

## 4. Chapter 4: Baseline

### 4.1 Overview of Eligibility and Clinical Assessments

Baseline assessments can be divided into a 2-3 day period when needed, for the participant's comfort and convenience. Keep in mind that the blood samples need to be submitted to a central laboratory and results are not received immediately. Every effort will be made to randomize participants within one week of their screening visit but participants must be randomized when they have attained 4-21 days of abstinence.

The initial assessment battery will consist of obtaining a breathalyzer and signed witnessed consent. A clinical interview will also be completed in order to rule out major psychiatric disorders. The first step will include all screening instruments necessary to determine study eligibility (i.e., clinical interview and drinking assessments). Blood and urine samples should be collected on the first baseline screening day as it takes 1-2 days to receive the lab report from Quintiles, Inc. The medical evaluation should occur after the site receives the lab results.

It is suggested that the medical evaluation and the rest of the drinking and psychosocial assessments be collected on the second baseline screening day. The medical evaluation will consist of vital signs and a breathalyzer, CIWA, Medical History, Physical Exam, Menstrual Calendar, and a report regarding the participant's lab results. The Psychosocial assessments consist of the Important People Inventory, Brief Symptom Inventory. The quality of life assessments consist of the World Health Organization Quality of Life and the SF-12 and data regarding treatment related expectancies will be collected by administration of the Treatment Experiences and Expectations form.

Although someone might become ineligible early on in the screening process, the clinical centers should continue to collect the Form 90, SCID-E (Alcohol and Drug Module) and the Concurrent Medication Form for those people. This information will be used to describe the ineligible population.

If the participant becomes ineligible at any time during the screening process, staff should use discretion when informing the person of the reason(s) for ineligibility.

The Eligibility Checklist (ELG) should be completed for anyone who completes any portion of the baseline screening assessments. Complete as much of the checklist as possible for those who become ineligible. If staff are not provided with enough information to respond to all items, leave those item(s) blank. Enter those items as permanently missing in the data management system. **All** items on the Eligibility Checklist **must** be completed for all randomized patients.

#### **4.1.1 Data Collection and Management**

Since the COMBINE Data Management System (DMS) is designed for self-administered assessments to be entered directly into the computer by the participant, the mode of data collection for self-administered assessments should be noted (Data Collection/Entry Checklist is located in Appendix A). If data are entered directly into the DMS and this is documented on the checklist, those blank paper forms can be removed from the participant binder. The checklist will provide documentation regarding the mode of data collection (i.e., entered directly into the DMS, collected on paper, permanently missing, not applicable) and when the data are

collected. This checklist will allow the sponsor monitor(s) to easily identify the mode of collection during site visits.

Case Report Forms that are considered to be source documents (i.e., Medical History, Physical Exam) should remain in the participant binder. If these data are entered directly into the DMS, the form should be printed, signed by the appropriate staff and inserted into the CRF binder.

Additional information pertaining to data collection and management is located in Chapter 7 section 7.11.

## **4.2 Communication Flow**

### **4.2.1 Communication within the Site**

Maintaining the boundaries between the data collection and the treatment arms is not always an easy task. The importance of the separation between the phases is embodied in the fact that different staff performs these two vital functions. Staff collecting data should be trained in maintaining this distinction. Staff should also acquire skills and resources to deal with situations that challenge the boundaries between the treatment and data collection phase. Chapter 8 discusses this issue in greater detail.

Outlining the flow of communication (what can be communicated and to whom?) is another way to maintain boundaries between research and treatment staff. The Communication Table is located in Appendix B. The table outlines the type of information that can be communicated between research and treatment staff.

### **4.2.2 Eligibility Questions**

Eligibility questions that cannot be answered locally by the PI or study physician should be forwarded to the Coordinating Center. If the site needs an immediate response (staff should inform the CC if this is the case), the Coordinating Center will attempt to respond. If the Coordinating Center is unable to respond the question will be forwarded to a designated representative of the Operations, Treatment, or Research Protocol Committee. Once the question is answered or the issue is resolved, the Coordinating Center will notify the site.

