Official Title: Novel Intervention for Chronic Complex TBI in OEF/OIF/OND Veterans

NCT: NCT05671692

IRB Document Date: 10/10/2024

Participant Name:	**Date:**
Study Title: Novel Intervention for Chronic Complex TBI in OEF/OIF/OND Veterans	
Principal Investigator: Gerald Grant, MD	**VAHCS**: Durham VAMC

OVERVIEW AND KEY INFORMATION

Please read this form carefully. You are being asked to participate in this research study because you have experienced a traumatic brain injury (TBI). This study is voluntary and will include only people who choose to take part. Ask your study doctor or study staff to discuss this consent with you, please ask him/her to explain any words or information that you do not understand. It is important that you understand the information on this form.

The purpose of this study is to determine if the drug pregnenolone improves psychological health, overall physical and mental functioning, cognitive symptoms, posttraumatic stress disorder (PTSD) symptoms, and pain in veterans who have had a traumatic brain injury (TBI). This study will also determine the most effective dose of pregnenolone that is safe and well-tolerated. Pregnenolone is a naturally occurring molecule made in the brain and other organs.

Your participation in this study will involve being randomized to take either pregnenolone or placebo (a placebo is an inactive substance, like a sugar pill). Pregnenolone will be given to you to take each day at home, with doses increasing to the highest well-tolerated dose up to 2000mg per day. You will participate in 6 study visits at the Durham VA Health Care System over 11 weeks for tests, exams and procedures that are for study purposes, with each visit lasting 1.5 - 3 hours. At each visit your symptoms will be assessed, and you may be able to continue receiving the study drug. In this research study, the term “study drug” means “placebo or active drug.”

There are no known severe risks associated with taking pregnenolone. In prior studies, pregnenolone was very well-tolerated with few side effects. There have been rare reports of stomach upset, headache, difficulty sleeping, irregular heartbeat, hair loss (in women), acne, and rash. The exact likelihood of your experiencing one of these side effects is currently unknown. Not all side effects of pregnenolone are known.

If you are interested in learning more about this study, please continue reading below.

WHY IS THIS STUDY BEING DONE?

The study is being done to find out if pregnenolone improves psychological health, overall physical and mental functioning, cognitive symptoms, posttraumatic stress disorder (PTSD) symptoms, and pain more than placebo in OEF/OIF/OND-era veterans with chronic complex TBI, and to determine the optimal safe, effective, and well-tolerated dose of pregnenolone. Pregnenolone is currently available over-the-counter (OTC) in the U.S. and sold as a dietary supplement. In this study, however, we will use pregnenolone that is custom-made to meet FDA standards for purity.

If you consent to participate in this study, you will either receive the study drug (pregnenolone) or placebo. Neither you nor your treating physician will know if you are receiving pregnenolone or placebo until the study is completed. This is part of the research study clinical care (not part of your routine care).

How Many People Will Take Part in this Study

Approximately 54 people will be enrolled in this study at the Durham VA Health Care System. 108 total people will take part in this study across different sites.

How Long will I be in this study?

Your participation in this study will last 11 weeks (which includes one follow-up phone call after 6 study visits) and will take approximately 12 hours of your time. You can choose to stop participating at any time without penalty. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

Your participation in this study is not a substitute for your regular medical care or check-ups.

What is involved in this study?

If you agree to participate in this research study you will be asked to sign and date this consent form. You will have the following tests and procedures to make sure that you are eligible:

- Physical exam and medical history
- Vital signs
- Blood tests

- Urine drug screen
- Electrocardiogram (ECG), a tracing of the electrical activity of the heart

If you are eligible and volunteer to participate in this study, you will be required to:

1. Give basic information about you, your military experiences, and your mental and physical health. You will be asked to fill out a form that asks your name, age, phone number(s), and addresses. It will also ask your military position, dates of service, type of service, and if you took part in combat. You will also be asked about your mental and physical health.

