RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: a Multicenter Observational Study of Hyperbaric Oxygen Therapy (HBOT) in Chronic Traumatic Brain Injury (TBI)/Post-Concussion Syndrome (PCS) and TBI/Post-Traumatic Stress Disorder (PTSD)

PROTOCOL NO.: NBIRR-01
WIRB® Protocol #20090761

SPONSOR: International Hyperbaric Medical Foundation (IHMF)
Harvey, Louisiana
United States

INVESTIGATOR: Name
Address
City, State Zip
Country

SITE(S): Name
Address
City, State Zip
Country

STUDY-RELATED PHONE NUMBER(S): Name
Phone Number

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

Purpose of Study:

This is an observational research study whose purposes are to see:

a) if 40 HBOT's (Hyperbaric Oxygen Therapy) or more (60, or 80 HBOT's) help, worsen, or have no effect on subjects with chronic TBI/PCS (Traumatic Brain Injury/Post-Concussion Syndrome) and/or PTSD (Post-Traumatic Stress Disorder).

b) if improvements or worsening of symptoms can be recorded with computerized and written tests for memory and thinking, and with questionnaires about the subject's quality of life and health.

c) determine the long-term outcome of the treatment.

You are asked to participate in this treatment because you have either TBI/PCS or PTSD. This treatment is thought to be effective based on previous positive experience in other subjects with TBI and TBI with PTSD.

The study device, hyperbaric oxygen therapy, is an approved device for a different use. It has not been approved for TBI or PTSD but can, under the authority of a licensed study doctor, be prescribed for this purpose. An investigational device is one which has not been approved for this use by the U.S. Food and Drug Administration (FDA). This is an observational study to help determine if a formal FDA application should be submitted for this use of Hyperbaric Oxygen Therapy.

Description of the Study:

You will be evaluated for progress compared to your own baseline.

There will be a maximum of 1000 subjects recruited for the study.

There will be between 10 and 100 centers participating.

You may have TBI or TBI plus PTSD or PTSD without TBI.

You will be followed over time using automated measurements of brain function.

You will answer questionnaires that are designed to identify TBI and PTSD, submit to computer and written tests that measure your ability to think, answer questionnaires that measure a person's happiness and satisfaction with life, and have a physical exam by the study doctor.

There is no requirement that you have any test other than what is provided in this study. If you have formal neuropsychological or imaging tests, these data will be collected and analyzed as part of this study. Please let us know when you have any testing.

The HBO therapy will be delivered by having you lie on a stretcher that is in a fully enclosed chamber (one person chamber). The purpose of the hyperbaric oxygen is to see if increased oxygen at pressure can help your TBI and/or PTSD. The pressure in the chamber will be increased to one and one-half times atmospheric pressure, or the equivalent pressure one would

obtain if breathing compressed air while SCUBA diving 16.5 feet underwater. There is no water in the chamber. The breathing gas that is delivered is pure oxygen. The treatment takes 60 minutes.

Alternatively, depending on the facility that provides the HBOT, you may be treated in a chamber that can accommodate multiple subjects. In this chamber you will breathe air as the chamber is compressed. Once the chamber pressure reaches one and one half times atmospheric pressure you will have a clear plastic hood placed over your head that will be secured with a rubber neck dam to prevent oxygen leak. You will breathe oxygen in this hood for 50 minutes. The hood will then be removed and the chamber brought back to surface pressure while you breathe chamber air.

You will then have another 39 of these treatments on a once a day, 5 day / week schedule. If after these 40 HBOT's you are unchanged or not improved based on objective criteria, including physical exam, the study doctor can request up to an additional 40 HBOT's delivered in two blocks of 20 treatments. This second set of 40 HBOT's will be delivered at a frequency of 5-6 HBOT's week. After either 40, 60, or 80 HBOT's, you will submit to the same cognitive tests, answer the same questionnaires, and may have some optional imaging studies upon the request of your treating physician (not the study doctor). These follow up studies will be continued for up to 2 years to determine long-term results.

Steps to follow for this study plan are:

1) inquire about study
2) have a telephone screening
3) schedule interview
4) examination and interview by study doctor
5) determination of enrollment
6) have baseline cognitive tests
7) begin supplements
8) receive treatment - 40 sessions HBOT 1.5 (daily on a 5 day per week schedule)
9) have repeat cognitive tests and questionnaire to determine percent back to normal
10) maybe receive another 20 sessions HBOT 1.5 (daily on a 5-6 day per week schedule)
11) have repeat cognitive tests and questionnaires to determine percent back to normal
12) maybe receive another 20 sessions HBOT 1.5 (daily on a 5-6 day per week schedule)
13) have repeat cognitive tests and questionnaires to determine percent back to normal
14) wait 3 months
15) have repeat cognitive tests and questionnaires to determine percent back to normal
16) wait 6 months
17) have repeat cognitive tests and questionnaires to determine percent back to normal
18) wait 1 year
19) have repeat cognitive tests and questionnaires to determine percent back to normal
20) wait 2 years
21) have repeat cognitive tests and questionnaires to determine percent back to normal

At the same time, beginning before or shortly after the first HBOT and continuing through the last HBOT, you are being asked to take vitamin C twice a day and vitamin E and a multivitamin once a day. These are recommended to protect subjects against too much oxygen. You will also receive modifilan (kelp extract powder) or pectasol (solubilized pectin) to help you with potential co-existing heavy metal toxicity.