## **4.3 Initial Evaluations and Informed Consent**

### **4.3.1 Breath Alcohol Content and Vital Signs**

Collect the candidates breath alcohol level and vitals and record the information on the Vital Signs Form (VSB) during each contact. Sites should use their discretion to determine if vital signs need to be collected at each baseline visit. BAC must be 0.00 mg/dl in order for the person to sign the consent form. If the person's BAC level is  $> 0.00$ , ask the person to reschedule the appointment. S/he should also be informed that if BAC  $> .05$  for the post-randomization research visits s/he will be asked to reschedule the appointment.

The BAC will be collected for participants assigned to MM and/or CBI. Vitals will not be taken for participants assigned to CBI unless this is requested.

BAC should be documented on the Form-90 AIR/ED.

### **4.3.2 Informed Consent**

In order to validly screen and recruit participants into the study, information collected beyond the point of the “pre-baseline” Telephone Quick Screen (TQS) should only be obtained after first explaining the study to the participant and obtaining their signature on the site-specific consent form. Each site must comply with local IRB guidelines in this regard under the aegis of the federal OHSR guidelines for clinical research with human participants.

The social contract for participation is established during the first baseline assessment when the informed consent document is read by the participant and discussed in detail with the staff person conducting the interview. It is important for the staff person to acknowledge the full range of potential risks, costs, and discomforts associated with the experimental design, as well as anticipated benefits of participation. Being “fully informed” means that the participant has had an opportunity to discuss concerns about any of the assessment, treatment, or follow-up procedures, and has had an opportunity to consider alternatives to participation in the study.

It is essential that the participant be informed that they will not be unblinded to their treatment assignment until **all** participants have completed the study.

During the course of the study, information that may be relevant to the participant’s willingness to continue participation in the trial may become available. If this information impacts the consent form and there are revisions made, the site should communicate the changes to those participants who signed an earlier version of the consent form. The method of communicating the changes (i.e., verbally informing the participant of changes to the consent form, formally re-consenting the participant, etc.) is to be determined at the local level by the Institutional Review Board. The site should write a note to the study file that indicates the method by which the participants were made aware of the changes to the consent form.

#### **4.3.2.1 Reiteration of Study Procedures**

Because the language of the official Informed Consent document may be technical enough to confuse some individuals, the staff member conducting the interview must explore the participant’s understanding of the procedures. Use the Informed Consent outline (“Preparing Clients for Treatment in an Alcohol Research Setting” in Appendix B) after the participant has read the Informed Consent document to review and discuss the important points before the consent document is signed.

#### **4.3.2.2 Initiate a Discussion About Adherence**

Participants should be made aware of how missing data and attrition affect the quality of the study. Ask the participant for his or her reasons or motivation for participating in a clinical trial. As part of the informed consent process, ask each participant about the following issues:

- 1) “Is there anything that may interfere with your ability to participate in the study as outlined?”
- 2) “In the event that you cannot be located, research staff must go to great length to relocate you and obtain an interview. This will include calling locators that you provide, visiting your last known address, and calling you at work. Does that pose a problem for you?”

### **4.3.2.3 Inform Participants About the Inclusion Visit**

The eligibility process requires several visits and multiple assessments. Participants should be made aware that they have not officially been enrolled in the study until they have been informed of the treatment assignment and attend the first treatment session. This provides them with an opportunity to change their mind *without jeopardizing the integrity of the study*, should they have “second thoughts” about participation.

### **4.3.3 Demographics**

Demographics are important in establishing documentation of the baseline characteristics of the study participant sample. The Demographic form (DEM) is interview-administered at the time of screening. Try to elicit complete responses from the prospective participant for all items on this form, since values should rarely be missing or unknown.

### **4.3.4 Determinants of Participation**

Participants who continue on in the screening process will be asked to complete the Reasons for Wanting to Participate Questionnaire (RWP) during the baseline-screening phase.

## **4.4 Specific Guidelines for the Baseline RA Interview**

Whenever the Research Assistant assessment occurs, start by introducing yourself to the participant and describe the role of the Research Assistant: *to collect research data before, during and after treatment in order to evaluate the effectiveness of the treatment*. Explain that research staff are separate from the treatment staff, and that information obtained from them during follow-up assessments will not be shared with the therapist.

