Date:

Title of Study: Gulf War Illness Inflammation Reduction Trial
Principal Investigator: Ronald R. Bach, PhD
Co- Principal Investigator: Gerhard J. Johnson, MD

VAMC: Minneapolis 618

INTRODUCTION

It is important that you read and understand the following explanation of the proposed research study before you agree to participate. This consent form describes:

- The purpose,
- The description of the study,
- The benefits,
- The risks and/or discomforts (including any potential for pain),
- Steps taken to decrease or eliminate the risks, discomforts, or possible pain,
- Any other treatments that may be available, and
- Confidentiality and use of research results.

Whether you decide to participate or not, treatment at the VA for which you are eligible will not be affected.

This consent form may contain words you do not understand. Please ask the study doctor or the study staff to explain any words or information unclear to you.

PURPOSE OF THE STUDY

You are being asked to voluntarily participate in a research study that will determine if treatment with an anti-inflammatory drug known as delayed–release prednisone (Rayos®), 10 mg, will improve the quality of life of Gulf War veterans suffering from Gulf War Illness. The Department of Defense (DOD) is providing funding for this study. You have been asked to participate in this study because you have symptoms of Gulf War Illness, as defined by the Kansas Case Definition. Your participation is expected to last 16 weeks, and approximately 100 people will participate in the study.

DESCRIPTION OF STUDY

The following information describes what will happen while you participate in the study.
If you agree to participate in this study, then you will be asked questions about your medical history, and current health status. You will have a physical exam with one of the study doctors to check to see that you are eligible to participate. This is called a screening physical.

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You will be asked to fast for 8 hours, (nothing to eat for 8 hours, water for medication administration is allowed), before your appointment time to enable us to take a blood sample, in the amount of approximately 3 Tablespoons, to check the levels of sugar in your blood, how well your kidneys are working, if you have diabetes, and if you have signs of an infection or inflammation.
If your blood test results and physical exam are satisfactory, you will be invited back to the VA to continue on with the active part of the study. At this point, we will contact you first by a telephone call and then follow-up with a letter.

You will talk with the Study Coordinator and schedule your first study appointment. If you agree to participate in this study, then you will be asked questions about your medical history and current health status. Next, blood samples (approximately 3 Tablespoons – 45ml) will be taken by inserting a needle into a vein of your arm. Finally, the tubes containing your blood will be transported to the laboratory for analysis.
This blood will be examined to check your blood counts and the levels of certain proteins in your blood. You will also be asked to answer questions regarding your current health and how you feel. The study statistician will have randomly assigned you to one of two groups. The study pharmacist will prepare the study drug package for you. You will be instructed how to take the study drug. You will either receive the drug we are testing in the study or you will receive a placebo tablet. A placebo tablet is a tablet that looks just like the study drug but does not contain any of the chemicals that make the drug active. It contains a non-harmful powder that does not have any drug action. Subjects have an equal chance, like the flip of a coin, of getting placebo or active drug.

The Principal Investigator and the Study Staff will not know if you are receiving the study drug or the placebo, but this information can be obtained in an emergency. You will be given enough pills to take every day for 8 weeks and a calendar on which you can mark that you have taken your pill every day.

You will also receive the telephone numbers for the Principal Investigator, Study Physicians, the Study Coordinator, and the Study Hotline. We will also make an appointment for you to return to the VA within a few days of when you finish taking the pills. At this appointment you will have blood drawn from a vein in your arm. This blood will be examined to check the tests done at the

beginning of the study and the levels of certain proteins in your blood. You will also be asked to answer questions regarding your current health and how you feel.