2. Donate blood. You will be asked to give about 3.5 tablespoons of blood on the first study visit. You will also be asked to give approximately 2.5 tablespoons of blood on Visits #2, 3, 4, 5, and 6. This is a total of approximately 16 tablespoons of blood over the 11-week study. Your blood will be used to study blood chemistry that may be related to brain disorders. Your blood will be tested for chemicals like neurosteroids (specific compounds that are active in the brain and occur naturally), other small molecules, and proteins that may be related to brain function.

3. Donate blood for genetic analysis (Visit 1) to determine why some people may respond to the study drug and others may not.

Your genes are made up of DNA. DNA is short for deoxyribonucleic acid. DNA contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has a major role in making proteins. Proteins are the building blocks of your body, cells, and organs.

a. Participation in genetic studies: The genetic studies described are for research purposes only. Therefore, you will receive no results from this study (except as described below). It is not the purpose of this study to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. The research tests are not being used as diagnostic tests for any disease or illness. Your participation in this study is not a substitute for your regular medical care or check-ups.

b. Research Results: Through this research, we may find that you have an abnormal gene or gene product (RNA or protein) which indicates a risk for developing a disease at some time in the future. It is also possible that the research results may indirectly provide unexpected personal information about you or your family (such as ethnic/racial background or an unknown genetic relationship between family members). Please talk with the study doctor if you have any questions or concerns about the genetic testing being done in this research study. He may also refer you to a genetic counselor for further information.

c. Incidental Findings: It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician unless the information indicates that you may be at risk for a serious illness known at the time of testing to be treatable. In that case, we will attempt to notify you using the contact information you have provided, so that you can speak with Dr. Grant. Study staff will not provide this information in a voicemail, email, or otherwise prior to contacting you. Please notify us of any change in your contact information.

If you do not want to be notified of any incidental findings, please initial below.

_____ Please do not notify me of any incidental findings obtained from this research.

If you prefer, we can ask you at the time of notification whether or not you want to receive incidental findings information. In this case, please initial below.

_____ Please ask me at the time of notification whether or not I want to receive incidental findings information.

If at any time during or after the study you change your mind about whether or not you would like to be notified, you can contact us at (984) 245-4703.

After providing the information to you, Dr. Grant may arrange for you to meet with him and/or a genetic counselor or refer you to another appropriate health care provider to review the incidental findings information with you or your physician.

d. Use and ownership of samples: By agreeing to participate in this research, you authorize DVAHCS and members of its staff to use your tissue, blood or other samples for the purposes described in this consent form. DVAHCS will maintain these samples indefinitely or until they are exhausted.

These samples will not be available to you for diagnostic or therapeutic purposes. Therefore, for any future diagnostic testing or treatments, a new sample will be obtained from you.

Blood collected as part of this study may be valuable for scientific, research, or teaching purposes or for the development of a new medical or commercial product. DVAHCS and/or the developers will assert all rights of ownership in the samples and all rights arising from use of the samples. Your samples may result in commercial profit. You will not be compensated or profit from use of your samples.

e. Secondary uses of specimens: With your permission, your blood and/or tissue samples may be shared anonymously with other investigators for research purposes. The samples may be used for study of disorders unrelated to the one(s) in your family. Such research will be strictly anonymous, in that no identifying information that would link the samples to you is provided to the researcher. An ethics board will review any such research prior to access being given to your samples. This secondary use will in no way compromise the study of the disorder(s) in your family or the use of your samples as part of this study._

f. Availability/withdrawal of samples: You will not have access to the sample once it is obtained. Samples may be stored indefinitely. If you decide to withdraw your permission to use your samples in this research project, please contact the study doctor, Dr. Grant, in writing and let him know you are withdrawing your permission for your samples to be stored and used for this or future research. His mailing address is Box 3862 Med Ctr, DUMC, Durham, NC 27710. At that time, we will ask you to indicate in writing if you want your unused

samples destroyed or if your samples (with all identifying information removed that would link the sample to you) could be used in research. Data collected using your sample before your withdrawal will continue to be used as part of the study.

