VA Department of Veterans Affairs	VA RESEARCH CONSENT FORM (Page 1 of 10)	OMB 2900-XXXX Estimated Burden: 15 min.

Participant Name: _____ Date:_____

Title of Study: Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans (Cases)

Principal Investigator: Dr. Ashok Tuteja VAMC: Salt Lake City (660)

DESCRIPTION OF RESEARCH BY INVESTIGATOR

TO POTENTIAL PARTICIPANTS: Federal regulations require written informed consent before participation in a research study. This is to be certain that research subjects know the nature and risks of the study, as they make a decision to participate or not to participate. You are asked to read the following information and discuss it with the investigator, so that you will be fully informed about this research study and how it may affect you. Your signature on this form means that you have been fully informed and that you freely give your consent to participate.

BACKGROUND: Many Gulf War Veterans have diarrhea, gas (bloating) and stomach pain of unknown cause. These symptoms can be because of a disease called irritable bowel syndrome diarrhea (IBS-diarrhea). The cause and treatment of IBS-diarrhea has not been studied well in Gulf War Veterans. The Department of Veterans Affairs is doing a study to find out if IBS diarrhea is caused by too many bacteria in the intestines.

In this study we will compare the presence of intestinal bacteria between Gulf War Veterans who developed IBS diarrhea with those who did not. We will also compare them with Veterans who were not deployed to the Gulf.

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part in this research study.

IBS is a disease of the intestines. Some patients with IBS have diarrhea and others have constipation. We are studying IBS-diarrhea. These patients in general have diarrhea, stomach pains and bloating (gas). The cause of these symptoms is not known. You are being invited to take part in this study because you are a Gulf War Veteran who has symptoms of IBS-diarrhea. We will compare the presence of bacteria in your intestines with that of the Gulf War Veterans and Reservists who do not have IBS-diarrhea.

The purpose of this study is to find out if too many bacteria in the intestines is the cause of IBS- diarrhea. If you decide to participate, you will come to the study doctor's office for 5 visits.

The following are the requirements for participation:

In order to participate in the study you:

1) Must be a Veteran who either went to the Gulf War or worked in the United States during the Gulf War
2) Must be men or women, age 32-75 years
3) Must have IBS-diarrhea
4) Must not have other bowel/ stomach diseases such as ulcerative colitis or Crohn's disease.
5) Must not have significant heart, lung or kidney disease
6) Must not have cancer (except skin cancer)

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7) Must not have effects of alcohol or drug abuse
8) Must not have unstable psychiatric disease
9) Must not be currently participating in another research protocol that could interfere or influence the measures of the present study.
10) Must not be on any antibiotic for at least 7 days.
This study does not allow women who are pregnant or currently breastfeeding infants.

STUDY PROCEDURE: Participation in this study involves the followings:

- Completion of three questionnaires inquiring about your bowel habits, quality of life, combat experience during the war and psychological profile. It will take approximately 45 minutes to complete these questionnaires.

The following procedures are normally performed on a patient with IBS-diarrhea. If you had these procedures within the last 6 months, they will not be repeated.

- Blood sample for routine blood tests. These tests are done to assure that you are otherwise healthy and to exclude known causes of diarrhea. The total amount of blood drawn is 1 ½ tablespoonful.
- Stool sample: to check for infection.
- Breathing test to check for the presence of bacteria in your intestines. This test involves blowing into a mouthpiece, which collects your breath into a plastic bag. In this test you will drink a cupful of solution containing lactulose. Lactulose is a sugar which is broken down by bacteria into gases, called hydrogen and methane. The samples of your breath will be collected every 15 minutes. This test will last 3 hours. This test looks for the presence of hydrogen and methane in the exhaled breath.
- Colonoscopy and biopsy: The colon is the part of intestine which connects anus to the small intestine. During a colonoscopy, a tube is passed through your anus. The colon is about 6 feet long. A visual examination of the colon and if possible a part of the small intestine will be performed. This procedure will be performed in the Gastrointestinal Laboratory at the George E. Wahlen VA Medical Center in
Salt Lake City.

