# CONSENT FORM

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| **TITLE:** | Seroquel XR for the Management of Borderline Personality Disorder (BPD) |
| **PROTOCOL NO.:** | IRUSQUET0454 |
| **INVESTIGATOR:** | S. Charles Schulz, MD |
| **SITE:** | University of Minnesota Medical School, Dept of Psychiatry |
| **TELEPHONE:** | 612.273.9820 |

## INTRODUCTION

You have been asked to take part in a clinical research study at the University of Minnesota Medical School, Department of Psychiatry. This consent form describes the purpose, procedures, possible benefits and risks of the study. Before agreeing to participate in this research study, it is important that you read and understand this form. You are encouraged to discuss any questions that you may have about this study with the study staff and study doctors. If you participate, you will receive a copy of this form to keep.

This study is being conducted by the following researchers in the Department of Psychiatry at the University of Minnesota Medical School: S. Charles Schulz, MD; Richelle Moen-Moore, PhD; Michael J. Miller, PsyD; Scott Crow, MD, and Ann Romine, RN. This study is receiving support funding from AstraZeneca Pharmaceuticals LP.

## BACKGROUND AND PURPOSE OF THE STUDY

You are being asked to take part in this research study of the investigational drug quetiapine fumarate extended-release (SEROQUEL XR™). You are being invited to participate in this research study because you have identified traits of borderline personality disorder (BPD).

Quetiapine fumarate extended-release (SEROQUEL XR™) is approved by the United States Food and Drug Administration (FDA) for the treatment of schizophrenia, mania, and bipolar depression. It is not approved for the treatment of borderline personality disorder; however other atypical antipsychotic medications, including Seroquel immediate-release, have been tested with positive results being seen as evidenced by reduction in BPD symptoms. The purpose of this study is to determine the safety and effectiveness of quetiapine fumarate extended-release (SEROQUEL XR™) in the treatment of borderline personality disorder (BPD) compared to placebo (inactive substance).

## NUMBER OF SUBJECTS / LENGTH OF PARTICIPATION

An estimated 99 subjects will take part in this study from 3 study sites.

Your total study participation will last up to 12 weeks (depending on washout period) and include up to 10 study visits. Study visits will take between thirty minutes and 2 hours, depending on which procedures are necessary for that visit.

During the study, you may be asked to return for an unscheduled visit any time your condition warrants medical attention or a dose adjustment is required at no cost to you.

## STUDY PROCEDURES

If you decide to participate in this study you will come in for **10** study visits. The assessment visits will take place at the Ambulatory Research Center (ARC), University of Minnesota Medical Center, Fairview -Riverside Campus, in the Riverside Professional Building, 606 24$^{th}$ Avenue South, suite 602, Minneapolis, MN 55454.

### *Screening Visit (Visit 1)*

The following tests and procedures will be performed to determine eligibility at Visit 1:

- Review of your medical, psychiatric and medication history.
- A physical examination including an eye examination and measurement of your vital signs (heart rate and blood pressure), height, and weight.
- Electrocardiogram (ECG – which measures the electrical activity of your heart)
- Collection of a fasting (no food or drink for 8 hours, except water) blood sample (15 milliliters or approximately one tablespoon) for routine laboratory tests.
- If you have diabetes mellitus type 1, a fasting glycosylated hemoglobin (HbA1c) will be obtained. Your (HbA1c) will need to be less than 8.6% to participate in the study.
- Collection of a urine sample for drug screen for illegal drugs. Results of the drug screen must be negative for you to participate in this study.
- Collection of a urine sample for pregnancy testing for potential child-bearing female subjects. Results of the pregnancy test must be negative for you to participate in this study. The urine pregnancy test will be repeated again at visit 6.
- Mental health history and assessment interview.

You may be asked to stop taking certain medications for depression, mood and anxiety for 14 to 28 days. This is called a washout period where the effects of these medications leave your body.

If you possibly could become pregnant during the study, you must talk to the study doctor about the method of birth control that you will use to avoid getting pregnant during the study and for 30 days after your study participation is completed.

### *Baseline Visit (Visit 2)*

The mental health history and assessment interview will determine whether you have traits of Borderline Personality Disorder (BPD). A minimum of 5 out of 9 BPD traits are required to meet eligibility for participation in the study. If you are eligible to participate in the study you will then come in for the second visit which is the Baseline Visit. At this visit you will receive the study medication with instructions and begin taking the study medication.

