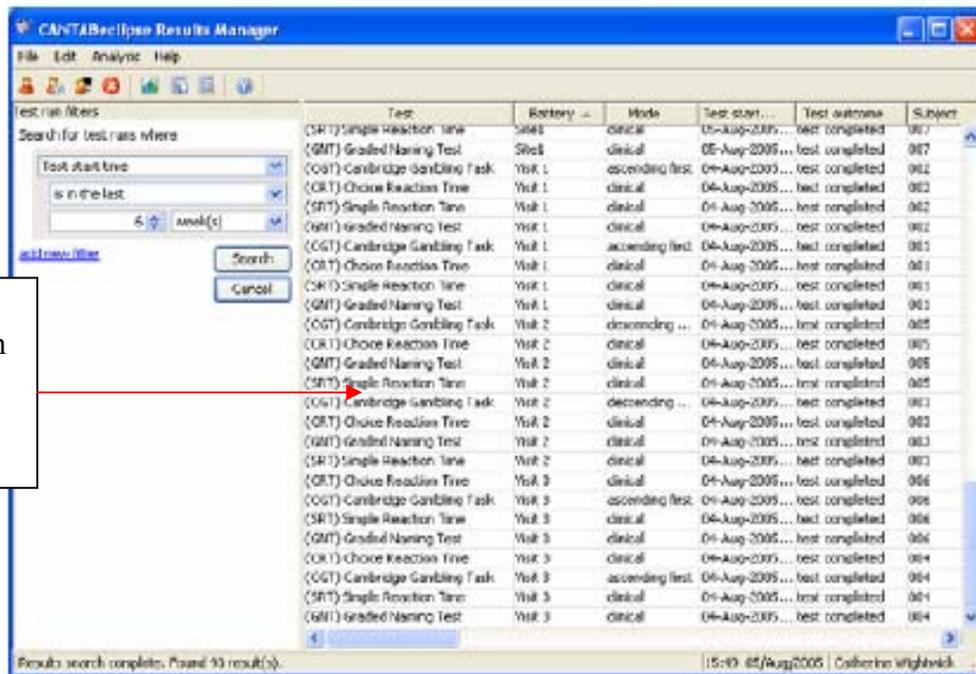


Figure 5-1 The CANTABeclipse Results Manager

The following are the selections for the reporting templates that need to be created:

CALERIE Baseline 2 (Session 1)

Test	Measure	Option	Mode	Session	Heading
(administrative details)	Subject ID				Default
(administrative details)	Session Start Time (<i>Date and Time</i>)				Default
(administrative details)	Username (<i>Site Name</i>)				Default
MOT	Mean Error		Clinical	1	Default
MOT	Mean Latency		Clinical	1	Default
RTI	Simple Reaction Time		Parallel	1	Default
RTI	Five-Choice Reaction Time		Parallel	1	Default
RTI	Simple Accuracy Score		Parallel	1	Default
RTI	Five-Choice Accuracy Score		Parallel	1	Default
VRM	Free Recall-Total Correct		Parallel 1 - immediate	1	Default
VRM	Free Recall – Total Novel Words		Parallel 1 - immediate	1	Default
VRM	Free Recall – Total Perseverations		Parallel 1 - immediate	1	Default
VRM	Recognition – Total Correct		Parallel 1 - immediate	1	Default
VRM	Recognition – Total False Positives		Parallel 1 - immediate	1	Default
VRM	Recognition – Total Correct		Parallel 1 - delayed	1	Default
VRM	Recognition – Total False Positives		Parallel 1 - delayed	1	Default
DMS	Percent Correct	(n ms delay – simultaneous)	Parallel 1	1	Default
DMS	Percent Correct	all delays	Parallel 1	1	Default
DMS	Percent Correct	0 ms delay	Parallel 1	1	Default
DMS	Percent Correct	4000 ms delay	Parallel 1	1	Default
DMS	Percent Correct	(12000 ms delay)	Parallel 1	1	Default
SWM	Between Errors		Clinical	1	Default
SWM	Within Errors		Clinical	1	Default
SWM	Total Errors		Clinical	1	Default
SWM	Strategy		Clinical	1	Default
RVP	Total Hits		Clinical	1	Default
RVP	Total Misses		Clinical	1	Default
RVP	Total False Alarms		Clinical	1	Default
RVP	Total Correct Rejections		Clinical	1	Default
RVP	Mean Latency		Clinical	1	Default
IED	Total Errors (Adjusted)		Parallel 1	1	Default
IED	Errors (Block 2)		Parallel 1	1	Default
IED	Errors (Block 5)		Parallel 1	1	Default
IED	Errors (Block 7)		Parallel 1	1	Default
IED	Errors (Block 9)		Parallel 1	1	Default
IED	Completed Stage Trials		Parallel 1	1	Default

