RESEARCH SUBJECT CONSENT FORM

Title:	Open-Label Study in Stable Schizophrenia Patients to Evaluate the Safety, Tolerability, and Pharmacokinetics of Switching from Oral Risperidone to Risperidone Implant (DLP-114)
Protocol No.:	DLP-114-03 IRB Protocol #20200594
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You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

Brief Overview of Subject Consent Form

You are being invited to take part in a research study. Taking part in this research is voluntary. Whether you take part is up to you, but if you do agree to participate in this study, you will sign this consent document.

The purpose of this research is to determine how well the placement and removal of the slow-release delivery system is tolerated, and determine the safety, tolerability, and pharmacokinetics (levels of study drug in your blood) when switching from oral risperidone to a slow-release risperidone system (DLP-114) in stable study participants with schizophrenia. DLP-114 is investigational, which means that it is not approved by the Food and Drug Administration (FDA).

We expect that your taking part in this research will last up to 236 days or up to 417 days, depending on which treatment group you are assigned to. If applicable, you may also be required to complete a conversion phase. This conversion phase may last a minimum of 2 weeks. During this time period, the Study Doctor may change your current oral antipsychotic treatment to an oral dose of risperidone to achieve an optimal dose of 3 mg per day.

The study medication will be provided via a slow-release delivery system which is placed just under the skin in one of the four quadrants of the abdomen. The system will be placed using sterile techniques and a local anesthetic, lidocaine, which numbs the placement area to ensure the participant comfort. A small, approximately 5 mm,

incision will be made just through the dermis (the second layer of skin). The system will be placed just under the skin using a placement tool. Following placement, the area will be cleaned using sterile technique and the incision will be closed using sutures and skin closure strips. The placement procedure should take approximately 20 minutes. You will be required to spend the night before the placement procedure and the following 3-6 nights at the research clinic.

The system will also be removed using sterile techniques and a local anesthetic, lidocaine, to numb the area and ensure participant comfort. The system will be located by palpation (examining by touch). After administration of lidocaine to numb the area to ensure participant comfort, the system will be immobilized and tented at one end and a small incision, approximately 5 mm, will be made in the dermis (the second layer of skin) and the system will be removed by the clinician. If there is any fibrous encapsulation of the system, a small incision may be made to allow for removal. Following removal of the system, the removal area will be cleaned using sterile technique and the incision will be closed using sutures and skin closure strips. The removal procedure should take approximately 10 minutes. You will be required to spend the night before the removal procedure and the night of the removal procedure at the research clinic.

In addition to signing this consent document and having the placement and removal procedures, the following assessments will be done at different visits throughout the study: collection of demographic information, and medical and medication history, measurement of height, weight, BMI and vital signs, physical examination, blood and urine collection safety tests, including hematology, chemistry, HIV, Hepatitis B, Hepatitis C, urinalysis and urine drug screen tests, collection of a blood sample or skin cells from inside your cheek to determine if you have certain genes, breath alcohol test, pregnancy test if you are a female, blood sample collection to measure study drug in your blood, electrocardiogram, rating scales to evaluate your schizophrenia symptoms and for safety, oral dosing with 3 mg risperidone with supervision and without supervision, you will be asked how you are feeling, inspection of your placement site, and ultrasounds to determine the location of the systems.

In addition to these assessments, if you are not already taking a stable dose of 2-3 mg of oral risperidone, you will be converted from your current antipsychotic to 3 mg of oral risperidone prior to the placement procedure.

There are possible side effects that you may experience during this study. You must tell the investigator or study staff about all side effects that you have. A list of known possible side effects is included further in the consent document, but some of the most common risks include sleepiness, weight gain, nausea, vomiting, diarrhea, constipation, Parkinsonism (tremor, slow movement, rigidity), dystonia (muscle contractions that cause slow, repetitive movements), anxiety, and dizziness.

Side effects of the placement procedure or the delivery system may include pain, infection, tingling, numbness, redness, scar, or itching or swelling in your abdomen at the placement site.

Other possible risks of the implant may include migration (movement of the implants), protrusion (the implant may stick out of the skin), expulsion (the implant may come out by itself), overdose of the ingredients in the implant (both risperidone and para-aminobenzoate [PABA]) should the device malfunction, or allergic reaction to PABA, including the risk of photosensitivity.

There is no guarantee that you will benefit from your participation in this study. Results from this study may benefit others in the future.

You do not have to be in this study to receive treatment for your schizophrenia. Your personal doctor can advise you regarding alternative therapies for your schizophrenia and their risks and benefits, including continuing with oral risperidone.