**Study Medication**
Your medication will either be quetiapine fumarate extended-release (Seroquel XR) or placebo (sugar pill). Neither you nor the study team will know whether you are taking Seroquel XR or placebo. Whether you receive Seroquel XR or placebo will be determined by chance, like the flip of a coin. You will be assigned to **1 of 3 groups** in the study. Of the 3 groups, 2 groups will receive Seroquel XR (active medication), and 1 group will receive placebo (inactive medication). **This means you will have a 2 out of 3 chance of getting Seroquel XR, and a 1 out of 3 chance of receiving placebo.** The 3 groups to which you will be assigned to are 1) Seroquel XR 150 mg per day, 2) Seroquel XR 300 mg per day, or 3) placebo. You will take by mouth the number of tablets instructed by your study doctor and will be instructed to take the assigned tablets at approximately the same time each day.

It is important that you take the study medication as directed. The study tablets must be taken every day. Any extra study medication tablets and the container, even if it is empty, must be returned to the research coordinator. The study medication should be taken only by you and should not be taken by anyone else.

The study coordinator will call you the day after your baseline visit to ask you how you are feeling after your initial dose of study medication and to address any questions or concerns you may have.

***Study Treatment Period (Visits 3-10)***
After the Baseline Visit you will return to the study clinic weekly for the next 8 weeks (visits 3-10). At each visit you will complete questionnaires about your behavior and mood and the study team will monitor your symptoms and any side effects you may have. Each of these study visits will last approximately 30 minutes to 1 hour.

At visit 6 you will have a urine pregnancy test (females) and weight. The final visit (visit 10) will include vital signs, weight, blood and urine tests (drug screen and pregnancy test for potential child-bearing female subjects), ECG, and side effect assessments. You will complete a final set of questionnaires regarding your behavior and mood at this visit. At the final visit we will also discuss your dosing titration off of the study medication and options for your post-study follow-up care. Follow-up visits will be scheduled with one of the study doctors accordingly.

**RISKS, DISCOMFORTS AND INCONVENIENCES**
There is a risk that the symptoms of your illness will not respond to the study medication. Your condition may worsen during the wash-out phase if you need to titrate off your existing medications before starting the study medication. You may experience increasing symptoms such as unstable mood, sleep disturbance, and the possibility of

suicidal feelings. Your symptoms could be severe and could require hospitalization and have consequences for your family, job, or your finances.

Your condition may worsen if the study drug has no effect on you. Also, as this is a study in which some patients will receive placebo (inactive substance), you may not improve if you are assigned to this part of the study. Throughout the study, your study team will closely monitor for the possibility of worsening symptoms at each clinic visit and will intervene appropriately. Telephone follow-up and additional visits may be used to evaluate your health and to check for increased symptoms. You are asked to contact your study doctor as soon as possible if these symptoms cause you any concern. If this happens, your study doctor will discuss with you whether you should continue in the study and other alternative treatments available for your condition.

If you or your doctor chooses to end your participation in the study, you will be given medication titration instructions by the study doctor to taper off your study medication. Acute withdrawal symptoms such as nausea, vomiting, and insomnia have very rarely been described after abrupt cessation of antipsychotic drugs including Seroquel. However, gradual withdrawal is advisable.

The study medication may cause some side effects. You may experience none, some or all of those listed below.

A common side effect for this type of drug, including the study medication, when beginning treatment is sleepiness. This may affect mental and physical abilities required to operate an automobile or machinery. You should exercise special caution when driving or using machinery since the study medication may cause drowsiness, lack of coordination or slowed reaction time.

You may experience lightheadedness, feeling faint or fainting when standing up, particularly if you wake up during the night during the first week of treatment. This is most common when you begin taking Seroquel XR or increase the dose of Seroquel XR and will usually pass with time. You should exercise caution if you wake up during the night (for example, to go to the bathroom) during the first week of treatment. Stand up slowly and carefully to avoid falling in case you do feel faint. If you awaken during the night and feel dizzy upon sitting up or standing, lie or sit back down and wait until you can get up without feeling faint.

Other relatively common symptoms are rapid heart beat, dry mouth, constipation, indigestion, feeling weak, swelling of arms and legs, weight gain, fainting and stuffy nose.

In some cases there may be a change in the amount of white blood (cells in your blood to help fight infections) or an increase in a type of white blood cells, “eosinophilia”, which is sometimes seen in allergic reactions. If you experience symptoms such as fever and/or sore throat and sores on the tongue or inside of the mouth please contact your study doctor. If the symptoms are severe, you should go to the Emergency Room.

Some patients have shown an increase in the amount of liver enzymes (indicating

possible liver injury or damage). If your blood tests indicate increased liver enzymes, the study doctor will discuss the results and recommendations with you.