CALERIE Month 6 (Session 2)

Test	Measure	Option	Mode	Session	Heading
(administrative details)	Subject ID				Default
(administrative details)	Session Start Time (<i>Date and Time</i>)				Default
(administrative details)	Username (<i>Site Name</i>)				Default
MOT	Mean Error		Clinical	2	Default
MOT	Mean Latency		Clinical	2	Default
RTI	Simple Reaction Time		Parallel	2	Default
RTI	Five-Choice Reaction Time		Parallel	2	Default
RTI	Simple Accuracy Score		Parallel	2	Default
RTI	Five-Choice Accuracy Score		Parallel	2	Default
VRM	Free Recall-Total Correct		Parallel 2 - immediate	2	Default
VRM	Free Recall – Total Novel Words		Parallel 2 - immediate	2	Default
VRM	Free Recall – Total Perseverations		Parallel 2 - immediate	2	Default
VRM	Recognition – Total Correct		Parallel 2 - immediate	2	Default
VRM	Recognition – Total False Positives		Parallel 2 - immediate	2	Default
VRM	Recognition – Total Correct		Parallel 2 - delayed	2	Default
VRM	Recognition – Total False Positives		Parallel 2 - delayed	2	Default
DMS	Percent Correct	(n ms delay – simultaneous)	Parallel 2	2	Default
DMS	Percent Correct	all delays	Parallel 2	2	Default
DMS	Percent Correct	0 ms delay	Parallel 2	2	Default
DMS	Percent Correct	4000 ms delay	Parallel 2	2	Default
DMS	Percent Correct	(12000 ms delay)	Parallel 2	2	Default
SWM	Between Errors		Clinical	2	Default
SWM	Within Errors		Clinical	2	Default
SWM	Total Errors		Clinical	2	Default
SWM	Strategy		Clinical	2	Default
RVP	Total Hits		Clinical	2	Default
RVP	Total Misses		Clinical	2	Default
RVP	Total False Alarms		Clinical	2	Default
RVP	Total Correct Rejections		Clinical	2	Default
RVP	Mean Latency		Clinical	2	Default
IED	Total Errors (Adjusted)		Parallel 2	2	Default
IED	Errors (Block 2)		Parallel 2	2	Default
IED	Errors (Block 5)		Parallel 2	2	Default
IED	Errors (Block 7)		Parallel 2	2	Default
IED	Errors (Block 9)		Parallel 2	2	Default
IED	Completed Stage Trials		Parallel 2	2	Default

CALERIE Month 12 (Session 3)