Whether treated in a single-person or multi-person chamber you will be closely attended by one of the hyperbaric study staff members outside or inside the chamber. If the study staff member is outside the chamber, communication will be by intercom.

You may choose to rest, watch television or a videotaped movie, or sleep while in the chamber. Sometimes, you may be asked questions related to this study while in the chamber being treated.

You will have the following tests and procedures:

1. A urine test for drugs.

2. Questionnaires for TBI and PTSD - these are written questionnaires that ask questions to identify and measure patients with TBI and PTSD. These will be completed at the beginning of the study and the end of the study. They take about 30 minutes to complete.

3. Cognitive tests - these are written or are computer tests that measure a subject's I.Q., speech and language level, and ability to think, remember, and concentrate. The tests are of two types: 1) those attended by a neuropsychologist or neuropsychometrists and 2) those performed independently by the subject on a computer. Depending on the resources available to each testing center, some subjects will have both the neuropsychologist tests and computer tests while others will have just the computer tests. The neuropsychologist tests will only be performed at the beginning of the study and after all HBOT has been completed. The computer tests will be administered after 40, 60, 80 HBOT's, and 6 and 12 months after the last HBOT. Each computer testing session takes about 30-45 minutes to complete and there may be up to 3 of these tests for a total of 2 hours of testing by automated computer-based tests that the subject will take with minimal supervision.

4. Quality of Life Questionnaires - these are written or computerized tests that measure your satisfaction with your life and health. They will be performed at the beginning of the study, after 40 HBOT's, and after completion of all of the HBOT treatments. These tests take about 2 hours to complete for each testing session.

5. The study doctor will do a history and physical examination. This is a comprehensive review of your medical history and a physical exam to document neurological and other abnormalities and ensure that you can safely undergo HBOT.

6. Women only: Every female subject of childbearing potential will be tested for pregnancy, initially and then monthly, while undergoing hyperbaric oxygen therapy. You will give a urine sample to perform this test. You MUST inform the study doctor if you have any reason to believe you may be pregnant. If so, a urine pregnancy test will be performed before any further HBOT treatment.

Risks to Subject:

While enrolled in the study, you are at risk for some side effects. You should discuss these with the study doctor and/or your regular doctor. There may be other side effects that are not known. Other drugs may be offered to try to make side effects less serious and uncomfortable. Many side effects go away shortly after the hyperbaric oxygen therapy is stopped, but in some cases side effects can be serious or long lasting or permanent.

Risks and side effects related to the procedures being studied include:

Hyperbaric Oxygen Therapy:

- There may be pressure-induced injury (barotrauma) of the middle ear (blood-tinged fluid accumulation behind the eardrum, if you cannot adjust the pressure in your ears as you would when traveling in an airplane); sinus (blood-tinged fluid in the facial sinuses if the subject has congested sinuses); inner ear (damage to the inner ear hearing and balance organs if the pressures cannot be adjusted to equal the middle ear space); or even a seizure. (There is no known risk of seizure at the pressure of 1.5 atmospheres used in this study.)

- Changes in pressure: Anytime the atmospheric pressure is changed, all of the air spaces within the body must remain in balance with these changes. If not, discomfort will result. You may experience this discomfort in the ears, sinus spaces, or teeth. If you do experience discomfort, you must advise the hyperbaric technician so that corrective action can be implemented immediately.

- If your lungs do not ventilate adequately during pressure changes, you may suffer a leak of air into the chest, or into the blood stream, causing a stroke, heart attack, or death. If you are at high risk for this complication, you may not participate in this study.

- Oxygen Toxicity: When provided in a hyperbaric chamber, oxygen can have strong effects. Some of these effects are beneficial in certain illnesses. It can be given in too little and too great a dose. Too much hyperbaric oxygen will affect the brain and produce one or more signs or symptoms. If the situation is not corrected a seizure may result. This is a rare occurrence at high pressures. The low pressure (1.5 atmospheres) featured in this study has not been reported to cause seizures.