### **4.4.1 Using the Research Timeline Handout:**

Provide a copy of the handout ***“Your Roles and Responsibilities as a Research Volunteer”*** (Appendix B) and review the content of the form. Be sure to cover the following points:

- Schedule of events during the three phases of the study: enrollment, treatment, follow-up
- Difference between treatment and research
- Structure of the interviews (listed on the timeline), including a Breathalyzer at each visit, completing the TLFB, as well as self-report forms on the computer or on paper and pencil, lab work, and interviews.
- Payment schedules and explain that the participant will be paid after completing each follow-up visit.
- The importance of continuing in research follow-up interviews even if the participant decides to discontinue treatment
- The importance of complete and accurate data
- We will be giving reminder letters and reminder calls
- Explain the timeline for COMBINE and the Cost Effectiveness study (optional).

Explain that the treatment phase of the study will last for 16 weeks and that the Research Assistants will collect data throughout this time. Explain that there will be a follow-up phase that will last for an additional 12 months, in which the participant will only be meeting with the Research Assistant. This data will be shared with the Coordinating Center and will be used to determine how helpful this particular treatment is.

Ask the participant if he/she has any concerns regarding the assessments, the time commitment, or any other aspect of the study. Respond to any questions that the participant raises, focusing primarily on clarifying study procedures and reinforcing the importance of the role of the research participant. If the participant identifies any concerns such as childcare, transportation, etc., refer these issues to the PC for resolution.

## **4.5 Initial Baseline Visit**

Baseline assessments can be divided into a 2-3 day period when needed, for the participant's comfort and convenience but this is not mandatory. The suggested order of assessments indicates that the clinical interview and the drinking assessments will be collected during the initial baseline visit.

### **4.5.1 Clinical Interview**

The clinical interview is needed to obtain an accurate alcohol diagnosis and to rule out other current substance dependence as well as other major psychiatric disorders that are exclusionary.

#### **4.5.1.1 SCID Module E Alcohol and Drug**

This SCID Module E module focuses on the assessment of alcohol and drug use, determining the number of diagnostic symptoms endorsed, as whether the individual is categorized as having alcohol and/or drug dependence diagnosis.

The full module is administered at baseline. The alcohol portion only is administered at weeks 16, 52, and 68.

##### **4.5.1.1.1 Specific Guidelines for Conducting the SCID-E**

- For alcohol, the **past 90 days** should be used as the time frame when assessing alcohol and/or drug dependence diagnoses at baseline. Once dependence has been confirmed, follow up with questions regarding physiological dependence and severity of dependence. If criteria for dependence have not been met, follow up with questions regarding alcohol abuse.
- For substances other than alcohol and opiates, complete the SCID dependence questions for all substance(s) coded 2 or 3 on the drug screening section for the **last 90 days**. Once dependence has been confirmed, it is not necessary to obtain information about whether physiological dependence or severity of dependence. Also, it is not necessary to obtain information about substance abuse.
- For opiates, complete the SCID dependence and abuse questions for opiates coded 2 or 3 on the drug screening section for the **past 6 months**. If dependence has been confirmed, it is not necessary to obtain information about either physiological dependence or severity of dependence.

The time frame for follow-up interviews (weeks 16, 52, and 68) is **since the most recent assessment**.

Information obtained from the SCID Module E should be recorded on the SCID Modules Form (SCM).

##### **4.5.1.2 Computerized SCID Screen Participant Questionnaire**

The SCID Screen Participant Questionnaire computer program for Windows, known as the mini SCID, is the computer administered screening version of the structured clinical interview for DSM-IV (SCID) created by

Michael First, M.D. The SCID Screen PQ Program probes a participant’s DSM-IV Axis I symptoms at a grade 7 reading level. Participants respond to SCID Screen PQ questions online. For those participants who are not comfortable with a computer screening, there is a written screen for the DSM-IV SCID by the same author.

The follow-up psychiatric interview is to be performed by an experienced clinician. Initial screening should be done with the “mini-SCID” software as a gross tool for indicating the need to either probe further, or administer specific modules in addition to Section E.