What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research is to determine how well the placement and removal of the slow-release delivery system is tolerated, and determine the safety, tolerability, and pharmacokinetics (levels of study drug in your blood) when switching from oral risperidone to a slow-release risperidone system (DLP-114) in stable study participants with schizophrenia. DLP-114 is investigational, which means that it is not approved by the Food and Drug Administration (FDA). The use of oral risperidone is also investigational.

About 24-30 subjects, between 18 to 70 years of age, will take part in this research across up to 3 study centers in the United States.

How long will I be in this research?

We expect that your taking part in this research will last up to 236 days or up to 417 days, depending on which treatment group you are assigned to. If applicable, you may also be required to complete a conversion phase. This conversion phase may last a

minimum of 2 weeks. During this time period, the Study Doctor may change your current oral antipsychotic treatment to an oral dose of risperidone to achieve an optimal dose of 3 mg per day. You will be compensated for your time and inconvenience related to your participation in this research study. Please see compensation details below on page 19.

What happens to me if I agree to take part in this research?

The study medication will be provided via a slow-release delivery system which is placed just under the skin in one of the four quadrants of the abdomen. The system will be placed using sterile technique s and a local anesthetic, lidocaine, which numbs the placement area to ensure the participant comfort. A small, approximately 5 mm, incision will be made just through the dermis (the second layer of skin). The system will be placed just under the skin using a placement tool. Following placement, the area will be cleaned using sterile technique and the incision will be closed using sutures and skin closure strips. The placement procedure should take approximately 10 minutes.

The system will also be removed using sterile techniques and a local anesthetic, lidocaine, to numb the area and ensure participant comfort. The system will be located by palpation (examining by touch). After administration of lidocaine to numb the area to ensure participant comfort, the system will be immobilized and tented at one end and a small incision, approximately 5 mm, will be made in the dermis (the second layer of skin) and the system will be removed by the clinician. If there is any fibrous encapsulation of the system, a small incision may be made to allow for removal. Following removal of the system, the removal area will be cleaned using sterile technique and the incision will be closed using sutures and skin closure strips. The removal procedure should take approximately 10 minutes.

The slow-release delivery system (DLP-114) consists of a hollow cylindrical titanium reservoir (1/8 in diameter and 2 inches in length) fitted on each end with a cap containing a thin micron membrane and filled with tablets of a powder form of the study drug, risperidone, plus excess of para-aminobenzoic acid (PABA). The study drug is released by passive diffusion of the drug through the micron membrane of the cylinder.

The evaluation of how much risperidone is absorbed by your body is done by analyzing the amount of risperidone that is present in the blood at various time intervals following administration of the oral risperidone or after placement of the study system (DLP-114).

Before any tests are performed, you will be asked to read and sign this consent document. The following tests will be performed to determine if you qualify to take part in this study:

<u>Screening Visit (Day -36 to -8)</u>
During this study visit, the following will be done:

- You will be asked to give your demographic information (name, age, race, etc.).
- You will be asked about your medical history and any medicines that you have

taken or are currently taking.

- Your vital signs will be taken (lying down and standing blood pressure and heart rate, breathing rate, and temperature).
- You will have a physical exam, including having your weight and height measured.
- You will have an electrocardiogram (electronic tracing of your heart).
- You will have rating scales given to you to evaluate your schizophrenia symptoms and for safety. Those scales are: Simpson Angus Scale (SAS), Barnes Akathisia Scale (BARS), Abnormal Involuntary Movement Scale (AIMS), Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression of Severity (CGI-S), and Columbia Suicide Severity Rating Scale (C-SSRS).
- You will have blood and urine samples collected for safety tests which include: hematology, chemistry, HIV, Hepatitis B, Hepatitis C, urinalysis and urine drug screen tests. The study doctor may be required by law to report the results of the HIV, Hepatitis B and Hepatitis C to the local health authority. If you have questions about this, please ask your study doctor.
- A blood sample or skin cells from inside your cheek will be collected to determine if you have certain genes. This is for research purposes only, and you will not be told the results of this test.
- You will have a breath alcohol test.
- If you are female that can have children, you will have a blood pregnancy test.
- You will be asked about how you are feeling.

If you qualify and wish to continue, you will be asked to administer oral risperidone at 3 mg/day for 3-6 days, unsupervised. The day after your last unsupervised dose, you will be asked to return to the clinical facility for your first outpatient visit on the morning of Day -4. You will be assigned to either Group 1 or 2. Group 1 will have the DLP-114 systems placed for 6 months and Group 2 will have the systems placed for 12 months. You have a 50% chance of being placed in each group. You cannot choose your study group.