Contact	Approximate Duration	Event	Administered/ Reviewed by
Initial Phone Call	15 minutes	Pre-Screening Phone Call, including Kansas Case Definition Questionnaire	Study Coordinator
Screening Visit (Week -1 or -2)	60 minutes	Informed Consent Process: , including Study Consent Form, HIPAA, Participant Information	Study Coordinator
	30 minutes	Screening for Exclusion Criteria: History, Physical Exam, and Review of Systems	Physician
	15 minutes	Screening for Exclusion Criteria: Screening Blood Tests	Nursing Staff
Randomization Visit (Week 0)	15 minutes	Initiation of Active Phase: Health Questionnaires	Study Coordinator
	10 minutes	Subject Receives Study Drug or Placebo	Research Pharmacist
	15 minutes	Blood Draw for Baseline, Safety and Biomarker Analysis	Nursing Staff
Week 2 Phone Call (+/- 7 days)	10 minutes	Telephone Call with Subject : Check on study drug/placebo compliancy, and any new health concerns.	Study Coordinator
Week 4 Phone Call (+/- 7 days)	10 minutes	Telephone Call with Subject : Check on study drug/placebo compliancy, and any new health concerns.	Study Coordinator
Week 8 Clinic Visit (+/- 7 days)	15 minutes	Conclusion of Active Phase: Health Questionnaires	Study Coordinator
	10 minutes	Blood Draw for Repeated Baseline, Safety and Biomarker Analysis	Nursing Staff
	30 minutes	Active Phase Completed: Physical Exam and Review of Systems	Physician
Week 16 Clinic Visit (+/- 7 days)	15 minutes	Evaluation of Possible Change in Symptoms using Health Questionnaires	Study Coordinator
	10 minutes	Blood Draw for repeated Baseline, Safety and Biomarker Analysis	Nursing Staff

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This study includes the creation of a database (computer record) of information. By initialing number 1 below you are choosing to have your information stored, OR by initialing number 2 below you are choosing to NOT have your information stored.

Please **initial** item 1 or 2 below:
1._____ I permit my information to be stored for future research.
2._____ I do not permit my information to be stored for future research.

RISKS AND/OR DISCOMFORTS
Approximately 4 tablespoons (60cc) of blood will be drawn from your arm, approximately 1 tablespoon (15cc) at each blood draw. Possible side effects from the blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of the puncture. There is also a slight possibility of infection. There may be other unknown side effects that could occur.

There are physical risks involved with taking prednisone, an anti-inflammatory drug. Common side effects for this drug include holding fluid in your body tissues, changes in how much sugar your body can handle, blood pressure going up, acting differently, mood changes, wanting to eat more and weight gain.

There are also possible ways that this drug can work with other drugs and some reasons not to take this medicine. As a general rule, do not be treated with live-attenuated (made less harmful) viral or bacterial vaccines when you are participating in this study. Some examples are listed below.
Viral: measles vaccine, mumps vaccine, rubella vaccine, chicken pox vaccine, oral polio vaccine, rotavirus vaccine (Sabin), yellow fever vaccine, and nasal-spray flu vaccine (including the seasonal flu nasal spray and the 2009 H1N1 flu nasal spray).
Bacterial: BCG (tuberculosis) vaccine, oral typhoid vaccine and epidemic typhus vaccine.

When the study is over and you want to receive a vaccine, check with your doctor to see if it is OK for you to have it.

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Possible drug interactions with:

The study team will review your list of current medications and discuss them with your primary provider. Please notify the study team if there are any changes in the medications that you are currently taking.

There may be other unknown side effects that could occur.

EMPLOYEES AS RESEARCH SUBJECTS

If you are a VA employee you are considered a special class of research subject who deserves special protections: 1) your decision to participate in this study should be free from pressure or coercion to participate; and 2) the VA research team will work to secure your information according to VA data security and privacy policies and every effort will be made to keep your information from your supervisor and co-workers. However, accidental disclosure or release of your private information could occur during the conduct of this study.

BENEFITS

There may be no direct benefit to you from being in the study. The knowledge gained from this study may benefit others in the future.

COMPENSATION

You will be paid $100.00 for each visit relating to the study (4 total), and reimbursed for travel expenses ($0.415 per mile). Because you are required to not eat before the required blood tests, you will also receive a $5.00 food voucher at the end of each visit to the MVAHCS.

You will receive your payment within 3 weeks of completing the study.

ALTERNATIVES (OTHER AVAILABLE TREATMENTS)

There are no known treatments for Gulf War Illness. Your only alternative is to not participate in the study.

