Experimental Research Subject's Bill of Rights

California law, under Health & Safety Code Section 24172, requires that any person asked to take part as a subject in research involving a medical experiment, or any person asked to consent to such participation on behalf of another, is entitled to receive the following list of rights written in a language in which the person is fluent. This list includes the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of the signed and dated written consent form.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

_____ _____

Signature of Subject Date

_____ _____

Signature of Witness Date

INFORMED CONSENT TO PARTICIPATE IN CLINICAL RESEARCH STUDY

Title: An Investigator Initiated, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy of Certolizumab Pegol (Cimzia) For the Treatment of Interstitial Cystitis(IC)

Sponsor: Philip C. Bosch, M.D.

Protocol Number: IC-201

Principal Investigator: Philip C. Bosch, M.D.
651 E. Pennsylvania Ave. Ste. 201
Escondido, CA 92025

24-Hour Telephone Number: (760) 743-3135

You are being asked to take part in this research study to evaluate an investigational treatment for interstitial cystitis (IC). This study includes only individuals who voluntarily choose to participate. Please take your time to make your decision. You may choose to discuss this with your regular doctor, your friends and your family. You are free to ask questions concerning this document.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this research study is to evaluate an investigational treatment for interstitial cystitis (IC). IC is a chronic bladder disease that includes the following symptoms:

- Urinary frequency during the day
- Urinary frequency at night
- Urinary urgency
- Bladder discomfort relieved by voiding

Presently, there is no cure for IC. The responses to current approved treatments are poor. Patients with IC have a poorer quality of life. The cause of interstitial cystitis is unknown.

This study is evaluating the drug certolizumab pegol (Cimzia) for improving the symptoms of patients with IC. Certolizumab pegol is an injectable anti-inflammatory medication. It has been available for use in the United States since the US Food and Drug Administration (FDA) approval for the treatment of Crohn's disease on April 22, 2008. Certolizumab pegol (Cimzia) has subsequently been FDA approved for the treatment of rheumatoid arthritis, psoriasis, and ankylosing spondylitis. These diseases have similar characteristics to IC. This study is experimental as it will evaluate a new investigational use of certolizumab pegol (Cimzia) for the treatment of IC. Cimzia (certolizumab) is not approved for the treatment of IC.

Patients participating in this study will be randomized (assigned randomly like flipping a coin) to receive injections of one of the following products:

1. Certolizumab pegol (Cimzia)
   or
2. Placebo (a substance containing no active medication)

This is considered a double-blind, randomized study in which neither the patient nor the study doctor will know which injection the patient will receive. Neither you, nor the doctor can choose whether you receive the active medication or the placebo. This allows for an unbiased evaluation of the results of the study. In case of an emergency, the study doctor will be able to find out which injection the patient was given.

HOW LONG IS THIS STUDY?

There will be 4-6 weeks of screening, 10 weeks of the actual study, and then a follow up 4 and 8 weeks after the completion of the study. The total time involved is about 5 months.

HOW MANY OTHER PEOPLE WILL BE IN THIS STUDY?

There will be 20 patients receiving certolizumab pegol (Cimzia) and 10 patients receiving placebo for a total of 30 patients. After evaluation in the initial 30 patients, the Study may potentially increase the study sample size to a total of 42 study patients (an added 8 patients receiving certolizumab pegol (Cimzia) and 4 patients receiving placebo).

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

If new information in relation to this study becomes available that may be relevant to the purpose and safety of the study and your willingness to continue participation in this study, you will be informed by the study doctor.

WHO IS ELIGIBLE FOR THE STUDY?

Females who have been diagnosed with interstitial cystitis for more than six months and are between the ages of 18 and 65 are eligible to participate in this research study.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to take part in this research study, you will be required to sign and date this informed consent form before any procedures take place.

Initial evaluation:

1. You will complete an initial questionnaire detailing your personal and medical history.
2. A complete medical history will be obtained.
3. You will be given a complete physical exam by the study doctor.
4. You will be instructed in behavior modification techniques to improve IC and/or Bladder Pain Syndrome (BPS) symptoms
5. You will be required to take a tuberculosis (TB) skin test.
6. You will be tested for Hepatitis B & C.
7. You may be asked to have an HIV test. This will dependent on how recent and/or how thorough your available medical records are.