Risperidone Conversion Phase

If you are eligible, you may be required to enter the conversion phase that lasts a minimum of 14 days (2 weeks) after Screening. During weekly visits in the conversion phase, patients who are stable on an antipsychotic other than oral risperidone (2-3 mg/day), will be tapered off their current antipsychotic and titrated, at the Study Doctor's discretion, to achieve an oral Risperidone dose of 3 mg/day. Following this conversion, patients will need to be stable on oral risperidone 2-3 mg/day for at least 2 weeks prior to being implanted.

Oral risperidone 1 mg to 3 mg/day will be self-administered either unsupervised or under the supervision of the Study Doctor or other trained designee. Compliance with oral study medication will be monitored by the study staff by counting the risperidone tablets during the applicable study visits.

Day -7 to Day -5 (unsupervised oral dosing)

If you are eligible for the study, you will begin unsupervised dosing with oral risperidone 3 mg/day, provided, starting on Day -7, or as early as Day -10, through Day -5.

Day -4 (outpatient visit)

When you arrive at the clinical facility on Day -4, the study doctor or someone they assign, will meet with you to explain all study procedures and encourage you to ask any questions. You will also be asked questions to make sure you understand the protocol requirements and safety monitoring.

The following assessments will be performed on each patient:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken previously.
- If you are female that can have children, you will have a urine pregnancy test.
- Your height and weight will be measured.
- Your vital signs will be taken while lying down prior to dosing with oral (by mouth) risperidone (blood pressure and heart rate, breathing rate, and temperature).
- Someone on the study staff will watch as you take a 3 mg dose of risperidone by mouth.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.

Day -3 and Day -2 (outpatient visits)

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Someone on the study staff will watch as you take a 3 mg dose of risperidone by mouth.
- Your vital signs will be taken while lying down prior to dosing with oral (by mouth) risperidone (blood pressure and heart rate, breathing rate, and temperature).

Day -1 (overnight in the clinical facility)

You will be admitted to the clinical facility on Day -1 and will stay until Day 7. If you have any significant safety issues during this study period, you may be required to remain in the clinical facility for further observation.

The following assessments/procedures will be performed on Day -1:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your vital signs will be taken while lying down prior to dosing with oral (by mouth) risperidone (blood pressure and heart rate, breathing rate, and temperature).
- You will have a sample of blood taken to measure study drug in your blood within 10 minutes prior to dosing with oral (by mouth) risperidone.
- Someone on the study staff will watch as you take a 3 mg dose of risperidone by mouth.

- You will have an electrocardiogram (electronic tracing of your heart).
- You will have a sample of blood taken to measure study drug in your blood at 0.5, 1, 2, 3, 4, 6, 8, 12 and 24 hours after dosing with oral (by mouth) risperidone.
- You will have blood and urine samples collected for safety tests which include: hematology, chemistry, urinalysis and urine drug screen tests.
- You will have a breath alcohol test.
- If you are female that can have children, you will have a urine pregnancy test.
- You will have rating scales given to you to evaluate your schizophrenia symptoms and for safety. Those scales are: Simpson Angus Scale (SAS), Barnes Akathisia Scale (BARS), Abnormal Involuntary Movement Scale (AIMS), Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression of Severity (CGI-S), and Columbia Suicide Severity Rating Scale (C-SSRS).

<u>Day 1 (DLP-114 placement day, overnight in the clinical facility)</u>
The following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Your vital signs will be taken prior to dosing with oral (by mouth) risperidone (lying down and standing blood pressure and heart rate, breathing rate, and temperature).
- Someone on the study staff will watch as you take a 3 mg dose of risperidone by mouth.
- Approximately 1 hour before DLP-114 placement, you will have a sample of blood taken to measure study drug in your blood.
- A physician will administer a numbing solution under the skin in your abdomen to ensure you are comfortable. He or she will then make a small incision, just through the skin and place 2 slow-release systems containing risperidone. The incision will be closed with a few stitches and a member of the study staff will assess your placement site.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature) every hour for the first 8 hours after the systems are placed. Your blood pressure and heart rate will also be measured while standing 4 hours after the systems are placed.
- You will have an electrocardiogram (electronic tracing of your heart) 4 hours after the systems are placed.
- You will have a sample of blood taken to measure study drug in your blood at 1, 2, 3, 4, 6, 8 and 12 hours after the systems are placed.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.

<u>Day 2 (overnight in the clinical facility)</u>
The following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.