g. Right to New Information: We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

h. Potential Risks and the Genetic Information Non-Discrimination Act (GINA): There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information, but this cannot be guaranteed. The genetic information obtained as a result of your participation in this research will be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, secure location at DUHS, accessible only by authorized members of the study team, and will not be disclosed to third parties except as described in this consent form, with your permission, or as may be required by law.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

I agree to genetic testing for the current study: ☐ Yes ☐ No

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Permission to Re-Contact for Future Research Studies
We would like permission to re-contact you for future research. If you answer "YES", should another study or studies become(s) available that we feel may be of interest to you, we will send you a letter in the mail about it. After a week, will contact you by phone. If you answer 'NO' below, then you will not be contacted for future research studies. Your choice to give permission to be re-contacted or not to give permission to be re-contacted will not affect your enrollment in the current study, nor your access to care at the Durham VAHCS.

I agree to be re-contacted: ☐ Yes ☐ No

Your samples and/or data may be stored and used for future studies without additional consent from you if identifiable private information, such as your name or medical record number, are removed.

Study Procedures: All study procedures are for research purposes only and would not be part of your usual care.

1. At Visit #1 (screening visit), a study physician will conduct a physical examination (prior to randomization to study drug or placebo). You will be asked to provide blood and urine specimens for laboratory testing, and urine toxicology screen. Blood samples for neurosteroids, other small molecules and proteins that may be relevant to brain function will be collected, in addition to blood samples for genetic testing. The total amount of blood drawn during Visit #1 is about 3.5 tablespoons (52 ml). You will also receive an ECG and your vital signs will be assessed. Female participants will receive a pregnancy test. You will receive several psychiatric and physical assessment instruments. You will receive placebo drug (no active ingredients) to take with you and be asked to swallow the tablets twice a day. Estimate of Time for Visit 1: approximately 3 hours.

2. At Visit #2, you will complete several questionnaires that assess your mental and physical health. Using a procedure like flipping a coin, you will have a 1 in 2 chance of receiving an inactive substance like a sugar pill (a placebo) instead of pregnenolone. Neither you nor your treating physician will know if you are receiving pregnenolone or the placebo until the study is completed. In case of an emergency, the study doctor can quickly find out which study group to which you are assigned. This is part of the research study clinical care (not part of your routine care). You will be asked to take the

study drug (swallow tablets) twice a day for two weeks and return any unused study drug during Visit#3. You will be asked to provide urine and blood samples and your vital signs will be assessed. Female participants will receive a pregnancy test. The total amount of blood drawn during Visit #2 is about 2.5 tablespoons (38 ml). Estimate of Time for Visit 2: approximately 1.5 hours.

3. At Visits #3, #4, and #5 you will complete brief questionnaires, will provide urine and blood samples and your vital signs will be assessed. The amount of blood drawn during these visits is about 2.5 tablespoons (38 ml). Female participants will receive a pregnancy test. At these visits you will receive a new supply of study drug (either pregnenolone or placebo, depending upon random assignment) to take with you and will be asked to return any remaining tablets of study drug. Estimate of Time for Visits 3, 4, and 5: approximately 1.5 hours each visit.

4. At Visit #6, you will receive several questionnaires, provide urine and blood samples, receive an ECG and your vital signs will be assessed. You will also receive instructions about how to taper your study drug. The total amount of blood drawn during Visit #6 is about 2.5 tablespoons (38 ml). Female participants will receive a pregnancy test. The physical exam will be repeated. You will be asked to return any remaining tablets of study drug. You will be given instructions to taper the study drug. Estimate of Time for Visit 6: approximately 2 hours.

5. You will receive a phone call between each study visit and a follow-up phone call one week after Visit #6. You will be asked about any potential side effects. You will also receive a questionnaire about suicide and be asked about any medication changes. Estimate of Time for Each Follow-Up Phone Call: approximately 10 minutes.

See the next page for the planned schedule of events.