Test	Measure	Option	Mode	Session	Heading
(administrative details)	Subject ID				<i>Default</i>
(administrative details)	Session Start Time (<i>Date and Time</i>)				<i>Default</i>
(administrative details)	Username (<i>Site Name</i>)				<i>Default</i>
MOT	Mean Error		Clinical	3	<i>Default</i>
MOT	Mean Latency		Clinical	3	<i>Default</i>
RTI	Simple Reaction Time		Parallel	3	<i>Default</i>
RTI	Five-Choice Reaction Time		Parallel	3	<i>Default</i>
RTI	Simple Accuracy Score		Parallel	3	<i>Default</i>
RTI	Five-Choice Accuracy Score		Parallel	3	<i>Default</i>
VRM	Free Recall-Total Correct		Parallel 3 - immediate	3	<i>Default</i>
VRM	Free Recall – Total Novel Words		Parallel 3 - immediate	3	<i>Default</i>
VRM	Free Recall – Total Perseverations		Parallel 3 - immediate	3	<i>Default</i>
VRM	Recognition – Total Correct		Parallel 3 - immediate	3	<i>Default</i>
VRM	Recognition – Total False Positives		Parallel 3 - immediate	3	<i>Default</i>
VRM	Recognition – Total Correct		Parallel 3 - delayed	3	<i>Default</i>
VRM	Recognition – Total False Positives		Parallel 3 - delayed	3	<i>Default</i>
DMS	Percent Correct	(n ms delay – simultaneous)	Parallel 3	3	<i>Default</i>
DMS	Percent Correct	all delays	Parallel 3	3	<i>Default</i>
DMS	Percent Correct	0 ms delay	Parallel 3	3	<i>Default</i>
DMS	Percent Correct	4000 ms delay	Parallel 3	3	<i>Default</i>
DMS	Percent Correct	(12000 ms delay)	Parallel 3	3	<i>Default</i>
SWM	Between Errors		Clinical	3	<i>Default</i>
SWM	Within Errors		Clinical	3	<i>Default</i>
SWM	Total Errors		Clinical	3	<i>Default</i>
SWM	Strategy		Clinical	3	<i>Default</i>
RVP	Total Hits		Clinical	3	<i>Default</i>
RVP	Total Misses		Clinical	3	<i>Default</i>
RVP	Total False Alarms		Clinical	3	<i>Default</i>
RVP	Total Correct Rejections		Clinical	3	<i>Default</i>
RVP	Mean Latency		Clinical	3	<i>Default</i>
IED	Total Errors (Adjusted)		Parallel 3	3	<i>Default</i>
IED	Errors (Block 2)		Parallel 3	3	<i>Default</i>
IED	Errors (Block 5)		Parallel 3	3	<i>Default</i>
IED	Errors (Block 7)		Parallel 3	3	<i>Default</i>
IED	Errors (Block 9)		Parallel 3	3	<i>Default</i>
IED	Completed Stage Trials		Parallel 3	3	<i>Default</i>

CALERIE Month 24 (Session 4)