**4.5.1.3 SCID Modules**

The interviewer should follow up with modules for disorders that, in the SCID PQ summary report, fall under the category “the following are supported or suggested by the person’s response.” Axis I categories are listed in Table 4.2 and are categorized under “assess” or “don’t assess”. The interviewer should also use clinical judgment in order to determine which modules should be administered.

**Table 4.1 Axis I Categories**

<b>Axis I Category</b>	<b>Assess :</b>	<b>Don’t assess :</b>
Schizophrenia and other psychotic conditions	Presence of psychotic symptoms suffices to satisfy primary goal	
Mood Disorders	<ul style="list-style-type: none"> <li>• Bipolar I</li> <li>• Bipolar II</li> <li>• Current Major Depressive Disorder*</li> </ul>	<ul style="list-style-type: none"> <li>• Dysthymic Disorder</li> <li>• Depressive Disorder NOS</li> </ul>
Anxiety Disorders	<ul style="list-style-type: none"> <li>• Panic Disorders*</li> <li>• PTSD*</li> <li>• OCD*</li> </ul>	<ul style="list-style-type: none"> <li>• GAD</li> <li>• Specific Phobias</li> <li>• Anxiety Disorder NOS</li> <li>• Social Phobia</li> </ul>
Eating Disorders	<ul style="list-style-type: none"> <li>• Anorexia Nervosa (because of medical needs)</li> <li>• Bulimia (because purging may affect medication absorption)</li> </ul>	
•		Presence of disorders not relevant to goals <ul style="list-style-type: none"> <li>• Somatoform Disorders</li> <li>• Dissociative Disorder</li> <li>• ADHD and Impulse Control Disorders</li> <li>• Sexual and Gender Identity Disorders</li> <li>• Sleep Disorders</li> <li>• Adjustment Disorders</li> </ul>

\*participant may be included in the study if severity of the disorder does not warrant medications

The SCID Modules Form (SCM) should be completed for all participants. If it is necessary to proceed with a SCID module, document this on the form. Information about lifetime prevalence and whether symptomatic diagnostic criteria are present or absent (past month) should be recorded.

When the SCID interview is complete, inform the participant about his/her eligibility based upon the diagnostic interview. Use general terms such as “you meet the study criteria with regard to alcohol and other drug abuse and dependence.” Acknowledge the difficulty and sensitivity of the material discussed during the

SCID interview. Reinforce the individual's cooperation and participation. Clarify any questions or concerns that the participant may have after completing this interview. Discuss treatment recommendations for individuals who are not eligible for COMBINE. Inform the eligible participants of the next step in the enrollment process.

#### **4.5.1.4 Psychiatric History**

The Psychiatric History Form should be administered during the screening visit to exclude the following conditions for which medication is the first line of treatment (even if the person is not currently taking medication for the condition) or to exclude people whose mental health conditions warrant medication treatment. The term "warrant" is based on current practice guidelines and clinical judgement.

- Schizophrenia
- Other psychosis
- Mood disorder
- Certain anxiety disorders
- Other mental or emotional problems
- Suicidal intention
- Self report of anorexia nervosa or bulimia or purging

This Psychiatric History form must be completed for everyone prior to randomization.

#### **4.5.1.5 Concurrent Medications**

The record of all medications, both over the counter (OTC) and prescribed, will be recorded on the Concurrent Medication Form (COM). Over the counter medication that consists of vitamins and herbal supplements should also be recorded. The participant should be reminded regularly, to report any concomitant medication being taken. On the day of screening, the participant should bring to the clinic, all medication being taken under prescription, as well as any OTC drugs used on a regular basis. Refer to the list of excluded medications (Appendix C) for any substances that would be contraindicated for use in combination with acamprosate and naltrexone.

Participants cannot be enrolled if they are currently undergoing therapy for alcohol abuse/ dependence and will continue to do so, or if they have taken either naltrexone or acamprosate in the last 30 days as part of a prescribed course of treatment. If a participant decides to engage in other pharmacologic therapy post-randomization, the information should be documented on the Concurrent Medication Form.

If research staff learns that a participant is taking concomitant medication that is not documented on the case report form, the staff should notify the Project Coordinator, who in turn will inform the MM clinician. This will preserve the boundary between the research and treatment staff.