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Schedule of Events:

Visit	**1**	**1.5**	**2**	**2.5**	**3**	**3.5**	**4**	**4.5**	**5**	**5.5**	**6**	**Follow Up**
	Screen	**Phone Call**	**Randomize**	**Phone Call**		**Phone Call**		**Phone Call**		**Phone Call**		**Phone Call**
Week	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Description	X											
Informed Consent and HIPAA Authorization	X											
Demographics	X											
Medical History	X											
Physical Exam and ECG	X										X	
Vital Signs	X		X		X		X		X		X	
Blood draw	X		X		X		X		X		X	
LFT, BMP, CBC	X		X		X		X		X		X	
Lipids	X										X	
Neurosteroids, other small molecules, proteins	X		X		X		X		X		X	
HbA1C	X										X	
TSH	X											
Genetic Analyses	X											
Serum HCG - females	X		X				X				X	
Urine Drug Screen	X						X				X	
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	
Hillside Adverse Events Scale		X	X	X	X	X	X	X	X	X	X	X
History of TBI	X											
Brief Symptom	X		X		X		X		X		X	

Inventory												
36-item Short-Form Health Survey	X		X		X		X		X		X	
WAIS-IV	X						X				X	
Stroop	X						X				X	
PCL-5	X		X		X		X		X		X	
Beck Depression Inventory II	X		X		X		X		X		X	
Brief Pain Inventory	X		X		X		X		X		X	
Sanford Sleepiness Scale	X		X		X		X		X		X	
Epworth Sleepiness Scale	X		X		X		X		X		X	
Columbia Suicide Severity Rating Scale	X	X	X	X	X	X	X	X	X	X	X	X
Global Impressions of Improvement					X		X		X		X	
Dispense Study Drug or Placebo	Placebo (for 2 weeks)		Placebo or 500mg Preg (for 2 weeks)		Placebo or 1000mg Preg (for 2 weeks)		Placebo or max tolerated dose up to 2000mg Preg (for 2 weeks)		Placebo or max tolerated dose up to 2000mg Preg (for 2 weeks)		Taper of study drug	N/A; follow up phone call

WHAT ARE THE RISKS AND DISCOMFORTS OF PARTICIPATING IN THIS RESEARCH STUDY?

There are no known severe physical risks associated with this study. There is the potential risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed. Some questions asked as part of this study may make you feel uncomfortable or increase distress. This discomfort or increased distress is usually temporary and well tolerated. You

do not have to answer questions and you can take a break at any time. You can call the study team at any time if you experience any discomfort related to the research.

Because this is an investigational drug, we do not know all its effects. You should contact the Investigator or a member of the study team if you have any questions or experience a side effect that you think might be related to the research. As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

Pregnenolone may cause some, all, or none of the side-effects listed below. There are no known severe risks that have been associated with taking pregnenolone. In prior studies, pregnenolone was very well-tolerated with few side effects.

- Stomach upset
- Headache
- Difficulty sleeping
- Irregular heartbeat
- Hair loss (in women)
- Acne
- Rash

REPRODUCTIVE RISKS

For Women: The effect of pregnenolone on the risk of birth defects, miscarriage, or other bad outcomes when taken during pregnancy or while breastfeeding is unknown. To reduce the risk of any harmful effects, women who are pregnant, trying to become pregnant, or breastfeeding are not allowed to participate in studies using pregnenolone. If you are a woman who could possibly become pregnant (you have not had a hysterectomy and/or both tubes and/or both ovaries removed) and you have a partner who is able to father children, a blood pregnancy test will be performed, and it must be negative to continue in the study. In women 40 years old and older, blood pregnancy tests may sometimes give a false positive or “indeterminate” result, and additional testing may be required to confirm your eligibility for the study. You will also have additional urine pregnancy tests at some study visits, as described above, and they also must be negative for you to continue in the study.

You and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for 30 days after your last dose of study drug or use a highly effective method of contraception for the same length of time. Highly effective methods include (a) partner vasectomy, (b) bilateral tubal ligation, (c) non-hormonal intrauterine devices (IUDs). Hormonal contraception methods are NOT permitted during this study (e.g., hormonal implants (such as Implanon), or other hormonal methods (birth control pills, injections, patches, vaginal rings). If you and your partner are not currently using one of these methods your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required for this study. Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test.

