COVER PAGE

Subject Information Sheet (SIS) and Informed Consent Form (ICF)

TITLE: Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Intramuscular Injections of Risperidone ISM® in Patients with Acute Exacerbation of Schizophrenia (PRISMA-3)

PROTOCOL NUMBER: ROV-RISP-2016-01

NCT NUMBER: NCT03160521

ICF VERSION 4.0

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SUBJECT INFORMATION SHEET AND INFORMED CONSENT FORM

Title: Multicenter, Randomized, Double-Blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Intramuscular Injections of Risperidone ISM® in Patients with Acute Exacerbation of Schizophrenia (PRISMA-3)

Protocol number: ROV-RISP-2016-01
EudraCT number: (applicable to EU countries only)

Sponsor name: Laboratorios Farmacéuticos ROVI, S.A.

Address of Sponsor: C/ Julián Camarillo, 35. 28037 Madrid, Spain

Principal Investigator: Insert Name, affiliation, location

Telephone number
Daytime:
After Office Hours:

Participant's name: _____

Introduction and Purpose of the Study

You are being asked to volunteer to take part in a research study of a drug called **risperidone.** Risperidone is a medication which is commercially available for many years, but new pharmaceutical form of this product Risperidone ISM® (long-acting injectable intramuscular formulation) has been developed and must be clinically tested. *Before you decide we would like you to understand why the research is being done and what it would involve for you.* ***You can take as much time as you need to read and understand the information provided in this form and to ask questions. One of the research team members will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish.***

This study is a multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety Risperidone ISM®, a new long-acting injectable form of the licensed drug risperidone. The study design includes a screening period, a 12-week treatment period, and a follow-up period or an optional long-term extension segment of the study of 1 year. Eligible subjects will be randomly assigned, under double-blind conditions, to receive Risperidone ISM® (either 75 or 100 mg) or placebo. It means that you have one third chance to participate in any of these 3 study arms. **This informed consent is applicable to the screening and a double-blind 12-week treatment period only**.

"Multicenter" means that it will be conducted in numbers of hospitals /doctors' offices (study sites). "Randomized" means that the study drug assignment will be done by chance (like tossing a coin) assigned by a computer. "Double-blind" means that neither you nor your study doctor will know what treatment you will be receiving. "Placebo-controlled" means that some of the subjects in the study will receive a dummy drug (placebo) which contains no active substance in it, but looks exactly the same as the experimental drug. Placebo and the experimental drug are referred to as "study drugs".

Your doctor will adjust your medication during the screening period and some drugs will be washed out. If you have never taken risperidone you must have a short-term use of oral risperidone (2 mg/day for 3 days during the screening period) in order to ensure a lack of any sign of hypersensitivity reactions before the first dose of the study drug is administered.

You will be admitted to the study site's inpatient unit sometime during the screening period (from 1 to 8 days before study day 1 which will be the first day of the first dose of study medication). It is generally anticipated that you may remain on the inpatient unit for at least 7 days after the first dose of study drug is administered, though inpatient duration will be flexible.

The study drug (Risperidone ISM® or placebo) will be administered as intramuscular (IM) injection either in the gluteal or deltoid muscle a total of 3 times, once every 4 weeks, during the 12-week treatment period (at study days 1, 29, and 57).

After the completion of planned double-blind study drug treatments and study evaluations you may be eligible to participate in an optional long-term extension segment of the study in which treatment with open-label Risperidone ISM® 75 or 100 mg would begin immediately. "Open-label" means that both you and your doctor will know if you receive 75 or 100 mg of study drug. If you don't participate in the extension segment, a safety follow-up phone contact will occur approximately 2 weeks after the end-of-treatment visit. After your participation in the study is finished, your doctor will continue your treatment as per routine medical practice.

This study will be done at approximately 48 sites in Europe and USA and will involve more than 400 subjects.

No study procedures related to this study will be performed until you have signed the Subject Information Sheet and the Informed Consent Form. An original or copy of the signed Subject Information Sheet and the Informed Consent Form will be given to you to keep.

The study has received favourable/ positive opinion by the Ethics Committee [insert name as applicable] on [insert date] and an authorization from the applicable competent authorities (insert name as applicable) on [insert date] according to the legislation in force.