- Approximately 24 hours after the systems are placed, the following will be done:
  - Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
  - A member of the study staff will assess your abdomen and the placement site.
  - You will have an electrocardiogram (electronic tracing of your heart).
  - Someone on the study staff will watch as you take a 3 mg dose of risperidone by mouth. This will be the last dose of risperidone that you will take orally.
- You will have a sample of blood taken to measure study drug in your blood at 24, 28, 32 and 36 hours after your systems are placed.

Day 3 (overnight in the clinical facility)

The following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Your vital signs will be taken approximately 48 hours after your systems are placed (lying down and standing blood pressure and heart rate, breathing rate, and temperature).
- A member of the study staff will assess your abdomen and the placement site.
- You will have a sample of blood taken to measure study drug in your blood at 48 and 52 hours after your systems are placed.

Day 4 (overnight in the clinical facility)

The following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Your vital signs will be taken (lying down and standing blood pressure and heart rate, breathing rate, and temperature).
- A member of the study staff will assess your abdomen and the placement site.
- You will have a sample of blood taken to measure study drug in your blood.

You may be discharged as early as Day 4 upon consultation with the study's medical monitor. If you are discharged prior to Day 7, the assessments listed below under "Day 7 (discharge from clinical facility)" will be performed on the day of discharge, and the assessments listed in "Day 14 to End of Study" will be performed on Day 7.

Day **7 (discharge from clinical facility)**

The following assessments/procedures will be performed:

- Your body weight will be measured.
- You will be asked about how you are feeling and any medicines you are currently assess for safety.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).

- You will have blood and urine samples collected for safety tests which include: hematology, chemistry, and urinalysis.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the placement site.
- You will have an electrocardiogram (electronic tracing of your heart).
- You will have a sample of blood taken to measure study drug in your blood.

You will be issued a study card indicating the name of the investigational product, the study number, the investigator's name, a 24-hour emergency contact number, and, if applicable, excluded concomitant medications. You will also be offered a safety alert bracelet bearing the same information, if desired, instead of or in addition to the study card.

Days 14 to End of Study – Group 1
Days 14, 21, 28, 42, 56, 70, 84, 98, 112, 126, 140, 154, and 168 (outpatient visits)
The following assessments/procedures will be performed at every outpatient visit:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- Your body weight will be measured.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the placement site.
- You will have a sample of blood taken to measure study drug in your blood.

The following assessments/procedures will be performed on the following outpatient visits (assessments may be performed more frequently based on symptoms at the study doctor's discretion):

- You will have a urine sample collected for a urine drug screen on Day 84.
- You will have blood and urine samples collected for safety tests which include: hematology, chemistry and urinalysis tests on Days 28, 84, and 140.
- If you are female that can have children, you will have a urine pregnancy test at Days 28, 56, 84, 112, and 140.
- You will have an electrocardiogram (electronic tracing of your heart) at Days 28, 84, and 140.
- You will have the CGI-I rating scale given to you to evaluate your schizophrenia symptoms on Days 14, 28, 56, 84, 112, 140 and 168.
- You will have the PANSS rating scale given to you to evaluate your schizophrenia symptoms on Day 84.
- You will have the following rating scales given to you to evaluate your schizophrenia symptoms and for safety on Day 168: SAS, BARS and AIMS.
- You will have an ultrasound on Day 14 to determine the location of the systems.

Day 183 (± 7 days) (overnight in the clinical facility)
The following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your body weight will be measured.
- You will have a urine sample collected for a urine drug screen.
- If you are female that can have children, you will have a urine pregnancy test.
- You will have an electrocardiogram (electronic tracing of your heart).
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- You will have the following rating scales given to you to evaluate your schizophrenia symptoms and for safety: CGI-I, PANSS, and C-SSRS.
- A member of the study staff will assess your abdomen and the placement site.
- You will have an ultrasound to determine the location of the systems.
- A physician will administer a numbing solution at the removal site to ensure your comfort. He or she will then make a small incision and remove the DLP-114 systems. The incision will be closed with a few stitches.
- You will have a sample of blood taken to measure study drug in your blood at 1, 2, 3, 4, 6, 8 and 12 hours following removal of the DLP-114 systems.
- You will have blood and urine samples collected 4 hours after removal of the systems for safety tests which include: hematology, chemistry and urinalysis tests.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature) every hour for the first 4 hours after the systems are removed.
- You will have an electrocardiogram (electronic tracing of your heart) 4 hours after the systems are removed.

Day 184 (overnight in the clinical facility)
On Day 184 (or 1 day after system removal) the following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Approximately 24 hours following removal of the DLP-114 systems:
    - Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
    - A member of the study staff will assess your abdomen and the removal site.
    - You will have a sample of blood taken to measure study drug in your blood.