If you do become pregnant during the study, your study doctor will stop the study drug, withdraw you from the study, and notify the sponsor. You will be followed for the duration of the pregnancy to better understand the potential effects of the study drug on pregnancy outcomes.

For Men
It is unknown whether pregnancies that began while the father was taking the study drug are at increased risk for birth defects, miscarriages, or other bad outcomes. To reduce the risk of any harmful effects, men who are trying to become fathers are not allowed to participate in studies using the study drug.

If you are able to father children and your partner is a woman who could possibly become pregnant (she has not completed menopause, or has not had a hysterectomy and/or both tubes and/or both ovaries removed), you and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for 90 days after the last dose of study drug, or use a highly effective method of contraception for the same length of time. Highly effective methods include (a) vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (such as Implanon), or (e) other hormonal methods (birth control pills, injections, patches, vaginal rings). If you and your partner are not currently using one of these methods your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required for this study.

You should not donate sperm for the duration of the study and for 90 days after the last dose of study drug.

Risks of Drawing Blood: Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Drug and Food Interactions: For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study. There may be risks, discomforts, drug interactions or side effects that are not yet known.

Social Risks: Although unlikely, genetic testing could possibly result in genetic discrimination by employers or insurance companies (making it difficult to be employed or insured) if you have a gene mutation that causes or increases the risk of an inherited disorder. Also, any breach of confidentiality impact insurability, employability, reproduction plans, family relationships, immigration status, paternity suits, or stigmatization. To protect you from the possibility of discrimination, your research records will be kept confidential to the extent allowed by law. Federal Privacy Regulations provide safeguards for the privacy, security, and authorized access. VA has no policies that would deny benefits based on genetic information. VA healthcare benefits cannot be denied by the results of a genetic test.

Psychological risks: If genetic or other findings are disclosed, psychological effects may result from learning the results of a test, learning that no effective therapy exists, or disclosing results to family members.

Unknown risks: There may be unknown risks. In addition, there may be future implications of finding potentially inheritable mutations for the patient and family member.

WILL I BENEFIT FROM TAKING PART IN THIS RESEARCH STUDY?

If you agree to take part in this study, there may be direct medical benefit to you. You may experience reduced complex TBI symptoms. You may not personally be helped by taking part in this study, but your participation may lead to knowledge that will help others.

WHAT OTHER OPTIONS OR ALTERNATIVES DO I HAVE?

Taking part in this study is your choice. You may choose to not participate. Instead of being in this study, you have the following alternatives:

1. Getting treatment or care for chronic complex TBI and/or mental health issues without being in a research study.
2. Taking part in another research study.
3. Getting no treatment.

Please talk to your doctor about these and perhaps other options.

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HOW WILL MY RESEARCH DATA BE PROTECTED AND SECURED?

Your information used for this study will be kept confidential as required by law. The results of this study may be used for scientific purposes or for publication, but these results will not include any information that would identify you. Your identity will not be disclosed without your consent, or unless required by law. Your research records will be maintained and destroyed according to VHA records retention requirements.

Your original research files will be maintained at DVAHCS per VA guidelines. Your research records may be reviewed by Durham VA staff who are responsible for the safe conduct of this research. We may also provide your research records to federal agencies such as the Office for Human Research Protections (OHRP), the VA Office of the Inspector General (OIG), and the Office of Research Oversight (ORO). The Food and Drug Administration (FDA) may choose to inspect research records that include your medical records. We may also disclose your information to Duke University Health System, Institute for Medical Research (IMR), the Department of Defense (DoD). We will disclose your name, mailing address and social security number to Duke University Health System so they can reimburse you for your participation in this study. An electronic copy of your data will be uploaded to the Duke Office of Clinical Research (DOCR) instance of RedCap. We will not share any information with these groups outside the VHA unless they agree to keep the information confidential and use it only for the purposes related to the study. Any information shared with these outside groups may no longer be protected under federal law. These groups may disclose your information to other groups. If the sponsor receives identified information, it is then the sponsor, and not the VA, who is responsible for the security of the information.