During this procedure, an intravenous line will be placed in your arm. This line is a catheter which will allow medication to be delivered directly into your bloodstream. You will be sedated, during which time you will be breathing on your own and even able to interact with your doctor and nurses but will be less likely to remember doing so. You will receive two drugs: Medazolam (a sedative drug, similar to Valium) and fentanyl (a pain killing drug, similar to morphine). Sometimes phenergan is also given to avoid nausea or enhance the effect of other drugs. Two biopsies (small tissue samples) will be collected from the small bowel, two from the right part of the colon and two samples from the rectum. The biopsy samples are very small, i.e., 1- 2mm (the size of the pencil tip) in size. They will be performed through the endoscope and you will not feel any discomfort from the biopsy procedure. The purpose is to determine if there is any inflammation in intestines. If any abnormal areas are

found, additional biopsies may be performed. If any incidental polyps (benign tumors) are detected, they will also be removed either with a biopsy forceps or with an electric snare. This decision will be clinical one and not related to the study, but again, you will not feel any discomfort related to this part of the procedure. The endoscope will then be removed and you will be allowed to awaken. The entire length of the procedure once you have been sedated should be between 20- 45 minutes. You will not be able to drive for the rest of the day.

If you decide you want to participate in the study and you have completed the 3 questionnaires, your first visit to the doctor's office will have the followings parts:

Part #1: The study will be discussed with you, and you will be asked to sign this consent form.
A physical examination will be performed. You will be asked about your health and any current illnesses or medication you are taking. You will be asked to give about 1 ½ tablespoonful of blood for routine laboratory testing to ensure everything is normal. A portion of your drawn blood will be tested to ensure that you are not pregnant. You will be asked to give a stool sample for microscopic stool examination.

Part #2: You will have the breathing test for bacterial overgrowth. This will last 3 hours.

Part #3: You will be asked to undergo colonoscopy with biopsy.

If the above tests do not confirm that you do have IBS-diarrhea or if you do not have too many bacteria in your intestine, your participation in the study will stop.

If you have IBS-diarrhea and there are too many bacteria in your intestines, you will participate in the treatment part of this study and you will be assigned by chance (similar to tossing a coin) to one of the following study groups:

Group A: If you are assigned to Group A, you will receive rifaximin (an antibiotic) 1 tablet (550mg) two times a day for 14 days.

Group B: If you are assigned to Group B, you will receive placebo (a sugar pill), 1 tablet two times a day for 14 days. A placebo pill looks like the real thing but is not. It contains no active ingredient.

The medications all look the same, so neither you nor your study doctor will know which medication you are receiving, although if your study doctor needs to find out for your safety, he can do so.

You will not be able to participate in this part of the study if you are on any of the following medications for 7 days prior to the study: warfarin (coumadin) antidiarrheal, e.g. lomotil and Imodium, hyocyamine (levsin), raglan, any laxatives and any antibiotic.

Visit #2: (second part of the study): You will be assigned to one of the two groups and have medication for 14 days.

Visit #3: (second part of the study): You will return to your doctor with all study drug (unused tablets) bottles. You will be asked to redo several questionnaires, relating to how bad your IBS is. You will also have a repeat a Breathing Test to determine the states of bacteria in your intestine.

Following this, you will return monthly for 6 months, when the questionnaires will be repeated. You will have two more Breathing Tests during this time: 1 month after completing the medication, and at the last visit.

RISKS: Questionnaires:
Potential risks include loss of confidentiality. All subjects will be assigned identification (ID) numbers to which data will be linked. Upon completion of the study all keys to the identity of the subjects will be destroyed. Subjects may feel uncomfortable while answering some of the questions. They will be informed that they may decline to answer any question.

Blood draw:
As a result of the blood draw you may feel pain, bleeding or bruising at the needle site and dizziness or fainting. Infection may occur around the needle site causing redness and pain, but this is rare. The total amount of blood that will be taken during the study is about one and a half tablespoonful.

Breathing Test for presence of bacteria:
There are no significant risks involved with this test. However some subjects may experience abdominal discomfort, bloating or diarrhea for a few hours afterwards.

Colonoscopy and biopsy:
Colonoscopy is generally a safe procedure but complications can occur. These can include an allergic reaction to the sedation or ointment that is spread on the endoscopy (tube) that is passed into the rectum and colon. The allergic reaction is usually treated with Benadryl (diphenhydramine). Severe allergic reaction may require epinephrine. Usually there is discomfort and feeling of fullness during this test. Bleeding might occur at the biopsy site, but is usually minor. Bleeding can stop on its own or be controlled through the colonoscope; rarely does it require follow up treatment. Rarely, a hole can be made in the side of colon or rectum that can require surgery but the likelihood is less than 1 in 500. You will also be asked to sign a separate consent form prior to this procedure. Upload a copy of the consent form in ROCIS.

Sedation:
Moderate sedation is used during the procedure. Allergic reactions may occur causing a rash. Rarely, excessive sedation can cause breathing difficulty. Death has been reported. There is continuous heart and breathing monitoring during colonoscopy and the chance of this happening is less than 1 in 1000.