Study Plan

The study design includes a screening period (planned duration 1 to 8 days) immediately preceding the administration of the study drug, a treatment period (duration 12 weeks), and a follow-up period (duration 2 weeks); not applicable for subjects who enter into a long-term extension segment of the study.

The screening period should be as brief as is clinically feasible (eg, target of 3 days preferred) but may last up to 8 days (in order to safely washout any prohibited medications) with an extension up to 14 days maximum. It is generally anticipated that you may remain on the inpatient unit for at least 7 days after the first IM dose of long-acting study drug is administered. However, inpatient duration may vary for individual persons, and potentially may be longer.

Study drug will be administered as IM injections. After initial dosing on study day 1, study drug will be administered once every 4 weeks during the 12-week treatment period (at study days 29 and 57).
Your visits to study center after you are discharged from in-patient unit may take several hours.

As mentioned, if you complete planned participation in this study through to the end of the treatment period you may be eligible to enter into an optional long-term extension segment of the study, during which open-label Risperidone ISM® (ie, either 75 or 100 mg) will be administered as IM injection once every 4 weeks for approximately 1 year, immediately upon completion of the end-of-treatment visit assessments and procedures. If you are eligible and decide to participate in the long-term extension segment, you should sign a separate Subject Information Sheet and the Informed Consent Form. If you do not enter into the extension segment you will have a final safety follow-up phone contact approximately 2 weeks after the end-of-treatment visit.

Eligibility

To be eligible for participation in the study, at screening you must meet all of the inclusion criteria and none of the exclusion criteria.

You may be withdrawn from the study at any time if you, investigator, or sponsor determines that it is not in your best interest to continue. Reasons for withdrawal may include, but are not limited to noncompliance, safety, development of a medical condition that requires treatment with a prohibited medication, a positive result on a pregnancy or urine drug screen test, or your withdrawal of consent without penalty or loss of benefits to which you are otherwise entitled. In addition, if your condition changes during the course of the study so that you no longer satisfy the inclusion and exclusion criteria, you may be withdrawn.

Study Procedures

Study Visit 1: Screening Visit (*Study Day -8 to -1)*

During the screening visit (period) the following tests and procedures will be done to determine if you qualify to take part in this study:

- Demographic data
- Medical and psychiatric history data
- A set of standard questions/scales/questionnaires that will assess your physical sensations and symptoms, your quality of life and how it is affected by your schizophrenia, as well as assessment scales to assess your movements (the way you move and whether you have movements you cannot control)
- Physical examination
- Ophthalmological examination - examination of the front part of your eyes, best correction visual field, visual acuity and intraocular pressure
- Height, weight and body mass index
- Vital signs (blood pressure, pulse rate, respiratory rate and body temperature)
- ECG (electrocardiogram, which records heart function)
- Review of your medications (including vitamins and herbal supplements)
- Blood samples (about 2 tea spoons, approximately 10 ml) for laboratory testing which will show the function of your blood and vital organs (eg liver, kidney)
- Blood sample (about 1/2 tea spoon approximately 2.5 ml) will be taken from you for a pregnancy test if you are female able to have kids
- Urine samples for laboratory testing and drug screening

You will receive a test treatment with oral risperidone (2 mg, 3 days) if you have never received risperidone before to show how well your body can tolerate it.

Blood testing (to the applicable visits)

Your samples will be coded before being shipped to a central laboratory and will be stored there awaiting analysis. The central laboratory is experienced in handling and testing samples from research studies. All samples will be destroyed once all tests are complete.

The samples will only be used for study related purposes, and no other analyses than study related analyses will be performed without you and the ethics committee's approval.

Hepatitis and HIV testing

Positive results for hepatitis B and C infection and/or HIV infection may be required to be reported to health authorities according to law. If hepatitis or HIV test is positive, you cannot take part in the study.

If you qualify for the study, you will be told about the study restrictions and when you to come to the clinic for study visits.

Study visits 2, 3, 4, and 5: In-patient Clinic Stay (Days 1-8)

If you agree to participate in the study, you will be hospitalized for up to 8 days before the study drug is administered. You must stay at least 2 days in the hospital after the injection, but it is anticipated that you will remain hospitalized up to 7 days after the injection, even longer if clinically indicated.