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to the Department of Defense and its affiliates. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration (FDA), representatives and affiliates of the Department of Defense, the Duke University Health System Institutional Review Board, the Durham VA Health Care System Institutional Review Board, study monitors, and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record.

FITBIR

Data from this study may be submitted to the Federal Interagency Traumatic Brain Injury (FITBIR) informatics system. FITBIR is a computer system run by the National Institutes of Health (NIH) that allows researchers studying traumatic brain injury to collect and share information with each other. With an easier way to share, researchers hope to learn new and important things about traumatic brain injury more quickly than before.

During and after the study, the researchers will send information about your health and behavior and, in some cases, your genetic information to FITBIR. However, before they send it to FITBIR, they will remove information such as name, date of birth, and city of birth and replace that information with a code number. Other researchers nationwide can then file an application to obtain access to your study data for research purposes. Experts who know how to protect health and science information will look at every request carefully to minimize risks to your privacy.

You may not benefit directly from allowing your information to be shared with FITBIR. The information provided to FITBIR might help researchers around the world treat future children and adults with traumatic brain injury so that they have better outcomes. FITBIR will report on its website about the different studies that researchers are conducting using FITBIR data; however, FITBIR will not be able to contact you individually about specific studies.

You may decide now or later that you do not want to share your information using FITBIR. If so, contact the researchers who conducted this study and they will tell FITBIR to stop sharing the research information. However, FITBIR cannot take back information that was shared before you changed your mind. If you would like more information about FITBIR, this is available online at http://fitbir.nih.gov.

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Certificate of Confidentiality

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);
2) you have consented to the disclosure, including for your medical treatment; or
3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the Food and Drug Administration (FDA).

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

DOES PARTICIPATION IN THIS RESEARCH STUDY COST ANYTHING?

There will be no costs to you for any of the research treatment or research testing done as part of this research study. Some Veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are not part of this study.

The Department of Defense will provide the study drug free of charge to you. At the end of the study, or if you decide to withdraw from the study before it ends, you may be asked to return all unused study drug. Your study doctor may request that you return for a checkup before you stop your study drug/biologic if he thinks that stopping it suddenly may harm you and may ask you to complete the tests that would ordinarily occur when a person completes the study.

WILL I RECEIVE ANY COMPENSATION (MONEY OR OTHER) FOR TAKING PART IN THIS RESEARCH STUDY?

You will be compensated $100 for your time after completing each study visit. Since this study involves 6 visits over 11 weeks, you may receive $600 for participating in all 6 study visits. If you participate in only three study visits, you will receive $300, etc.

Additionally, you will receive an allowance for travel that depends on how far you live from the Durham VA. The amount you get is calculated using the table below that shows the travel allowance for some typical cities in North Carolina.

A Duke ClinCard will be issued to you by Duke University after your first study visit and it will be reloaded with your visit compensation following each visit. Your name, mailing address and social security number will be provided to Duke University for the purpose of issuing your ClinCard, which will be mailed to you following your study visit. You will be asked to sign a Duke University "Personal Data Disclosure Form for Research Study Participants" consenting to this release of information.

Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual totals $600 or more in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University adding up to $600 or more during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

Distance (round trip miles)	Allowance	Typical towns and cities
0-50	$10	Raleigh, Durham, Cary, Chapel Hill
50-100	$20	Henderson, Wake Forest, Burlington
100-200	$30	Greensboro, Fayetteville, Goldsboro
200-300	$40	Salisbury, Greenville, Rocky Mount
300-400	$50	Wilmington, Charlotte, Hickory
> 400	$60	

WHAT WILL HAPPEN IF I AM INJURED WHILE PARTICIPATING IN THE RESEARCH STUDY?