The Concurrent Medication Form should be completed for all participants at each visit.

#### **4.5.2 Lab Examination**

Blood and urine samples should be collected on the first baseline screening day as it takes 1-2 days to receive the lab report from Quintiles, Inc. The medical evaluation should occur after the site receives the lab results.

The lab examination will include a pregnancy test for females, CBC with differential and platelets, blood chemistry panel (including glucose, LDH, GGT, SGOT, SGPT, alkaline phosphatase, bilirubin, uric acid, serum creatinine, BUN electrolytes, calcium, inorganic phosphorus, total protein and albumin), urinalysis, and urine drug screening. CDT and pharmacogenetic samples will also be collected at baseline. These frozen samples should be shipped to Quintiles Laboratories, Inc. on a monthly basis. Refer to Appendix F for more information about collection of pharmacogenetic samples.

Note that Quintiles Laboratories will analyze only those samples that are outlined in the COMBINE protocol and the Quintiles lab manual. If there is a need for additional tests/analysis, they should be done locally.

Refer to the Laboratory Specimen and Procedures manual from Quintiles, Inc. for more details regarding specific laboratory samples, sample collection schedule, shipment, etc. The Quintiles manual should be placed in this COMBINE Manual of Operations.

#### **4.5.2.1 Lab Reports**

Quintiles Laboratories will supply the lab report in hard copy. Keep the copies of all lab records in the participant file. The PI or the designated staff member (i.e., MD) must sign lab results. All significant results should be initialed, and action taken or reason for no action should be indicated on the lab report itself or in the chart note for the session.

If your site requires the birth date to be deleted from the lab report before it is inserted into the participant binder, staff can black out the date (i.e., tape or marker). A written explanation for crossing the date or putting tape over it should be inserted into the regulatory binder.

Remember to provide necessary lab information to the MM clinician for the Clinician Report Form and/or CBI therapist for the Personal Feedback Report prior to the initial session(s).

#### **4.5.2.2 Lab Sample Labeling Errors**

If, after sending a sample, staff becomes aware that they labeled the sample with incorrect identifiers (i.e., an incorrect screening ID number), the site should call the Quintiles Investigator Services Department (1-800-676-8452). Staff should report the scenario and the correct information for the participant(s) involved. Once the report is given to the QLAB, the database will be corrected and a revised report will be sent to the site showing the correct information. The report is a “header” report and not a full lab report. It will consist of the investigator and participant information. A description of the modification will also be noted (i.e., change participant screening ID number from \_\_\_ to \_\_\_).

### **4.5.3 Drinking Assessments**

#### **4.5.3.1 Form-90 AIR/ED**

The Form-90 AIR/ED obtains primary outcome data through a detailed, comprehensive assessment of daily alcohol use and patterns. It also incorporates economic outcome data that covers 4 domains: health care, crime, labor market, and motor vehicle accidents.

The measure uses a modified calendar review method to assess daily alcohol use, weekly patterns and atypical episodes of drinking as well as other drug use. This measure will be used to assure that participants meet the minimum and maximum eligibility criteria for alcohol use for entry into the study.

If applicable, relay relevant information to the CBI therapist (for Personal Feedback Report). Information pertaining to quantity/frequency should be taken from the AED and forwarded to the MM clinician as it is to be documented on the Clinician Report Form.

Consuming 1-2 nonalcoholic beers/day will not effect the 4-day abstinence requirement. If a participant reports that they have consumed nonalcoholic beer, this should be recorded as an abstinent day on the calendar. If s/he consumed any amount of alcohol, it should be recorded as a drinking day.

Reference the Form-90 Manual for more detailed instructions. Questions that pertain to administration of the Form 90 should be directed to Roberta Chavez, M.A., the Assessment Coordinator, at the New Mexico Training and Monitoring Center.

#### **4.5.3.2 Drinker Inventory of Consequences**

This self-administered questionnaire was developed with the goal of being a consensus instrument for the treatment field for assessing negative consequences of drinking. The items survey negative consequences in a variety of domains: physical, interpersonal, intrapersonal, impulse control, and social responsibility.