- Visual Changes: Some subjects undergoing hyperbaric oxygen therapy develop a temporary change in seeing ability, called myopia (near-sightedness). Closer focus (reading a book or a magazine, for instance) becomes improved while distant vision is blurred. This visual change is usually associated with higher pressures and longer courses of HBOT, and is largely self-correcting once the hyperbaric exposures have been completed. It is very unlikely in this study.

- Fire: Increases in oxygen concentration and pressure increase the risk of fire. The chamber has been specially designed to minimize this risk. This is a rare event, because by using only cotton clothing and bedding, and eliminating all other personal items that may produce a spark, this risk is greatly minimized. If a fire or related explosion occurs, the consequences may cause death. To our knowledge, this has only happened once in North America.

- Transient emotional instability: Some subjects may experience a temporary (3 days or less) increase in emotion that consists of episodes of sadness and crying approximately half way through the first course of 40 HBOT's. PTSD symptoms may worsen temporarily for about one to two weeks during treatment, typically around the 20th treatment. Often, increased support from friends, family, medical professionals, or institutions is needed at this time for a few days or more.

- Questionnaires for TBI/PCS and PTSD, cognitive tests, and Quality of Life Questionnaires: No known risks from these tests.

For more information on the research to be performed, or any risks, benefits, or alternative treatments, subjects should ask their regular doctor or any of the site study doctors listed on the front page of the consent form.

If you suspect that you have become pregnant, you must notify the study doctor.

Your condition may not get better or may become worse during this study.

Benefits to Subjects:

The possible benefits of taking part in this study may include 1) improvement in thinking ability, 2) quality of life, and 3) reduction in PTSD symptoms. However, there may be no benefit at all.

There may or may not be any direct medical benefit to you. Preliminary studies have shown benefit to subjects. It is the purpose of this study, to confirm this in a greater number of subjects. It is hoped the information learned from this study will benefit other patients with TBI/PCS and/or PTSD in the future.

Costs:

The cost of the automated neuropsychiatric tests and all testing related to the observation of the treatment will be covered by the sponsor. All costs related to the treatment of HBOT are not covered.

All study drugs, visits, and procedures not covered by the sponsor will be billed to the subject. At this time, the sponsor does not have the funds to pay for the treatment. The sponsor will pay for all of the automated neuropsychiatric testing. If the sponsor or funding source does not pay for the treatments and procedures you will be billed for them. It is anticipated that your insurance company will not cover the costs of the treatments in this study plan, because the study plan is considered experimental. Usually, costs for procedures or tests that are not part of routine care guidelines are not covered by insurance companies. If you have any question, we urge you strongly to talk with the insurance company.

Medicare, in particular, makes it very clear that they do not cover costs that are incurred as part of a research study plan that is an observational study plan and the use of HBOT therapy for your condition is considered investigational - this is why the present study is being done.

Ancillary diagnostic testing that is NOT required by the study may be recommended by your study doctor. For purposes of planning and estimation, the costs of testing that are NOT required in this study are:

- psychometric screening, evaluation, and quality of life questionnaires ($1000 per exam, subjects who undergo testing by a neuropsychologist will have 2 or 3 of these);
- MRI of the brain with radiologist's reading ($2,000);
- SPECT brain imaging with radiologist's reading ($1,750 per SPECT; subjects will have 3 or 4 of these); and
- functional brain MRI (approximately $2,000 per study; there could be 2-3 of these tests).

The costs of testing and treatment that are required for this study are:

- hyperbaric medicine evaluation, screening, and exam ($450);
- HBOT (approximately $200/HBOT-this will vary according to the center at which the subject receives their HBOT, subjects will have 40-80 of these);
- pregnancy tests during the course of the study ($30 each, female subjects will have 3 or 4 of these);
- urine toxicology test for drugs of abuse ($30 each, subjects will have 3 or 4 of these);
- transportation costs to and from the city with the hyperbaric clinic or hospital (will vary according to the subject's proximity to the center); and
- lodging, food, and transportation costs to and from testing and treatment centers ($100-150/day, subjects will be in the treatment phase of the study for 6-19 weeks. Follow-up computer testing will occur at 6 and 12 months).

There are some tests that may be recommended by your study doctor, however, these are not part of the study unless expressly stated elsewhere in this consent form. Costs of additional testing, such as EEG, angiograms, MRI, CT, or PET imaging, or Doppler studies should be discussed with the ordering study doctor. These tests can vary in cost and may or may not be covered by insurance. These tests are not required for the study.

Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include the costs of treating possible side effects. Otherwise, you might have unexpected expenses from being in this study.

Payment for Participation:

You will not be paid for your participation or reimbursed for your time and travel.