The VA will provide necessary medical treatment should you be injured by being in this study. You will be treated for the injury at no cost to you. This care may be provided by the Durham VAHCS or arrangements may be made for contracted care at another facility. Every reasonable safety measure will be taken to protect your well-being. You have not released this institution from liability for negligence. In case of research related injury resulting from this study, you should contact your study team. If you have questions about compensation and medical treatment for any study related injuries, you can call the medical administration service at this VA Medical Center at 919-286-6957.

WHAT ARE MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

Withdrawal of Samples and/or Data for Future Use

If you agree to allow your samples and/or data with information that would link your sample and/or data to you to be kept for future research, you can change your mind at any time. To withdraw your samples and/or data, contact Dr. Gerald Grant in writing and let him know you are withdrawing permission for your identifiable samples to be used for future research. Dr. Grant's mailing address is:

Durham VA Health Care System
Attention: Gerald Grant, MD
508 Fulton St
Durham, NC 27705

If your identifying information, such as your name or medical record number, are removed from your samples and/or data, we will no longer be able to identify and withdraw the samples and/or data.

ARE THERE REASONS THAT MY RESEARCH PARTICIPATION MAY END EARLY?

The investigator may withdraw you from the study without your consent for one or more of the following reasons: You have serious side effects, your condition worsens, or your study doctor decides it is no longer in your best interest to continue in the study, or failure to follow instructions of investigator and/or study staff.

Reasons why this might occur include:

- if you do not meet eligibility criteria;
- if you do not take your study drug for 3 days (6 doses) or longer in between study visits or if you do not come to your visit appointments for two weeks in a row;
- if you experience a change in mental health treatment (medications or therapy) or if your mental health problems become worse;
- if you undergo medical hospitalizations for more than 24 hours;
- experience a seizure or a stroke;
- develop a rash (that is consistent with a drug reaction on the trunk);
- become pregnant;
- by physician request;
- or if it is not in your best interest to continue.

If you decline to participate or are withdrawn, you will be notified and your study doctor will discuss other options with you. We will tell you about new information that may affect your health, condition, welfare, or willingness to participate in this study.

WILL THE RESULTS OF THIS RESEARCH STUDY BE SHARED WITH ME?

Clinically relevant results of this research will be communicated with you if could possibly benefit medically from the information. Your individual study results will not be shared with you. However, once the data are analyzed (after completion of the entire study), you may request to see your data. It is not the purpose of this study to look for or provide you with any medical information or diagnoses about your present condition or other illness.

DO ANY OF THE RESEARCHERS HAVE A FINANCIAL INTEREST RELATED TO THIS RESEARCH STUDY?

This project is funded by the Department of Defense. A portion of the salaries of Dr. Grant's research staff are being paid by the sponsors of this research.

WHERE CAN I FIND OTHER INFORMATION ABOUT THIS RESEARCH STUDY?

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHO DO I CONTACT IF I HAVE QUESTIONS OR CONCERNS ABOUT THE RESEARCH STUDY?

If you have questions about the research or need to talk to the study team, you can contact *Dr. Gerald Grant at (984) 245-4703* during regular business hours, after hours, and on weekends and holidays. You may also contact the study coordinator at *(919) 384-8582* during regular business hours. If you have questions about the research or your rights as a research participant, would like to obtain information, offer input, or have other concerns or complaints, you may contact the administrative officer of the research service at (919) 286-0411, extension 177632. If you would like to check that this study is approved by the Durham VAHCS's Institutional Review Board, please call the research office at (919) 286-6926 or (888) 878-6890, extension 176926.

AFFIRMATION FROM PARTICIPANT

I have read this form or it has been read to me. My rights as a research participant have been explained to me, and I voluntarily consent to participate in this study. I have received an explanation of what the study is about and how and why it is being done. I authorize the use and

Participant Name:	**Date:**
Study Title: Novel Intervention for Chronic Complex TBI in OEF/OIF/OND Veterans	
DVAHCS Principal Investigator: Gerald Grant, MD	**VAHCS**: Durham VAMC

disclosure of my identifiable information as described in this form. I will receive a signed copy of this consent form.

Signature of Participant **Date**

Signature of Person Obtaining Consent **Date**