You will be told if the test results for TB, Hepatitis B, Hepatitis C, or HIV are positive. A positive result from these tests will be reported to the local health department as required by state law. The results from these tests are confidential and results will not be shared outside of this study except as required by state law. There is always a chance that a breach in confidentiality could happen; this means that people that were not originally supposed to have this information could see these results. Please speak to the study staff or your personal doctor, if you want to know more about what it could mean to you if somebody outside of this research study has access to this information.

Re-Evaluation Visit

You will be reassessed at least one month later for inclusion/exclusion criteria and determine study eligibility. At this Re-Evaluation Visit:

1. You will undergo laboratory work including blood and urine samples.
2. If you are able to become pregnant your blood will be tested for pregnancy. You should not participate in this research if you are pregnant, or planning to become pregnant while in the study.

Study Visits:

If after your re-evaluation visit, you are still eligible to participate in this study, you will come back approximately one week later (Baseline, Week 0) to begin the study.

Baseline and Visits 1-3 (Weeks 0,2,4,8)

At your Baseline Visit, you will be randomized to receive a skin (subcutaneous) injection of either certolizumab pegol (Cimzia) or the placebo.

At this study visit and again at your visit on Week, 2, 4 and 8, the following procedures will take place:

1. You will receive your injection
2. You will be required to complete two questionnaires evaluating your interstitial cystitis symptoms at each visit.
3. A urine sample will be done at each visit.
4. A general health questionnaire will be done at each visit.
5. A physical exam will be performed if indicated.

Visits 4 (Weeks 10)

At this study visit, the following procedures will take place:

1. You will be required to complete two questionnaires evaluating your interstitial cystitis symptoms at each visit.
2. A general health questionnaire will be done at each visit.
3. A physical exam will be performed if indicated.

Follow-Up

A follow-up phone evaluation will be done with you four weeks (Week 14 and 18) after completion of the study. A final blood test, urine analysis, and tuberculosis skin test will be done.

You are advised to tell your regular health care providers and any emergency care providers that you are participating in this research study.

WHAT ARE THE POSSIBLE RISKS WITH THIS STUDY?

The study drug has been associated with the following side effects, including redness or swelling at the injection site, rash, upper respiratory infection, or urinary tract infection. Serious side effects reported include infections caused by viruses, fungi, or bacteria, tuberculosis, cancer and demyelinating diseases (any condition that results in damage to the protective covering called a myelin sheath

that surrounds nerve fibers in your brain and spinal cord). Please ask the study doctor if you have any questions.

More rare side effects may include, but not limited to:

- shortness of breath;
- swelling of the ankles, hands, or feet;
- unexplained weight loss or weight gain;
- swelling or itching of the face, tongue, lips, or throat;
- trouble breathing;
- skin or eyes look yellow:
- tiredness (fatigue);
- poor appetite or vomiting;
- pain on the right side of your stomach (abdomen);
- dizziness;
- numbness or tingling;
- problems with your vision;
- weakness in your arms or legs;
- fever
- bruising or bleeding;
- unusually pale skin;
- new or worsening joint pain;
- butterfly-shaped rash on the nose and cheeks.

Please notify the study doctor immediately if any of these side effects occur.

The package insert of Certolizumab Pegol (Cimzia) is available for you to read. Please ask the study doctor for a copy and for more information that is available for patients taking this drug, so that you can read about the potential side effects and warnings associated with taking this study drug.

Any of the drugs used in this study can interact with other medications, including over-the-counter, herbal and vitamin medicines. Please inform the study doctor of all the medications you are currently taking.

Especially tell your healthcare provider if you take the following medicines due to a higher chance for serious infections:

- Kineret (anakinra), Orencia (abatacept), Rituxan (rituximab), or Tysabri (natalizumab).