The DrInC will be collected at baseline (uses past 90 days as the time frame) and at weeks 8, 16, 26, 52 and 68 (uses "since last interview" as the time frame). If applicable, relay relevant baseline information to the CBI therapist (for Personal Feedback Report) and the MM (for the Clinician Report Form).

#### **4.5.3.3 Alcohol Abstinence Self-Efficiency Scale**

The AASE Scales assess participants' confidence to abstain (AASE part 1) and temptation to drink (AASE part 2). Both parts are self-administered and are collected at baseline and are also collected during weeks 16 and 26.

#### **4.5.3.4 Obsessive Compulsive Drinking Scale**

The primary instrument that will measure baseline and change in "craving" will be the Obsessive Compulsive Drinking Scale (OCDS) which has been determined to be reliable, and to have good construct, congruent and face validity (Anton, Moak, & Latham, 1995, Moak et. al. 1998, Bohn et. al. 1996) and to be capable of measuring change during a pharmacotherapy trial (Anton, Moak, & Latham, 1996).

The OCDS is a 14-item self-administered rating scale with two sub-scales, which quantifies thoughts of alcohol, urges to drink, resistance to these thoughts and urges, and social interference of these thoughts and urges. The OCDS will be given during the baseline screening visit and again on the day of randomization (before the participant is informed of treatment assignment). It will also be given to participants during weeks 1, 2, 4, 6, 8, 10, 12, 16, and 26.

#### **4.5.3.5 Drinking Questionnaire**

The OCDS will be supplemented by two additional questions taken from the 5-item Craving Questionnaire developed by Weiss et al. (1995, 1997). This questionnaire, originally developed to assess craving in cocaine dependent participants, has been shown to have internal consistency and predictive validity in an outpatient population of cocaine dependent participants. These items will assess 1) conditioned craving (i.e., the strength of one's desire to drink when exposed to a stimulus previously associated with drinking, such as a beer ad), and 2) the participant's perception of his/her likelihood of drinking if he/she were in the environment previously associated with drinking. They will be used to complete the evaluation of craving during the trial.

These questions are self-administered and are given during screening, on the day of randomization (before the participant is informed of treatment assignment) and during weeks 1, 2, 4, 6, 8, 10, 12, 16, and 26.

#### **4.5.3.6 Alcohol Dependence Scale**

The Alcohol Dependence Scale (ADS) is a self-report measure that provides a quantitative measure of the severity of alcohol dependence consistent with the concept of the alcohol dependence syndrome. The 25

items cover alcohol withdrawal symptoms, impaired control over drinking, awareness of a compulsion to drink, increased tolerance to alcohol, and salience of drink-seeking behavior. The ADS will be given at baseline only.

#### **4.5.3.7 University of Rhode Island Change Assessment Scale**

Assessment of motivational readiness to change will use a version of the University of Rhode Island Change Assessment Scale (URICA; McConaughy, DiClemente, Prochaska & Velicer, 1989) that has been adapted for use in alcoholism treatment. Four subscales are derived, each having six items, each representing precontemplation, contemplation, action and maintenance (resisting relapse). Similar versions of this measure have been used in a number of prior alcoholism treatment studies (DiClemente & Hughes, 1990; Isenhardt, 1994; Carney & Kivlahan, 1995). This measure demonstrated solid psychometric properties in Project MATCH with Alpha internal consistency coefficients for the four subscales ranging from .74 to .82 in the aftercare arm and .75 to .86 in the outpatient arm.

The URICA will be given at baseline only. If applicable, the score should be forwarded to the CBI therapist for the Personal Feedback Report.

#### **4.5.3.8 Family History**

The Family History form obtains information about blood relatives' drinking problems, which is based on whether they experienced legal problems, health problems, marital or family problems, work problems or difficulties with responsibilities around the house, social problems, or had treatment for alcoholism. There are also four questions that involve the participant's mother and/or father smoking history. The FAH is an interviewer-based form and should be administered at baseline only.