Day 185 (discharge from the clinical facility)

On Day 185 (or 2-days after system removal) the following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Approximately 48 hours following removal of the DLP-114 systems:
  - Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
  - A member of the study staff will assess your abdomen and the removal site.
  - You will have a sample of blood taken to measure study drug in your blood.
- You will have a physical exam.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- You will resume taking your original oral (by mouth) risperidone dose of 2-3 mg.
- You will be discharged from the clinical facility.

Day 186 (outpatient visit)

On Day 186 (or 3 days after system removal) the following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the removal site.
- You will have a sample of blood taken to measure study drug in your blood.

Day 190 (End of Study, outpatient visit)

On Day 190 (or 7 days after system removal) the following assessments/procedures will be performed as the End of Study Visit:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your body weight will be measured.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the removal site.
- If you are female that can have children, you will have a urine pregnancy test.

Days 14 to End of Study – Group 2

Days 14, 21, 28, 42, 56, 70, 84, 98, 112, 126, 140, 154, 168, 182, 196, 210, 224, 238, 252, 266, 280, 294, 308, 322, 336, and 350 (outpatient visits)

The following assessments/procedures will be performed at every outpatient visit:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- Your body weight will be measured.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the removal site.
- You will have a sample of blood taken to measure study drug in your blood.

The following assessments/procedures will be performed on the following outpatient visits (assessments may be performed more frequently based on symptoms at the study doctor's discretion):

- You will have a urine sample collected for a urine drug screen on Days 84, 182 and 266.
- You will have blood and urine samples collected for safety tests which include: hematology, chemistry and urinalysis tests on Days 7, 28, 84, 140, 182, 238, 280 and 322.
- If you are female that can have children, you will have a urine pregnancy test at Days 28, 56, 84, 112, 140, 182, 210, 238, 280, 308 and 336.
- You will have an electrocardiogram (electronic tracing of your heart) at Days 28, 84, 140, 182, 238, 280 and 322.
- You will have the CGI-I rating scale given to you to evaluate your schizophrenia symptoms on Days 28, 56, 84, 112, 140, 168, 182, 210, 238, 266, 280, 308, 336 and 350.
- You will have the PANSS rating scale given to you to evaluate your schizophrenia symptoms on Days 84, 182 and 280.
- You will have the following rating scales given to you to evaluate your schizophrenia symptoms and for safety on Days 210, 238, 266, 336 and 350: SAS, BARS and AIMS.
- You will have an ultrasound on Day 14 to determine the location of the systems.

Day 364 (± 7 days) (overnight in the clinical facility)

The following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your body weight will be measured.
- You will have a urine sample collected for a urine drug screen.
- If you are female that can have children, you will have a urine pregnancy test.
- You will have an electrocardiogram (electronic tracing of your heart).

- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- You will have the following rating scales given to you to evaluate your schizophrenia symptoms and for safety: CGI-I, PANSS, and C-SSRS.
- A member of the study staff will assess your abdomen and the removal site.
- You will have an ultrasound to determine the location of the systems.
- A physician will inject a numbing solution at the removal site to ensure your comfort. He or she will then make a small incision and remove the DLP-114 systems. The incision will be closed with a few stitches.
- You will have a sample of blood taken to measure study drug in your blood at 1, 2, 3, 4, 6, 8 and 12 hours following removal of the DLP-114 systems.
- You will have blood and urine samples collected 4 hours after the systems are removed for safety tests which include: hematology, chemistry and urinalysis tests.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature) every hour for the first 4 hours after the systems are removed.
- You will have an electrocardiogram (electronic tracing of your heart) 4 hours after the systems are removed.

Day 365 (<u>overnight in the clinical facility</u>)
On Day 365 (or 1-day after system removal) the following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Approximately 24 hours following removal of the DLP-114 systems:
    - Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- A member of the study staff will assess your abdomen and the removal site.
    - You will have a sample of blood taken to measure study drug in your blood.

<u>Day 366 (discharge from the clinical facility)</u>
On Day 366 (or 2-days after system removal) the following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking.
- Approximately 48 hours following removal of the DLP-114 systems:
    - Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
    - A member of the study staff will assess your abdomen and the removal site.
    - You will have a sample of blood taken to measure study drug in your blood.

- You will have a physical exam.
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- You will resume taking your original oral (by mouth) risperidone dose of 2-3 mg.
- You will be discharged from the clinical facility

Day 367 (outpatient visit)
On Day 367 (or 3 days after system removal) the following assessments/procedures will be performed:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the removal site.
- You will have a sample of blood taken to measure study drug in your blood.