The reason for hospitalization is that the use of some medication you are currently taking may be stopped, and therefore closer medical follow up may be required. Additionally, during these visits in-patient stay you will be monitored for adverse events, and it will be easier to do a group of questionnaires and laboratory tests. Your stay in the hospital after the first dose of the study medication is needed so that medical staff can observe how you initially react to the treatment, to record any adverse event and to check the injection site. The in-patient period will provide you constant medical care which can be beneficial for you.

During the in-patient clinic stay ECGs and vital signs assessments will be done at all study visits. You will be also asked if there have been any changes in your health or medication you are taking. Body weight will be checked at day 1 and day 8). At days 1, 4, and 8 of your hospitalization the study staff will administer questionnaires and assessment scales similar to the screening visit, to make sure it is safe for you to continue in the study.

Additionally they will perform laboratory tests (including blood and urine tests), at day 1 and 8.

Urine sample will be collected at visit 2 (Day 1) for dipstick urine drug screen testing and the sample will also be sent to the central laboratory for analysis. Your doctor may ask for this test to be done again any later visit.

At visit 2 (Day 1) you will be administered a dose of Risperidone ISM® or placebo by intramuscular injection, with examination of the injection site appearance and sensitivity on the same day.

During the Day 1 and Day 3 visits, you will have also some additional tests done:

- Blood sample (about 1 tea spoon, approximately 5 ml) for pharmacokinetic (PK) testing to show the levels of the study drug in your body.

  Pharmacokinetic Sample Collection

"Pharmacokinetic" testing is a procedure which is done to see what your body does to the drug and to show the levels of the drug in your blood. A blood sample (about 5 mL) for pharmacokinetic testing will be taken at Day 1, Day 3, Day 29, Day 31, Day 57, Day 59, and Day 85. The pharmacokinetic samples will be obtained before administration of study drug if the study drug administration and pharmacokinetic sampling occur on the same day. Additional sample may be required in a case of a serious adverse event.

Please note that a group of approximately 75 subjects will have additional sampling on days 8, 15 and 22. If you are in this group of patients, you will be asked to sign consent form additionally if you agree to participate. It also means that you need to visit the study site on day 22 for blood sampling. Patients who are not a part of this group will not come to additional visit 7 on day 22.

- Blood sample (approximately 5 ml, about 1 tea spoon) for genotyping testing may be taken at Day 1 or at any time point after randomization. If you decide to participate in this additional research study, you should sign a separate Subject Information Sheet and the Informed Consent Form.

  Genotyping

  DNA (deoxyribonucleic acid) is a molecule that carries most of the genetic instructions and makes your genes unique. DNA determines a lot about you, including your physical appearance and how likely you are to get certain diseases, and why your body might process drugs differently than other people. The researchers will look at your DNA in order to determine how your body breaks down drugs and/or the genes that are potentially related to the response or adverse events a drug may have. You will be provided with a separate detailed written information regarding genotyping so that you can decide if you are willing to participate in this testing.

Study Visit 6
Treatment Week 2 (Treatment Day 15)

At visit 6 the study staff will perform physical examination, laboratory tests and ECG, will check your weight and body mass index, and vital signs, and will administer questionnaires and assessment scales as it was done at previous visits, to make sure it is safe for you to continue in the study. You will be asked if there have been any changes in your health and for any new medication you may have begun to take from previous visit.

Study Visit 7
Treatment Week 3 (Treatment Day 22)

A group of approximately 75 patients who had additionally signed the consent form will have additional visit on day 22 for blood sampling for pharmacokinetic testing. If you are

in this group you will need to come to this visit. You will also be asked if there have been any changes in your health and for any new medication you may have begun to take from previous visit. Your vital signs will be checked and ECG will be done.

Study Visits 8 and 11: Study Drug Administration Visits
Treatment Weeks 4 and 8 (Study Days 29 and 57)

At visits 8 and 11 the study staff will perform laboratory tests (including blood and urine tests), ECGs, vital signs assessments, body weight, and administer questionnaires and assessment scales as it was done at previous visits, to make sure it is safe for you to continue in the study. You will be asked if there have been any changes in your health and for any new medication you may have begun to take from previous visit. IM study drug (risperidone or placebo) will be administered by IM injection. The injection site appearance and sensitivity will be examined after injection.