### **4.6 Scheduling the Second Baseline Visit**

Once the initial baseline visit is completed, discuss with the participant what will be happening at the next baseline visit. Example: "Okay, John, now we need to schedule your second visit. We usually schedule it 2 days after this visit so that we will have the lab results back. The next visit will last approximately 2-3 hours. You will first be meeting with our Project Coordinator to discuss any questions you may have. The visit will also include a physical, some more self-reports, and a short interview with me. The doctor will also discuss your lab results with you."

The Research Assistant or Administrative Assistant will place a reminder call the day before the participant's scheduled appointments. The Research Assistant will also send out a reminder letter a few weeks before each major follow-up interview is due, to prompt the participant to call and schedule an appointment. If the participant does not respond to the letter or misses the scheduled appointment, the Research Assistant will refer the issue to the Project Coordinator. The Project Coordinator can then further explore any special

needs of the participant and offer ways to increase compliance. Tips for contacting participants are located in Chapter 8.

## **4.7 Second Baseline Visit**

Vitals and BAC should be collected at each visit and the baseline Concurrent Medication form should be updated.

### **4.7.1 Medical Assessments**

Records of adverse events and laboratory determination are central to the study because of obligations to participant well-being and safety. This section describes the procedures to be used to measure the physical parameters.

#### **4.7.1.1 Specific Guidelines for Conducting the Medical Evaluation**

This visit will occur with the RN/Physician, usually 2 days after first screening visit so that lab results will be back.

- Begin the interview by asking the participant if he/she has any questions since last visit.
- Reinforce the participant's commitment and cooperation as well as their importance to the study.
- Orient the participant to what will occur in this visit as well as to the role of the physician/medical monitor.
- Complete the History and Physical
- Conduct an ECG (if indicated--see protocol). Review the results with the Medical Consultant if abnormal.
- Lab results within acceptable range for randomization will be discussed with the participant by the MM therapist.
- CBI-only participants' lab results will be discussed with the participant in collaboration with MD, NP, or PC as determined by each site.
- Labs greater than 3x the upper limit normal will be discussed with the participant by the MD/NP, and referred to primary medical doctor as indicated. Retest as indicated. Consider Hepatitis C testing.
- Abnormal physical findings will be discussed with the participant during the physical exam and referred for follow up with primary care doctor.
- If eligible, review requirement of 4 days of abstinence. Problem-solve with participant about how to achieve this. Discuss potential for acute withdrawal symptoms and develop a plan in case this occurs.
- Attempt to schedule inclusion visit as soon as possible, considering the participant's preference for initiation of treatment.

**Table 4.2 Medical Measurements**

<b>Medical Assessment Module</b>			
	<b>Day 1</b>	<b>Day 2</b>	
Vitals and BAC (VSB)		X	Completed at each contact
Medical History (MHE)		X	Completed for all potential participants
Physical Exam (PHE)		X	ECG if clinically indicated
CIWA-Ar (CIW)		X	As needed on day 1 or 2. Must complete on day of randomization
Menstrual Calendar (MCA)		X	Completed at baseline for all female candidates
Concurrent Medication (COM)		X	Complete at each visit for all potential participants
Lab Results		X	Repeat blood work if necessary

**4.7.1.2 Medical History**

The Medical History form (MHE) is interview based, and must be completed prior to randomization to rule out any potential exclusion criteria (in conjunction with the physical exam and lab screen). Based on the responses from the Demographics form, inquire about the prospective participant’s medical history. Questions should be adapted to the appropriate literacy level of the prospective study participant.

**4.7.1.3 Physical Exam**

The Physical Examination form (PHE) is critical for documentation of the physical health of the prospective COMBINE participant at screening. Perform an abbreviated physical examination and record the findings. If indicated, a full exam can be conducted. If a problem is detected, clinical referral should be provided. Should any abnormal conditions be detected as a result of the examination, indicate the condition and degree of severity. Some abnormalities may be severe enough to exclude the participant from the study (see Chapter 2: Eligibility).

Record a standard 12-lead resting ECG if there is any personal history of heart conditions, and note any abnormalities upon interpretation.

An abbreviated physical examination will be performed at the screening visit. A physical checkup, including breath alcohol testing, vital signs and an ECG (as needed) will be performed.