Rifaximin:
No serious side effects have been associated with rifaximin. The less serious side effects include: dizziness, flatulence, stomach pain, bowel urgency, constipation, fever, rash, nausea and vomiting. We will review the other medications you are taking in an effort to be sure that there is no known drug interact with your medications and rifaximin.

Placebo
Participants assigned to the placebo group will receive placebo instead of active medication for the duration of the study. The risks of receiving placebo are the same as not receiving any treatment for your condition.

While taking placebo, it is possible that your IBS may not get better or become worse. Any concerns you may have about this should be discussed with the study doctor.

If you experience an allergic reaction (difficulty breathing; closing of your throat; swelling of your lips, tongue, or face; or hives), bloody diarrhea, chest pain, or shortness of breath after leaving the Gastroenterology Laboratories, please call 911 immediately, and then contact the study doctor. Dr. Tuteja can be reached 24 hours a day through the George E. Wahlen VAMC, GI lab at (801) 584-1236 from 8 AM to 5 PM or through the GI fellow on-call at (801) 582-1565.

BENEFITS: Rifaximin might help your IBS, but there is no guarantee that this study will help you. Your condition might not improve or might get worse while you are in this study. If you receive placebo, this does not contain active medication. The information we get from this study may help us to better treat future patients with IBS-diarrhea.

ALTERNATIVE PROCEDURES: If you do not want to be in the study, you may choose not to participate without any penalty or compromise of your care. You will continue to be treated for your illness with usual medications.

CONFIDENTIALITY: All information gathered during this study will be treated confidentially. Individuals will be identified only by initials and numbers. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognized from it. Only those who work with this study will be allowed access to your information. Your identity will not be disclosed in any publication.

The information gathered from this study will be stored in locked secure cabinets in the Division of Gastroenterology, George E. Wahlen V.A. Medical Center and the University of Utah Hospital. The computerized data is saved on password-protected computers, also in secured Gastroenterology research offices. The principal investigator, co-investigator, and study coordinator will have access to this data. Your study data will be kept as confidential as possible under local, state and federal laws. By signing this informed consent form, you authorize such access.

AUTHORIZATION FOR USE OF MY PROTECTED HEALTH INFORMATION

Signing this document means that you have authorized the researchers in this study, and others working with us to use information about your health for this research study. This health information would include all records protected by 38 U.S.C. Section 7332 that pertains to Drug Abuse, Alcoholism or Alcohol Abuse, Testing for or Infection with Human Immunodeficiency Virus (HIV) and Sickle Cell Anemia. You can choose whether or not you will participate in this research study. However, in order to participate you have to sign this consent and authorization form.

This is the information we will use:

- Name

Participant Name: _____ Date:_____

Title of Study: Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans (Cases)

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- Address
- Social Security Number
- Telephone number
- Family medical history
- Allergies
- Current and past medications or therapies
- Information from a physical examination, such as blood pressure reading, heart rate, breathing rate, and temperature
- Current and past pertinent medical information (other medical diseases)
- Information from questionnaires regarding your bowel symptoms, quality of life, and psychological profile.
- Information from Breathing Test for the presence of bacteria.

Others who will have access to your information for this research project are the University of Utah's Institutional Review Board (the committee that oversees research studying people) and authorized members of the **VA Salt Lake City Health Care System (VASLCHCS)** workforce who need the information to perform their duties (for example: to provide treatment, to ensure integrity of the research, and for accounting or billing matters).

If we share your information with anyone outside the **VASLCHCS** you will not be identified by name, social security number, address, telephone number, or any other information that would directly identify you, unless required by law.

In records and information disclosed outside of the **VASLCHCS** your information will be assigned a unique code number. We will keep the key to the code in a locked file. We will destroy the key to the code at the end of the research study. ~~You may revoke this authorization.~~

You may revoke this authorization. **This must be done in writing.** You must either give your revocation in person to the Principal Investigator or the Principal Investigator's staff, or mail it to **Ashok K. Tuteja, GI Lab (111 G); Foothill Blvd. Salt Lake City, UT 84148**. If you revoke this authorization, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

This authorization does not have an expiration date.

PERSON TO CONTACT: If you have questions, complaints or concerns about this study, or if you think you may have been injured from being in this study, you can contact **Ashok Tuteja, M.D.** at (801) 584-1236.

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Dr. Tuteja can be reached at this number during the hours of 8 AM to 5 PM. Dr. Ashok Tuteja can also be reached 24 hours a day through the George E. Wahlen VAMC, GI lab or through the GI fellow on-call at (801) 582-1565.