- Medicines called Tumor Necrosis Factor (TNF) blockers such as Remicade (infliximab), Humira (adalimumab), Enbrel (etanercept), or Simponi (golimumab).

An allergic reaction is possible. This reaction can be a mild rash or itching to a severe rash, including trouble breathing or swallowing. Please tell the study doctor immediately if you experience any of these symptoms.

Blood sampling has risks which include bruising, dizziness, or pain.

There may be risks to being in this study that cannot be predicted.

Please discuss these risks with the study doctor and your regular doctor. Many side effects subside shortly after the study drug is stopped, however, in some cases side effects can be serious or long-lasting. Rarely are side effects permanent.

Side effects occurring during the trial can be treated by the study doctor, if this is deemed necessary. It is important to inform the study doctor of any side effects.

ARE THERE PREGNANCY RISKS?

Women of child-bearing age may not participate in this study if they are pregnant or nursing. Since no adequate and well-controlled studies of the study drug in pregnant women have been performed, women should not become pregnant while participating in this study.

Women who think they are pregnant must tell the study doctor immediately. If you are of able to become pregnant, please discuss adequate methods of birth control with the study doctor.

For more information about these risks and side effects, contact the study doctor**.**

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There will be no direct benefit from participating in this study. Your symptoms may improve, stay the same or get worse.

ALTERNATIVES:

Your alternative is to NOT participate in this study and remain on your current treatment for IC. Your study doctor can give you more information on alternative current treatments for IC, and their risks.

CONFIDENTIALITY

Your personal information will be kept confidential to the extent permitted by law. The study cannot guarantee absolute confidentiality. By signing this document,

you give permission to access your medical records at any time for data verification purposes.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include:

- The study staff and researchers involved in the study
- UCB- the pharmaceutical company that produces certolizumab pegol (Cimzia)
- The U.S. Food and Drug Administration (FDA)
- Aspire Independent Review Board (IRB)

The results from the study, including laboratory tests, may be published for scientific purposes. Your identity will be kept confidential.

In the rare event that your information is required to be disclosed by law to another entity, privacy laws may not apply.

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.

WHAT ARE THE COSTS?

There are no costs associated with being in this study. You are responsible for your regular health care while in this study.

INVESTIGATOR PAYMENT

The study doctor and the study site have received grant funding to conduct this study.

WILL YOU BE COMPENSATED DURING THE STUDY?

You will not be compensated for participating in this research study.

WHAT HAPPENS IF THERE ARE COMPLICATIONS OR INJURIES?

If you experience a serious side effect, complications, or are injured because of participation in this study, please contact the study doctor promptly. The study doctor can be reached at the phone number listed on page 1 of this document. The study doctor will provide any necessary medical treatment to help you promptly recover from the injury.

RIGHTS AS A RESEARCH SUBJECT

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. However, if you decide to stop participating in the study, you are encouraged to talk to the study doctor and your regular doctor first.

RESPONSIBILITIES AS A RESEARCH SUBJECT

You will be asked to adhere to all instructions issued by the study doctor and study staff.

You should answer all asked questions truthfully.

If you do not comply with instructions, may be removed from the study.

The study doctor may also exclude you from this study if he deems it detrimental to your health, or if you do not meet the study requirements.

WHO TO CALL WITH QUESTIONS

For questions, concerns or complaints about the study or a research-related injury, contact the study doctor (760) 743-3135.

This study was reviewed by IRB. The IRB will review the study to protect the rights and welfare of study participants. If you have problems, concerns, suggestions, questions, or information about the study, or for information regarding study subject's rights, please call Aspire's Study Participant Advocate at 1-877-366-5414 (toll free).

Aspire IRB has approved the information provided in this informed consent form and has granted approval for the investigator to conduct the study. IRB does not approve your participation in the study. It is your responsibility to evaluate the information in this informed consent form and decide if you wish to participate in this study.

SIGNATURE AND CONSENT TO BE IN THE STUDY

Your signature below means that you have read the above information and have had the opportunity to ask questions concerning your participation in the study. Your questions have been answered to your satisfaction. Your signature confirms that you have received and read a copy of the California Experimental Bill of Rights. Your signature confirms that you agree to participate in this research and

that you have been told that you can discontinue this study at any time. You will be given a signed and dated copy of this agreement. By signing this consent form you are not giving up any of your legal rights.