CONFIDENTIALITY AND USE OF RESEARCH RESULTS

The results of this study may be published or presented but your identity and records will not be revealed unless required by Federal Law. A Federal Law allows the U.S. Food and Drug Administration, Office for Human Research Protections, Government Accountability Office and other Federal agencies, including the U.S. Army Medical Research and Materiel Command (USAMRMC), The Department of Defense (DOD), the Research and Development Committee and/or the Institutional Review Board (IRB)/Human Studies Subcommittee of the VA Medical Center to review records for the purpose of fulfilling their responsibility to protect research subjects. Because of the need for these inspections, absolute confidentiality cannot be guaranteed.

COSTS TO YOU FOR PARTICIPATING

There is no cost to you for taking part in this study. All the study costs, including any study medications provided by the sponsor, will be paid for by the VA Medical Center. **Veterans who must make a co-payment for their usual medications or treatments will continue to be required to make such a co-payment for non-study related drugs.** There should be no additional medical costs to you for taking part in this study. However, frequent clinic visits may result in transportation costs and possible wages lost due to time missed from work.

WHAT TO DO IF YOU HAVE A MEDICAL EMERGENCY

In the case of a medical emergency call 911 and seek immediate medical attention.

WHAT TO DO IF YOU HAVE QUESTIONS OR MEDICAL PROBLEM

If you have questions about the study or are seeking advice about a medical problem that may be related to this study call (612) 467-1100. If you do not live in the metropolitan area, you may call the toll-free number: 1-866-414-5058.

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MEDICAL CARE IF YOU ARE INJURED

In case you are injured from this research study, treatment will be available, including first aid, emergency treatment and follow-up care, as needed, by the VA Medical Center. In the event you cannot reach a VA facility, the VA will pay for necessary medical care for any injury or illness directly related to your participation in this research study. If you receive this type of medical care, you must contact the Research Investigator for this study. You can find contact information in the section of this consent titled "Compensation for Any Injuries".

COMPENSATION FOR ANY INJURIES

You have not released the VA Medical Center from liability by signing this form. This includes but is not limited to: 1) free medical care other than as described in this consent form, 2) payment of lost wages, or 3) compensation for pain and suffering. Compensation for those items from the VA may be available under applicable Federal Law. You should immediately report any injuries resulting from your participation in this study to either Dr. Bach at (612) 467-4418 or Dr. Johnson at (612) 467-4134. If they are unavailable when you call, leave a message along with your name and contact phone number. A member of the study team will return your call as soon as possible.

OTHER INFORMATION

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.

NEW INFORMATION

You will be given any new significant information that is discovered during the course of this study which may influence your willingness to continue the study.

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RESEARCH SUBJECT'S RIGHTS: I have read or have had read to me all of the above. The Principal Investigator or the Study Coordinator 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. **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 my identity and records will not be revealed unless required by law.

I authorize the use of my bodily fluids and substances, or tissues.

I have been informed that because this study involves articles regulated by the FDA (Food and Drug Administration), the FDA may choose to inspect research identifying me as a subject of this investigation.

In the case of a medical emergency, I have been told to call 911 and seek immediate medical care. If I am seeking advice about a medical problem that may be related to this study or I have questions about the study I have been told to call (612) 467-1100. If I do not live in the metropolitan area, I may call the toll-free number: 1-866-414-5058. If any medical problems occur in connection with this study the VA will provide emergency care.

If I have any questions about the rights of a research subject, or would like to:

- obtain information
- discuss problems or concerns, or have questions about this study
- offer input regarding this research study

and would like to speak to an individual who is not part of the research team of this study, I may contact the Patient Representative at (612) 725-2106. If I wish to verify the validity of the study and its authorized contacts, I may call the patient representative or contact the IRB office at 612-629-7387.

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My questions have been answered and I voluntarily consent to participate in this study. By signing this form, I have not given away any of my legal rights, which I have as a subject of this research study. I will receive a signed copy of this consent form.

Subject's Signature Date Time

Signature of Person Obtaining Consent Date

Printed Name of Person Obtaining Consent

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