Alternatives to Participation in the Study:

The alternative to participation in this study is to have cognitive rehabilitation and psychotherapy (therapy with a psychiatrist, psychologist, or trained mental health professional), medications administered by other medical professionals. You will not be restricted from any other treatment while in this study.

In consultation with your study doctor, you may choose to undergo other studies, such as imaging, blood tests, brain blood flow studies, or electrical evaluations of brain function. You are encouraged to discuss other testing with your study doctor. Tests that are often done to evaluate subjects with your condition include MRI (magnetic resonance imaging - use of a magnetic field to produce an image) of the brain (if you have not had an MRI of the brain since you developed TBI or PTSD), SPECT brain imaging, and functional MRI.

Voluntary Participation/Withdrawal:

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Tell the study doctor if you are thinking about withdrawing from the study so that you may do so safely. If you decide not to continue participation in the study you should seek medical advice for alternatives and talk to your regular doctor first. There are no known serious consequences, to our knowledge, of sudden withdrawal from the study.

The study doctor or sponsor may stop you from taking part in this study, without your consent, at any time for the following reasons:

- if it is in your best interest,
- if you do not follow the study procedures,

- if the study is stopped,
- if your health worsens,
- if another treatment option appears to be appropriate, new information becomes available to the study doctor, sponsor, or monitoring groups,
- for any other cause which prevents your continuing in the study,
- you do not later consent to any future changes that may be made in the study plan,
- or for any other reason.

New Findings:

Should significant new findings take place during the course of the research that might change your decision to be in this study, that information will be provided to you. You may be asked to sign a revised consent form if this occurs.

Subject's Right to Privacy:

The results of the study will be released to the sponsor. If the results of the study are published you will not be identified in any way. Your personal information may be disclosed if required by law.

Private Insurance Exclusion: Your insurance company is allowed access to your private health information because you have authorized this release when you signed the agreement to the health insurance policy. You can decline disclosure of medical records to insurance carriers however, this will likely result in their denying payment of claims for therapy. In many cases, because this therapy is not covered by insurance, it may not be necessary to submit the claim to your insurance carrier.

Military Personnel: If you have already been disability rated by the military you should know that your results are private and cannot be accessed to personally identify you and possibly reevaluate your disability. You are seeking this treatment as a private citizen and to the best of our knowledge, the military is not allowed to access to your individual records.

TriCare Exclusion Pending Reimbursement Approval: As some research subjects will be active duty, retired military, etc., complete confidentiality cannot be promised as access to these records can be obtained for subjects using military TriCare. Presently, TriCare does NOT cover the treatment of TBI/PTSD with hyperbaric oxygen therapy. Until TriCare reimburses this treatment, claims for such treatments will not need to be submitted to TriCare.

Release of Information:

Organizations that may inspect and/or copy your study-related medical records for quality assurance and data analysis include: the sponsor, the U.S. Food and Drug Administration (FDA), the Western Institutional Review Board® (WIRB®), and the study doctors and study staff. While every effort will be made to maintain your privacy, absolute confidentiality cannot be guaranteed. Records will be kept private to the extent allowed by law.

Privacy of Medical Records and Confidentiality From Military:

As an individual, your records and clinical status or change in this study are confidential from the military. These records produced in this study are confidential to the study and cannot be used by the military to revise determinations of disability. We cannot control or determine if or when the military will periodically review your disability. The military will be notified of the general results of the study (without individual records) so that they may make an informed decision about whether or not to provide reimbursement to others who may need treatment. Therefore, we encourage you to do your best in the evaluations that are part of this study because it is important to have accurate results.

Compensation for Injury:

The study doctor will arrange for medical care for any emergency medical problem that you may experience as a direct result of your participation in this research. This will be provided on a fee-for-service basis. There are no funds available to pay for any disability, study related, or unknown complications that result from participation in this study or for damages such as lost wages, etc.

Source of Funding:

Funding for this research study will be provided by International Hyperbaric Medical Foundation (IHMF).

Questions:

Contact _____ at _____for any of the following reasons:

- if you have any questions about your participation in this study,
- if at any time you feel you have had a research-related injury or a reaction to the study drug, or
- if you have questions, concerns or complaints about the research.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
3535 Seventh Avenue, SW
Olympia, Washington 98502
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com.

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will be given a signed and dated copy of the consent form.

Signatures:

I have read the information in this consent form (or it has been read to me). The study has been discussed with me and all my questions have been answered. I agree to participate in this study.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

By signing this consent form, I have not given up any of my legal rights.

_____	_____
Signature of Subject	Date
_____	_____
Person Conducting Informed Consent Discussion	Date
_____	_____
Signature of Investigator (if different from above)	Date

---------- Use the following only if applicable ----------

If this consent form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject. The subject freely consented to be in the research study.

_____ _____

Signature of Impartial Witness Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling subjects who do not speak English.