_____ _____
SIGNATURE OF SUBJECT DATE

_____
PRINTED NAME OF SUBJECT

I confirm that a copy of this consent form has been given to this person to read and that this person has been told about the study. The contents of the consent form describing the study has been discussed with this person and I have made every effort to answer all questions to his or her satisfaction. I have watched this person sign the consent form.

_____ _____
INVESTIGATORS SIGNATURE DATE

Philip C. Bosch, MD
INVESTIGATOR

Authorization to Use and Disclose Your Personal Health Information

Title: An Investigator Initiated, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy of Certolizumab Pegol (Cimzia) For the Treatment of Interstitial Cystitis(IC)

Sponsor: Philip C. Bosch, M.D.

Protocol Number: IC-201

Principal Investigator: Philip C. Bosch, M.D.
651 E. Pennsylvania Ave., Suite 201
Escondido, CA 92025

24-Hour Telephone Number: (760) 743-3135

INTRODUCTION

This authorization may have words that you do not understand. Please ask the study doctor or staff to explain any words or information that you do not understand.

The purpose of this form is to explain how details about your health **and your personal information** that you give us during this study will be used and shared with others.

By signing this form, you allow the study doctor to use and share your personal health information collected during the course of this study. Please read this with the Informed Consent that you already signed for the above-mentioned study. All participation information is explained in that consent form.
You do not have to sign this form. However, if you choose not to sign this authorization, you may not participate in the study.

INFORMATION THAT MAY BE USED AND SHARED

Information that may be used and given to others may include past, present and future health information collected during this study. Your personal information includes, but is not limited to the results of study related procedures as described in the informed consent. [e.g., subject questionnaires, laboratory tests, medical history and other study-related materials that are unique and specific to your participation in this clinical study].

Your personal health information will be used to carry out the research, to review records on the information collected in this study, to check how the study was carried out, or for other uses permitted by law.

THIS INFORMATION MAY BE SEEN BY

- The study doctor and staff
- The study sponsor, UCB, Quest Labs
- Aspire Independent Review Board (IRB)
- The U.S. Food and Drug Administration
- The Department of Health and Human Services
- Government agencies that require reporting of reportable diseases
- Individuals or companies that monitor the quality of research practice

There may be other information that may be used and given to others that have not been stated above. You should discuss this with the study doctor or a member of the staff and ask any questions that you may have about the sharing of your health information.

HOW LONG IS THIS AUTHORIZATION IN EFFECT

This authorization to use and disclose your personal health information expires when the study is finished, which should be complete by 1/1/2019. You must notify the study doctor in writing that you no longer want to share your information. Information collected before the termination of your authorization may still be used for study purposes.

If you decide that you no longer wish to have your personal health information shared, you may withdraw at any time. However, once you do so, you can no longer continue to participate in the study.

In addition:

- You must provide a written request to the study doctor, listed on page 1, and tell him or her that you no longer want to share your information.

Revoking your authorization and choosing to no longer participate in this study, does not affect your treatment or any other benefits to which you would otherwise be entitled.

- You will no longer be a part of this research study
- The study doctor and staff can continue to share any of the information that they already have.

Once the study doctor has shared your information with someone outside the study, it may no longer be protected. There is a chance that your information will be shared with others in ways that are not listed here and released without your permission.

You have a right to see and copy of your information; however, you will not be able to see it while the research study is going on.

AUTHORIZATION

I agree to share my information as described in this form and I have received a signed and dated copy for my records.

_____	_____	_____
Printed Name of Study Participant	Signature of Study Participant	Date

The information contained in this document was fully and carefully explained to the study participant or the study participant's legal representative. If applicable, I certify to the best of my knowledge that the study participant's legal representative is authorized to sign this informed consent.

Philip C. Bosch, MD	_____	_____
Investigator	Signature of Investigator	Date