More uncommon side effects are allergic reactions and fits (seizures).

Rare side effects that have been reported are fever, very marked drowsiness, muscle stiffness, marked increase in blood pressure or heart beat, reduced consciousness and priapism (long-lasting and painful erection).

There is a rare, but potentially serious, side effect associated with this class of drugs, including the study medication called neuroleptic malignant syndrome (NMS), a potentially life-threatening disorder that includes symptoms such as fever, tight muscles, changes in blood pressure and heart rate, confused thinking, and an increase in the amount of “creatine phosphokinase”, a substance in the muscles.

This class of drugs may also cause a movement disorder called tardive dyskinesia (TD). Symptoms of this disorder are that certain muscle groups (e.g. the tongue and lip muscles) will move even if the person does not want them to move. In most cases the symptoms stop when the medication is withdrawn, but in some cases they are permanent.

In recent studies in bipolar depression, extrapyramidal symptoms that can be muscle tightness, restless feelings, tremor, stiff walking, or lack of coordination were more common in patients treated with Seroquel than in patients with no treatment.

Seroquel was recently approved in the U.S. by the FDA (October 2006) for the treatment of depressive episodes associated with bipolar disorder. All medications used to treat depression (i.e. antidepressants including quetiapine) received a warning from the FDA regarding the risk of suicidal thoughts and actions in some children and teenagers, as well as adults. You should watch for warning signs, especially when beginning therapy or changing dose, which include thoughts about dying, attempts to commit suicide, new or worsening depression, new or worsening anxiety, feeling very agitated or restless, panic attacks, difficulty sleeping, new or worsening irritability, acting aggressive, being angry, or violent, acting on dangerous impulses, or an extreme increase in activity and talking.

Extended-release Seroquel, regular Seroquel, and the non-active tablets (placebo) contain lactose, which may cause discomfort if you are lactose intolerant.

There have been reports of hyperglycaemia (high blood sugar) and diabetes in patients treated with Seroquel and other drugs like it. Also, increases in fatty substances such as triglycerides or cholesterol may occur. Further, people taking Seroquel can have increase in weight and waist size. These side effects, taken together, are now known as the “metabolic syndrome.” In general, these symptoms and laboratory tests go away when the medications are stopped, but may last for some period. You will be tested for changes in glucose, triglycerides, and cholesterol at the beginning and at the end of the study.

You may experience an allergic reaction to Seroquel XR. Symptoms of an allergic reaction include rash, hives, or difficulty breathing in extreme circumstances. If you experience an allergic reaction, you should contact your study doctor. If the symptoms are severe, you should go to the Emergency Room.

Studies with Seroquel and other drugs of this type have shown an increased risk of death in elderly patients with dementia and behavioral disturbances.

There may be risks involved in taking this medication that have not been identified in the studies done so far, but every precaution will be taken and you are encouraged to report anything that is troubling you. Your study doctor and the study staff will monitor your condition closely.

With your cooperation regarding the instructions given by your study doctor, frequent examinations and laboratory tests, the risk of unwanted side effects may be minimized. We ask you to report any health problems during the study to your study doctor.

There are some types of medications that are not allowed to be taken with study medication, including but not limited to, medications in the same class as Seroquel, medications for depression, medications for mood, and some medications for anxiety and sleep. Your study doctor will discuss these limitations on using medications with you. Your study doctor will also provide you with a list of over-the-counter medications and herbal drugs that cannot be taken during the course of the study.

During the washout and if you receive placebo your condition will not be treated with active medication and may become worse, stay the same or improve.

There is a risk that the symptoms of your illness will not respond to the study medication. Your condition may worsen if the study medication has no effect on you. If this happens, your study doctor will discuss with you whether you should continue in the study and other alternative treatments available for your condition.

Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.

Fasting for 8 hours could cause dizziness, headache, stomach discomfort or fainting.

**WOMEN OF CHILDBEARING POTENTIAL**

Taking the study medication may involve unknown risks to a pregnant woman, an unborn child, or breastfeeding infant. Therefore, if you are pregnant, planning to become pregnant during the research study period or are breastfeeding a child, you cannot participate in this study.

If you are a woman of childbearing potential:

- You confirm to the best of your knowledge that you are not pregnant and you do not intend to become pregnant during this study.
- You must avoid becoming pregnant by using one of the following methods of

birth control during this study: double-barrier method (condoms or diaphragm with spermicide), oral contraceptive (birth control pills), implant (Norplant®), dermal contraception (patch), long-term injectable contraceptive (Depo-Provera®), intrauterine device (IUD) or tubal ligation.