Test	Measure	Option	Mode	Session	Heading
(administrative details)	Subject ID				<i>Default</i>
(administrative details)	Session Start Time (<i>Date and Time</i>)				<i>Default</i>
(administrative details)	Username (<i>Site Name</i>)				<i>Default</i>
MOT	Mean Error		Clinical	4	<i>Default</i>
MOT	Mean Latency		Clinical	4	<i>Default</i>
RTI	Simple Reaction Time		Parallel	4	<i>Default</i>
RTI	Five-Choice Reaction Time		Parallel	4	<i>Default</i>
RTI	Simple Accuracy Score		Parallel	4	<i>Default</i>
RTI	Five-Choice Accuracy Score		Parallel	4	<i>Default</i>
VRM	Free Recall-Total Correct		Parallel 4 - immediate	4	<i>Default</i>
VRM	Free Recall – Total Novel Words		Parallel 4 - immediate	4	<i>Default</i>
VRM	Free Recall – Total Perseverations		Parallel 4 - immediate	4	<i>Default</i>
VRM	Recognition – Total Correct		Parallel 4 - immediate	4	<i>Default</i>
VRM	Recognition – Total False Positives		Parallel 4 - immediate	4	<i>Default</i>
VRM	Recognition – Total Correct		Parallel 4 - delayed	4	<i>Default</i>
VRM	Recognition – Total False Positives		Parallel 4 - delayed	4	<i>Default</i>
DMS	Percent Correct	(n ms delay – simultaneous)	Parallel 4	4	<i>Default</i>
DMS	Percent Correct	all delays	Parallel 4	4	<i>Default</i>
DMS	Percent Correct	0 ms delay	Parallel 4	4	<i>Default</i>
DMS	Percent Correct	4000 ms delay	Parallel 4	4	<i>Default</i>
DMS	Percent Correct	(12000 ms delay)	Parallel 4	4	<i>Default</i>
SWM	Between Errors		Clinical	4	<i>Default</i>
SWM	Within Errors		Clinical	4	<i>Default</i>
SWM	Total Errors		Clinical	4	<i>Default</i>
SWM	Strategy		Clinical	4	<i>Default</i>
RVP	Total Hits		Clinical	4	<i>Default</i>
RVP	Total Misses		Clinical	4	<i>Default</i>
RVP	Total False Alarms		Clinical	4	<i>Default</i>
RVP	Total Correct Rejections		Clinical	4	<i>Default</i>
RVP	Mean Latency		Clinical	4	<i>Default</i>
IED	Total Errors (Adjusted)		Parallel 4	4	<i>Default</i>
IED	Errors (Block 2)		Parallel 4	4	<i>Default</i>
IED	Errors (Block 5)		Parallel 4	4	<i>Default</i>
IED	Errors (Block 7)		Parallel 4	4	<i>Default</i>
IED	Errors (Block 9)		Parallel 4	4	<i>Default</i>
IED	Completed Stage Trials		Parallel 4	4	<i>Default</i>

B. To **Archive Data**

- Use filters to find the subject and session you wish to archive.
- Select all tests
- Go to “File”
 - “Export selected to archive”

C. To **Generate Data Reports**

- Use the filters to find the subject and session for which you wish to create a report
- Select all tests
- Click on **Analysis Tab**
 - Choose **Summary Data**
 - Choose the appropriate **Reporting Template (i.e. CALERIE Baseline 2, CALERIE Month 6, etc.)**
 - Choose **Generate Report (not Datasheet)**
 - Choose “one report page per session”
 - Do NOT include “norms comparison”
- Select “View”
 - You will then be directed into the report page
 - Go to the **File** tab
 - Choose “**print**”

D. **Print the Report**

- Copy the header information by hand (or label) on the top of each report page (the face page will already have this information).
 - Headers should include the following information:
 - CALERIE
 - Subject ID
 - Date of Birth
 - Battery
 - Session start time (this includes the date by default)
- **The printed file will be included in the data sent to the Data Center** (save another copy in the subject’s paper file at your site).

E. **Save the Data to the Network Drive**

9.12 **Electrocardiogram Procedures**

ECGs will be performed by study personnel trained in standard lead placement. Training will initially be conducted during the common study training sessions as a part of the CPX testing training.

Timing:

The ECG will be obtained at the following time points, coincident with the measurement of serum potassium: screening, baseline, and at 1, 3, 6, 9, 12, 18, and 24 months. In addition, for the CR group, ECGs will be performed at months 2, 4 and 5 after starting the intervention, otherwise, the time oints are consistent with both treatment groups

Procedure:

1. The 12-lead ECG will be obtained supine using standard lead placement.
2. The ECG will be read within 24 hours by the study physician or designated trained alternate.
3. Details of the reading will be noted on the accompanying form:
 - A. Evaluate the quality of the ECG.
 - B. Evaluate rate.
 - C. Evaluate rhythm, including extra systoles.
 - D. Evaluate P wave and PR interval.
 - E. Evaluate QRS duration for blocks.
 - F. Evaluate QRS axis.
 - G. Evaluate for Q-waves.
 - H. Evaluate ST segment.
 - I. Evaluate the QT interval.
4. Special attention will be paid to the following intervals for signs of potassium toxicity, which will be recorded on the form if present:
 - A. PR interval prolongation
 - B. ST segment depression
 - C. QRS interval prolongation
 - D. Disappearance of the P wave
 - E. QT interval prolongation
5. Specifically, symmetric peaking of the T-wave, significant changes in prolongation of the above mentioned intervals compared with previous studies or beyond normal values (PR > 0.20 ms; QRS > 0.12 ms; QTc > 0.48 ms) will be reported within 24 hours to the study site physician for follow-up.
6. Comparison will be made to prior studies and note made of any significant changes.
7. The ECG will be reviewed for abnormality and clinical relevance. It must be signed and dated by the reading physician.
8. Copies of the reading forms will be filed at the sites and copies sent to the CC for filing and future reference as needed.