Day 371 (End of Study, outpatient visit)
On Day 371 (or 7 days after system removal) the following assessments/procedures will be performed as the End of Study Visit:

- You will be asked about how you are feeling and any medicines you are currently taking or have taken since your last visit.
- Your body weight will be measured.
- Your vital signs will be taken while lying down (blood pressure and heart rate, breathing rate, and temperature).
- You will be given the Columbia Suicide Severity Rating Scale (C-SSRS) to assess for safety.
- A member of the study staff will assess your abdomen and the removal site.
- If you are female that can have children, you will have a urine pregnancy test

Blood samples for safety labs and to measure the study drug in your blood will be collected at the times noted above. An approximate total of no more than 250 mL (about 1 cup) of blood will be collected in Group 1 patients and 500 mL (about 2 cups) in Group 2 patients throughout the study.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be expected to:

- Tell the truth about your medical history, prescription and over-the-counter drugs you are taking, current medical conditions and symptoms, and answers to the rating scale questions.
- Follow the instructions of the study staff regarding what medications you should not take while in this study.
- Allow additional breath alcohol or urine drug testing as the study doctor determines necessary.

- Allow additional urine pregnancy testing if you are a female that can have children, if the study doctor determines it is necessary.
- Return to the clinical facility for all scheduled visits and remain at the clinical facility overnight on the days noted above.
- Tell the study doctor if you have received electroconvulsive therapy within the last 6 months or experienced depressive symptoms within the past 30 days that required treatment with an antidepressant.
- Tell the study doctor about any problems you have during the study.
- Report any side effects.
- If you decide not to return for study visits, your study doctor will continue to make efforts to reach you. The study doctor may share information about you, such as your name, address, and telephone number with other parties to help locate you so that the DLP-114 systems can be removed and to ensure that the experimental treatment is safe for you.
- At any point in the study, if there is scarring, abnormal bleeding, infection, etc., with DLP-114 system location, non-identifying pictures of the DLP-114 system location may be taken by the site staff.
- If you are a female, use appropriate contraceptive methods from screening until the end of the study. If you are a male, use appropriate contraceptive methods and do not donate sperm following dosing with study drug until the end of the study. Appropriate contraception is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm or cervical cap, or a condom. Total abstinence is also acceptable.
- Refrain from strenuous exercise and from participation in any contact sport activities for 7 days following the placement of the DLP-114 systems.
- Avoid caffeine or alcohol during the times when you stay at the clinical facility.

Could being in this research hurt me?

Side effects of risperidone may include:

- Back pain
- Abnormal decrease in blood pressure upon standing
- Difficulty sleeping
- Sleepiness
- Increased appetite
- Weight gain
- Feeling tired
- Rhinitis (swelling of the membranes in the nose)
- Upper respiratory tract infection
- Vomiting
- Saliva increased
- Constipation
- Parkinsonism (tremor, slow movement, rigidity)

- Dystonia (muscle contractions that cause slow, repetitive movements)
- Abdominal pain
- Anxiety
- Nausea
- Dizziness
- Dry mouth
- Tremor
- Rash
- Akathisia (agitation, distress, and restlessness)
- Indigestion
- Blurred vision
- Diarrhea
- Throat pain
- Laboratory abnormalities

There have been reports of hyperglycemia (high blood sugar) in patients taking atypical antipsychotics including risperidone. While it is not known if the DLP-114 system is associated with an increased risk of high blood sugar, subjects should understand that there is a potential increased risk of high blood sugar with the use of risperidone until more information on the medication becomes available.

Studies with risperidone and other drugs of this type have shown a risk of death in elderly patients with dementia and behavioral disturbances.

Neuroleptic Malignant Syndrome (NMS) is a serious, potentially life-threatening disorder that includes symptoms such as fever, tight muscles, changes in blood pressure and heart rate, as well as changes in thinking and understanding. If the study doctor suspects you are developing NMS, you will be evaluated and treated immediately by the appropriate consulting physicians. If you appear to be developing NMS, your participation in the study will be stopped.

Tardive dyskinesia is a syndrome of potentially irreversible, abnormal, involuntary movements of the tongue, jaw, body, arms and legs. There is no known treatment for tardive dyskinesia, although the symptoms may lessen or disappear completely if the antipsychotic medication is stopped.

Side effects of the DLP-114 placement procedure and any anesthesia used may include:

- pain, tingling, numbness, redness, scar, itching or swelling in your abdomen at the placement site.