INSTITUTIONAL REVIEW BOARD: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

MEDICAL TREATMENT OR COMPENSATION FOR INJURY: If you are injured as a result of being in this study, the VA will provide the necessary medical treatment in accordance with federal law. If you want to make a legal claim against the VA or anyone who works for the VA, special laws may apply. The Federal Tort Claims Act (28 U.S.C. 1346(b), 2671-2680) is a federal law that controls when and how a person can bring a claim against the U.S. Government. If you sign this document ~~you~~ you're not giving up your right to make a legal claim against the United States.

VOLUNTARY PARTICIPATION: Your decision to participate in this research study is entirely voluntary. It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the relationship you have with the investigator or staff nor standard of care you receive. You will be informed of any new information that may affect your decision to continue in the study.

UNFORESEEABLE RISKS: It is possible that if the treatment is given to a pregnant woman it will harm the unborn child. Therefore, pregnant women must not take part in this study; neither should a woman who plans to become pregnant during the study. Women who are at risk of pregnancy will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy and must use an acceptable form of birth control. Acceptable forms of birth control include hormonal control, spermicides, condoms and an intrauterine device (IUD). If a woman becomes pregnant during the study, she will be withdrawn from the study and will be referred to her primary physician for further follow up. *Any woman who finds that she has become pregnant while taking part in the study must immediately tell her research doctor.* There may also be unforeseeable risks associated with this study.

RIGHT OF INVESTIGATOR TO WITHDRAW: You may withdraw from the study at any time without penalty. Dr. Ashok Tuteja, can withdraw you without your approval. Possible reasons for withdrawal include an adverse or unexpected reaction to the breathing test solution.

COSTS TO SUBJECTS AND COMPENSATION: You will not incur any costs as a direct result of participation in this study. Your insurance company will be billed for the tests. Costs incurred during follow up with your health care provider or during the treatment of bacteria in your intestine, if indicated, will be billed to you or your insurer in the ordinary manner.

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You will receive a total payment of $200.00 if you complete all 10 study visits. If you do not complete all visits you will receive $20.00 for each visit completed.

NEW INFORMATION: Sometimes during the course of a research project, new information becomes available about the treatment/drug that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from this study, your research doctor will make arrangements for your care to continue. If you decide to continue in the study, you will be asked to sign an updated consent form. Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

NUMBER OF SUBJECTS: We expect that approximately 354 people *(165 cases, plus 189 controls)* will be in this study.

TISSUE BANKING: Please read each sentence below, think about your choice, and mark "**YES**" or "**NO**". **No matter what you decide to do, your decision will not affect your medical care.**

May the VASLCHCS or its research partners retain your blood, colon biopsy specimen, and stool sample(s) after the end of this research project for use in future research?

- **YES, my sample(s) may be saved for future Irritable Bowel Syndrome research**
- **NO, my sample(s) must be destroyed at the end of this research project**

If yes, may the VASLCHCS or its research partners keep your name and other identifying information with your sample(s)?

- **YES, my personal identifiers and medical information can be kept with my sample(s). All information will be kept secure and confidential.**
- **NO, my name and identifiers must be removed from my sample(s). My sample(s) cannot be linked back to me.**

If you granted permission for the sample(s) to be used in future research by the VASLCHCS or its research partners, the Institutional Review Board will review and approve each new project. The Institutional Review Board may require that you be contacted for your permission prior to the use of the sample(s) in a new project if it determines consent is required for your protection.

You have the right to withdraw your consent in the future. You need to notify the investigator of your decision. If you decide to remove identifiers from your sample(s), you will not be able to withdraw your sample later because it cannot be linked back to you.

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RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the preceding information. Dr./Mr./Ms _____ has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but I will not be identified in publications by name, photograph, or other identifiers. My records, including my name and results of my participation, may be revealed as required by laws and regulations of state and federal agencies. A copy of this consent form will be filed in my medical record chart at the VA Salt Lake City Health Care System.

If I have any questions about this study or if any problems arise during the study, I can call:

Dr./Mr./Ms. _____ at _____ DURING THE DAY and Dr. /Mr./Ms._____ at _____ AFTER HOURS. If any medical problems occur in connection with this study, the VA Salt Lake City Health Care System will provide emergency care.

If I have concerns or questions about this research study that the investigator has not answered, I can contact an official of the Institutional Review Board for Human Studies by calling 801-581-3655 or the VA Salt Lake City Health Care System Research Compliance Officer at 801-584-1271.

I understand my rights as a subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done. I will receive a signed consent form or a photocopy of it.

I agree to participate in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

_____ Participant's Name	_____ Participant's Signature	_____ Date
_____ Name of person obtaining authorization and consent	_____ Signature of person obtaining authorization and consent	_____ Date
_____ Witness Name	_____ Witness Signature	_____ Date

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Signature of Investigator