**4.7.1.4 Menstrual Calendar**

The Menstrual Cycle Calendar is a way to record the pattern of a woman’s menstrual cycle in a calendar format. It is an important indication of any irregularities and/or missed periods due to early pregnancy.

Medical staff will complete this form at baseline during the physical exam/medical history. The MM clinician will complete the form at each visit during the treatment phase.

**4.7.1.5 Clinical Institute Withdrawal Assessment for Alcohol**

The CIWA-AR is a 10-item interviewer-administered scale that contains 10 alcohol withdrawal signs and symptoms and is commonly used as a tool to guide the clinical management of alcohol withdrawal. The CIWA-AR will be administered as needed during the baseline screening phase but the assessment **must** be administered on the day of randomization. This measure is used to determine participant eligibility. For those participants whose CIWA-AR is  $\geq 8$  on the day of randomization, but who are otherwise eligible for

randomization, the CIWA-AR can be repeated to determine eligibility as long as 21 days of abstinence is not exceeded.

## **4.7.2 Psychosocial Assessments**

### **4.7.2.1 Important People Instrument – Initial**

The Important People and Activities (IPA) instrument was developed to operationalize the construct of network support for drinking. The IP has been modified to incorporate new questions that will assist in evaluating the influence of network support on important treatment issues.

Administration time for the IP will be 12 minutes on average. Scoring of the overall support for drinking measure will be retained from the MATCH study. The new questions asked will be single item variables that will be weighted by a measure of the importance of each network member and summed across the network. The IP will be administered at baseline and also during week 16 and week 26. If the form is not obtained at week 26, then obtain the information at week 52. Reference the IP Manual for additional information.

### **4.7.2.2 Brief Symptom Inventory**

The Brief Symptom Inventory (BSI) is an 8-minute 53-item self-report questionnaire, which yields continuous scores for nine dimensions of psychopathology. Derived from the SCL-90, it provides a symptom picture for the past week.

The BSI will be administered at baseline and during weeks 8, 16, 26, 52, and 68.

## **4.7.3 Quality of Life**

### **4.7.3.1 World Health Organization Quality of Life Assessment Instrument**

The World Health Organization has developed a measure of quality of life that has been used with a number of medical disorders in a number of countries (Anderson, et al., 1996; Szabo, 1996). This self-report measure consists of 25 items that are rated on 5-point Likert scales. For each of these, the individual is asked to provide information about relatively objective factors (e.g., assessments of his or her behaviors, states, and capacities) and more subjective evaluations of these factors (e.g., satisfaction with or concern about these behaviors, states, or capacities).

The measure will be given at baseline and at 6 month follow-up intervals (weeks 26, and 52).

### **4.7.3.2 SF-12**

A 12-item (two minute) questionnaire was developed from the SF-36® Health Survey for use in monitoring outcomes for general and specific populations. This survey form has been shown to yield summary physical & mental health outcome scores.

The SF-12 is a 12-item self-administered quality of life assessment that will be given at baseline and during weeks 16 and 52.

## **4.7.4 Treatment Related Expectancies**

### **4.7.4.1 Treatment Experience and Expectations**

This questionnaire asks participants about prior substance abuse treatment episodes, how helpful they feel their prior treatment was, how strongly they feel a current need for treatment, how helpful they expect the medications and counseling of the present trial to be, and how confident they feel that they will be drinking less or sober/abstinent from alcohol in 4 months. Most of these items are rated on 5-point Likert scales (0 - 4), with higher scores reflecting more positive appraisals and expectancies.

The TEE will be administered at baseline only.

## **4.8 Completion of Baseline Assessments**

Once the participant completes the baseline assessments, staff should work with the participant to schedule the randomization visit as soon as possible.

### **4.8.1 Preparing for the Randomization Visit**

Keep in mind that participants who complete all baseline eligibility measures but drink before 4 days of abstinence are met, technically, are not eligible until the day of randomization when the CIWA and the TLFB are completed. The participant will not be randomized until they have achieved 4 consecutive days (96 hours) of abstinence.

It is possible to “check in” with participants as a way of supporting sobriety before the randomization visit (initial session). If the participant returns to drinking before the randomization visit, it is possible to administer the TLFB by phone to obtain information about quantity and frequency.