Rare side effects of the DLP-114 system itself may include:

- system expulsion (systems may come out of your body on their own) and system migration (systems may move slightly from where they are initially placed)

Please notify the study doctor if you think the system (s) have come out.

Risperidone may interact with other medications. Follow the instructions you are given by the study staff regarding which medications you should not take during this study. Please seek treatment immediately and tell the study doctor and study staff if you have any side effects during the study whether or not you think they are caused by the study drug. If the study doctor suspects that there are issues with the DLP 114 systems once placed, you could have an ultrasound to locate the DLP-114 systems and they may be removed.

Other less common side effects have been reported. The study doctor or staff can discuss these with you.

The risperidone system is investigational, and the dose delivered may not be equivalent to the oral risperidone you have been currently taking. Currently your schizophrenia is stable, however you may be at risk of developing schizophrenia symptoms.

Risks of Study Procedures

- Blood samples will be collected during this study. To draw blood, a needle is inserted into a vein in the arm and a blood sample is withdrawn. Although one blood draw is usually sufficient, a second one may be necessary if the first is not successful. Whenever you have blood samples collected, there will be a small risk of discomfort, fainting, bleeding, pain and/or bruising, as well as swelling at the site where the blood was taken. It is rare, but an infection may occur at the site of the needle stick. A plastic catheter (cannula) may be inserted into a larger vein to collect multiple blood samples. Common effects could be pain, swelling and redness at the vein site. This is usually a temporary condition which resolves when treated with warm moist packs.
- Electrocardiogram (ECG): Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.

Ultrasound: For standard diagnostic ultrasounds there are no known harmful effects on humans. Ultrasound will be used by the study doctor to help find the exact location of the DLP-114 systems.

Unforeseen Risks
Since the use of the study drug is investigational when taken alone or in combination with other medications, there may be other risks that are unknown. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening.

Pregnancy/Birth Control
Taking the study drug may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant or are breastfeeding a child, you cannot participate in this study.

If you are a female that can have children and are sexually active, you must use an effective method of birth control while you are participating in this study in order to reduce the risk of pregnancy. If you are already using a method of birth control, the study doctor or study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

If, during this study, you become pregnant, you should notify the study doctor as soon as possible. The study drug will be stopped, your DLP-114 systems will be removed and your participation in this study will be ended. Information about your pregnancy and its outcome and the infant's medical records for up to 30 days after delivery, if applicable, will be collected with your permission and used to learn more about the effects of the study drug on pregnancy.

Males
Exposure to the study drug may involve unknown risks to a pregnant woman, an embryo, or a fetus (unborn baby). If you are having sexual intercourse with a woman who can become pregnant, you and your partner must use an acceptable form of birth control while you are participating in this study.

If you agree to participate in this study, you are expected to inform your female sexual partner(s) that you are participating in a research study of an investigational drug, and that the effects of the drug on an unborn baby and on a pregnant woman are unknown. You are also expected to provide your female sexual partner(s) with the information in the Pregnancy/Birth Control section of this Informed Consent and to provide her with contact information for the study doctor for any additional questions.

If your female partner becomes pregnant while you are participating in this study, tell your study doctor or study nurse promptly. At that time the study doctor may seek the pregnant woman's permission to review her medical records and the infant's medical records for up to 30 days after delivery, if applicable. The study doctor will share the information about your pregnant partner and the baby with the study sponsor to help understand the effects, if any, that the study drug may have on the pregnancy and the child.

Payment for all aspects of obstetrical care, or child-related care will be your responsibility.

In addition to these risks, taking part in this research may harm you in unknown ways.

Will it cost me money to take part in this research?

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

Will being in this research benefit me?

There is no guarantee that you will benefit from your participation in this study. Results from this study may benefit others in the future.

What other choices do I have besides taking part in this research?

You do not have to be in this study to receive treatment for your schizophrenia. Your personal doctor can advise you regarding alternative therapies for your schizophrenia and their risks and benefits, including continuing with oral risperidone.

What happens to the information collected for this research?

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor
- Government agencies, such as the Food and Drug Administration
- The Institutional Review Board (IRB) that reviewed this research
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

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.

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by an Institutional Review Board (“IRB”). An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or researchquestions@wcgirb.com if:

You have questions, concerns, or complaints that are not being answered by the research team.

You are not getting answers from the research team.

You cannot reach the research team.
You want to talk to someone else about the research.
You have questions about your rights as a research subject.

What if I am injured because of taking part in this research?