Study Visits 9 and 12
Treatment Weeks 4 and 8 (Study Days 31 and 59)

- Visits 9 and 12 will occur 2 days after Study Drug Administration Visits. At these visits the study staff will perform ECG, vital signs assessments, and you will be asked if there have been any changes in your health and for any new medication you may have begun to take from previous visit. Blood sample will be taken for pharmacokinetic testing.

Study Visits 10 and 13
Treatment Weeks 6 and 10 (Study Days 43 and 71)

At visits 10 and 13 the study staff will perform ECG and vital signs assessments, and administer questionnaires and assessment scales as it was done at previous visits, to make sure it is safe for you to continue in the study. You will be asked if there have been any changes in your health and for any new medication you may have begun to take from previous visit.

Study Visit 14: End of Treatment Visit or Early Termination Visit
Treatment Week 12 (Study Day 85)

Similar to the screening visit, at the final visit the following tests and procedures will be done:

- A set of standard questions/scales/questionnaires that will assess your physical sensations and symptoms, your quality of life and how it is affected by your schizophrenia, as well as assessment scales to assess your movements

- Physical examination
- Ophthalmological examination
- Weight and body mass index
- Vital signs
- ECG
- Review if there have been any changes in your health and for any new medication you may have begun to take from previous visit
- Blood samples
- Urine samples for laboratory testing and an optional urine drug screen

Study Visit 15: Safety Follow-up Contact (Via Telephone)
Study Day 99

At final study day you will be contacted by phone to inform if there have been any changes in your health and for any new medication you may have begun to take from previous visit.

This safety follow-up telephone contact will be done earlier in the case of an early termination, but it is not applicable for subjects who enter into a long-term extension segment of the study.

Subject's Responsibilities

While you are in this research study (after your inpatient stay is finished), you will be required to:

- Come to the study clinic for all of your scheduled visits, complete all required study procedures, follow the instructions listed in this Subject Information Sheet and Informed Consent Form, and follow instructions given to you by the study staff.
- Remain in the facility for the duration of all your in-clinic stays.
- Notify the study doctor of any changes in your health and medications or if your availability to take part in this study changes. 'Medications' include prescriptions and non-prescription drugs as well as vitamins or supplements.
- Agree to continue to take your normal medications for your condition, as prescribed by your doctor, throughout this study. The study doctor will change your regular medication during this study only if it is necessary for your health.
- Agree to not donate blood for at least 30 days after you leave the study.
- For females able to have children, agree to use an acceptable form of birth control for the duration of the study and for ≥ 6 months after the last dose of IM study drug has been administered, such as intrauterine device (IUD), a condom (with or without spermicide), diaphragm or cervical cap with spermicide), oral contraceptive pills or other hormonal methods (patches, contraceptive implant or a vaginal ring). The study doctor or study staff will discuss this with you in more detail.

- All male subjects must agree to use an acceptable barrier method of birth control for the duration of the study, such as a condom with or without spermicide. Men with an exclusive surgically sterile female partner, as well as men who have themselves had a vasectomy (surgical sterilization), are exempt from the requirement to use contraception. The study doctor or study staff will discuss this with you in more detail.
- Avoid certain medicines, supplements, and beverages. Your study doctor will explain to you in detail which drugs/vitamins /supplements/herbal extracts/beverages you should not take.
  Please consult him/her prior to starting any new treatment.

For your safety and the safety of others, it is important that you do not drink alcohol during this study, and especially you should not drink alcohol before or during any of the study visits. Please discuss with your doctor about any of these restrictions if you need any additional information or clarification.

Benefits and Risks

In the outpatient clinical setting, nonadherence with prescribed oral antipsychotic medication regimens is frequently seen and has been associated with relapse and worsening of the disease. Long-acting formulations of antipsychotic medications, developed to promote treatment adherence, have helped to improve compliance and thus efficacy. Initially developed long-acting formulations of antipsychotic agents are known to be associated with a number of safety and tolerability concerns that limit their acceptability in current clinical practice.