9.12.1 ECG Interpretation Form
CALERIE Study ECG

ECG (check one) Normal Abnormal

If Abnormal

Rhythm <i>(check all that apply)</i>	P Wave <i>(check all that apply)</i>	Axis <i>(check one, if applicable)</i>	Conduction <i>(check all that apply)</i>
<input type="checkbox"/> AIVR <input type="checkbox"/> Atrial fibrillation <input type="checkbox"/> Atrial flutter <input type="checkbox"/> AV sequential pacing <input type="checkbox"/> Ectopic atrial tachycardia <input type="checkbox"/> Nodal rhythm <input type="checkbox"/> NSR <input type="checkbox"/> Paced rhythm <input type="checkbox"/> Sinus bradycardia <input type="checkbox"/> Sinus tachycardia <input type="checkbox"/> SVT <input type="checkbox"/> Ventricular pacing	<input type="checkbox"/> LAE <input type="checkbox"/> RAE	<input type="radio"/> Normal <input type="radio"/> LAD <input type="radio"/> RAD	<input type="checkbox"/> 1° AV Block <input type="checkbox"/> 2° AV Block - Type I <input type="checkbox"/> 2° AV Block - Type II <input type="checkbox"/> 3° AV Block <input type="checkbox"/> Incomplete LBBB <input type="checkbox"/> LBBB <input type="checkbox"/> Left Ant Hemiblock (LAD > -30°) <input type="checkbox"/> Left Post. Hemiblock (RAD > +120°) <input type="checkbox"/> Nonspecific IVCD <input type="checkbox"/> RBBB <input type="checkbox"/> Incomplete RBBB <input type="checkbox"/> WPW
Arrhythmias <i>(check all that apply)</i>	QRS Complex <i>(check all that apply)</i>	ST-T Waves <i>(check all that apply)</i>	
<input type="checkbox"/> Couplets <input type="checkbox"/> PAC's <input type="checkbox"/> PJC's <input type="checkbox"/> PVC's <input type="checkbox"/> Ventricular tachycardia	<input type="checkbox"/> Anterior MI <input type="checkbox"/> Inferior MI <input type="checkbox"/> LVH <input type="checkbox"/> Lateral MI <input type="checkbox"/> Posterior MI <input type="checkbox"/> RVH	<input type="checkbox"/> Early repolarization <input type="checkbox"/> Low voltage <input type="checkbox"/> LV ischemia <input type="checkbox"/> Nonspecific ST-T changes <input type="checkbox"/> Poor R wave progression <input type="checkbox"/> Prolonged QTc <input type="checkbox"/> Secondary repolarization changes (LVH, RBBB) <input type="checkbox"/> Secondary repolarization changes (RVH) <input type="checkbox"/> ST elevation (persistent) c/w LV aneurysm <input type="checkbox"/> ST elevation c/w acute infarction <input type="checkbox"/> ST elevation c/w acute pericarditis <input type="checkbox"/> Subendocardial injury <input type="checkbox"/> Transient ST elevation c/w variant angina	

PLEASE NOTE ANY OF THE FOLLOWING:

- PR interval prolongation
- ST segment depression
- QRS interval prolongation
- Disappearance of the P wave
- QT interval prolongation

Signed _____

Date _____