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. There are no plans to provide other compensation beyond that which is listed in this informed consent document. You will not lose any of your legal rights, or release the Sponsor, the study doctor, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

If you are injured during this study, your study doctor will discuss with you the available medical treatment options.

Can I be removed from this research without my approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled by the FDA or the sponsor; or
- For administrative reasons, including the target number of subjects has entered the study.

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

What happens if I agree to be in this research, but I change my mind later?

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

If you decide to leave this research, contact the research team so that the study doctor can ensure the systems are removed and safety assessments are completed.

What happens if I do not return to the clinic for a scheduled visit after I have received the system?

If you fail to return for a scheduled visit a reasonable effort will be made to contact you to determine a reason for the failure to return and encourage you to return for removal of the systems. If unsuccessful in contacting you, the Investigator or their staff will

contact your caregiver/emergency contact. Once contact is established, the Investigator will assess your ability to continue in the study. If you do not contact the site, the sponsor will request for a third party to locate you to have the systems removed. If we cannot locate you using the plan outlined above the research site will request that all listed contacts continue to monitor for you and request that they call the emergency numbers if contact is made with you. The research site will also continue to monitor their psychiatric network in efforts to locate you.

Will I be paid for taking part in this research?

For your time and inconvenience related to your participation in this research study, you will be paid $100 for each outpatient visit you complete, $100 for each conversion phase visit you complete and $150 for each inpatient night you complete. If you are assigned to Group 1, you will receive an additional $300 payment on Day 1 for the placement visit and Day 183 for the system removal visit. After completion of Day 190 you will receive $350. If you are assigned to Group 2, you will receive an additional $300 payment on Day 1 for the placement visit and Day 364 for the system removal visit After the completion of Day 371 you will receive $350. If you are assigned to either group, you will receive an additional $200 at Day 42 and Day 84, and if you are in Group 2, you will also receive an additional $200 at Day 140.

You will be compensated for completed visits at least quarterly with final payment within 30 days of the end of your participation from the study. If you do not complete the study for any reason, you will be paid for the study visits you do complete.

If your test results say that there you are taking drugs that are not allowed during the screening process and throughout study participation or you are discovered participating in any other study during a visit, the visit is considered incomplete and you will not be paid for that visit and will be terminated from the study as this is prohibited.

If you have any questions regarding your compensation for participation, please contact the study doctor at the telephone number listed on page one of this consent document.

Statement of Consent:

Your signature documents your consent to take part in this research.

Signature of adult subject capable of consent	Date
Signature of person obtaining consent	Date

CALIFORNIA HIPAA AUTHORIZATION

Federal regulations give you certain rights related to your health information. These include the right to know who will receive the information and how it will be used. The study doctor must obtain your authorization (permission) to use or release any health information that might identify you.

What information may be used and shared?

The study doctor and study staff will use and share your health information as part of this research study. Except when required by law, you will not be identified by name, address, telephone number or other facts that could identify the health information as yours.

Examples of the information that may be used are:
Medical records (from any doctor, hospital or other healthcare provider)

Information created or collected during the research. This could include your medical history, and dates or results from any physical exams, laboratory tests or other tests.

Who will receive information about you?

The study doctor and study staff will share your personal health information with:

- the sponsor, including persons or companies working for or with the sponsor
- the Independent Review Board
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- other regulatory agencies

Why will this information be used and/or given to others?

The sponsor and the groups above will use your health information:

- to complete this research
- to evaluate the results of the study
- to check that the study is being done properly
- to obtain marketing approval for new products resulting from this research

Is my health information protected after it has been given to others?

Your health information may be further shared by the groups above. If shared by them, the information will no longer be covered by this Authorization. These groups are committed to keeping your health information confidential.

What if I decide not to allow the use of my health information?

You do not have to sign this form. If you do not sign this form, you cannot take part in this research study.

May I withdraw or revoke (cancel) my permission?

YES. You may withdraw your permission to use and disclose your health information at any time. You can do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in the research study.

What happens if I want to withdraw my authorization?

Information that has already been gathered may still be used and given to others. If you withdraw your permission, no new health information will be gathered unless you have a side effect related to the study.

If you withdraw from the study but do not withdraw your Authorization, new health information may be collected until this study ends.

Will my authorization expire?

This Authorization will expire December 31, 2060, unless you withdraw it in writing before then.

May I review or copy the information obtained or created about me?

YES. You have the right to review and copy your health information. However, your access to this information may be delayed until the study is complete.

Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

AUTHORIZATION
By signing this form, I allow the use or disclosure of my health information. I will receive a signed and dated copy of this Authorization.

_____
Printed Name of Subject

_____ _____
Signature of Subject **Date**