If you are female, a urine pregnancy test will be done at Visit 1, Visit 6, and Visit 10 to confirm that you are not pregnant. Results of the pregnancy test must be negative for you to participate in this study.

If at any time during this study you think you might be pregnant, or later learn that you were pregnant during the study, you must contact the study doctor immediately for further instructions.

If you become pregnant during the study, you will be withdrawn from the study. All costs for care related to your pregnancy, childbirth, and post-partum/newborn care will be your responsibility. The sponsor will request access to your records concerning your pregnancy, childbirth and postpartum care as well as your infant's medical records.

**UNFORESEEN RISKS**
Since the study drug is investigational for this indication, there may be other risks that are unknown at present, including possibly life-threatening reactions.

**NEW INFORMATION**
You will be given any new information about the study medication that becomes known during the course of this study that might reasonably affect your willingness to continue to take part in the study.

**POSSIBLE BENEFITS**
Although Seroquel XR is being tested as a treatment for BPD, there is no guarantee that you will receive any medical benefit. Study drug and study procedures will be provided at no cost. You may receive information about your health from the physical examinations, laboratory tests, and psychological evaluations done in this study. Your participation will provide information about the study medication and BPD that may benefit others in the future.

**ALTERNATIVE TREATMENT**
You do not have to take part in this study to be treated for your illness or condition. Other treatments and therapies for your condition are available, including psychotherapy or medication therapy. Although there are currently no medications approved by the Food and Drug Administration (FDA) for the treatment of Borderline Personality Disorder, Seroquel XR is available by prescription off-study. The study doctor can discuss with you the important benefits and risks of these treatments and therapies.

**CONFIDENTIALITY**

To help protect your privacy, the researchers have obtained a Certificate of Confidentiality from the National Institutes of Health. With this certificate, the researchers cannot be forced to disclose the information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the Federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself and your involvement in the research. If an insurer, employer or other person obtains your written consent to receive research information, then the researcher may not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant of the research project to prevent serious harm to you or someone else. This may occur under the following circumstances such as the present danger of child abuse, suicide, and/or homicide.

The Certificate of Confidentially does not represent an endorsement of the study by the Department of Health and Human Services or National Institutes of Health.

Records of your participation in this study will be held confidential except as disclosure required by law or as described in this informed consent document under the section PROTECTED HEALTH INFORMATION (PHI). The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records, which identify you by name. Therefore, absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

## COMPENSATION FOR PARTICIPATION

You will be compensated $30.00 for each visit in the form of a check that will be mailed to your home 2-3 weeks after your last study visit. Study drug and study procedures will be provided at no cost. We will also provide free parking and have transportation options available to you as needed.

## RESEARCH RELATED INJURY

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment, and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. The sponsor of the study has some funds available to pay for care for injuries resulting directly from being in this study. If you think that you have suffered a research related injury and that you may be eligible for reimbursement of some medical care costs, let the study physicians know right away.

**PROTECTED HEALTH INFORMATION (PHI)**
Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

**VOLUNTARY NATURE OF THE STUDY**
Participation in this study is voluntary. Your decision whether or not to participate in this study will not affect your current or future relations with the University of Minnesota or University of Minnesota Medical Center, Fairview. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Your participation in the study may also be stopped by the study doctors if health risk or protocol violation is determined. If you stop being part of the study, the study doctor will talk to you about any medical issues regarding the stopping of your participation, as well as follow-up care options.

**CONTACTS AND QUESTIONS**
You may ask any questions you have now, or if you have questions later, you are encouraged to contact the researchers at the following phone numbers: Dr. S. Charles Schulz at (612) 273-9820 or the study coordinator Ann Romine at (612) 627-4843.

If you have any questions or concerns regarding the study and would like to talk to someone other than the researcher(s), you are encouraged to contact the Fairview Research Helpline at telephone number 612-672-7692 or toll free at 866-508-6961. You may also contact this office in writing or in person at University of Minnesota Medical Center, Fairview Riverside Campus, 2200 Riverside Avenue, Minneapolis, MN 55454.

You will be given a copy of this form to keep for your records.

**STATEMENT OF CONSENT**
I have read the information above and my questions have been answered to my satisfaction. I understand I may withdraw from the study at any time without affecting any future relations with the University of Minnesota Medical Center, Fairview. I consent to participate in the study.

Participant's Name (Print): _____

_____
Signature of Participant Date

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Signature of Person Obtaining Consent Date