Risperidone ISM® formulation is an alternative long-acting injectable form of the atypical antipsychotic, risperidone. As a once monthly IM injection, Risperidone ISM® provides rapid achievement (within 24 hours) of therapeutic levels of risperidone with sustained therapeutic plasma levels for a period of up to 4 weeks without the initial need for daily oral risperidone supplementation.

However, please note that your symptoms of schizophrenia may not improve and could even worsen if you take part in this study.

<u>Possible Side Effects of Risperidone</u>

Risperidone ISM® injection has been previously tested in 3 clinical trials. Adverse events reported in adult subjects so far include:

- Endocrine disorders: hyperprolactinemia - higher levels of prolactin in the blood. Prolactin is the hormone that controls the process of lactation.
- Gastrointestinal disorders: dry mouth, odynophagia (is painful swallowing, in the mouth or gullet).

- General disorders and administration site conditions: injection site erythema (redness of the skin) and injection site pain.
- Nervous system disorders: dizziness, headache, oromandibular dystonia (this is a condition involving slow or sustained involuntary contraction of the muscles of the mouth, tongue or jaw), sedation, and somnolence.
- Psychiatric disorders: insomnia.

These side effects observed in previous clinical studies occurred in more than 5% of study subjects; nevertheless it does not mean that all of them were side effects related to the study drug.

Frequency and severity of related side effects in previous studies

The most frequently reported related side effect was hyperprolactinaemia (27.7%); in 4.0% it was moderate and in 96.0% it was mild. The second most frequently reported side effect was injection site pain (21.1%); in 3.9% was moderate and in 96.1% was mild. The third most frequently reported side effect was somnolence (6.3%); in 13.0% of cases it was moderate and in 87.0% it was mild.

Description of serious side effects in previous studies

A total of 6 serious side effects related to Risperidone ISM® were observed in 4 subjects in previous studies. These serious side effects were 3 oromandibular dystonias (this is a condition involving slow or sustained involuntary contraction of the muscles of the mouth, tongue or jaw; 2 were severe and 1 was moderate), 2 tachycardias (is a heart rate that exceeds the normal resting rate; they were moderate) and 1 sedation which was moderate. In all of these cases the subjects recovered from the serious side effect.

<u>Possible Discomforts and Reactions Caused by Study Drug Injection</u>
Sometimes people have reactions at the spot where medications have been injected. Reactions can include pain, tenderness, hardening of the area, swelling, redness, bruising, or itchiness. Very rarely a blood clot may form or an infection may occur. For your safety, call the study doctor right away if any of the following things happen at the injection site: intense pain, the area feels hard or has lumps, lots of swelling or blistering occurs, or if an open wound appears or a dark scab forms.

<u>Discomforts of Blood Tests and ECGs</u>
You may experience some discomfort, bruising, or slight bleeding on your arm where the blood samples are taken. Some people may feel faint or lightheaded for a few minutes after having blood taken.

During the in-hospital stay, instead of getting many needle sticks, you may have your blood samples taken through an indwelling catheter. A catheter is a small flexible tube that is put in your forearm. Catheters are used to limit the number of needle sticks. They make taking blood much easier since the blood can be taken directly through the tube

instead of using a needle each time. Catheters can sometimes cause discomfort. You may get a bruise or swelling or an infection. These effects normally clear up in a few days.

The ECG may cause some discomfort or skin irritation where the adhesive (sticky) pads are applied to your body.

Unknown/Unforeseeable Risks

In addition to the risks or discomforts listed above, there may be other risks that are currently not known. Also, the risks or discomforts described may occur more often or be more severe than has been seen before.

Reproduction Risks

The effects of risperidone on a fetus are unknown. In animal studies, the risperidone has shown possible birth defects. Even with using an approved birth control method, a pregnancy can still occur. Also, pregnancy tests are not always accurate. There is always a possibility that a female is pregnant even if her pregnancy test results indicate that she is not pregnant.

Sexually active females able to have children and men who are sexually active must use a medically acceptable birth control method while in this study and up to six months after the last study drug administration. Your study doctor will discuss this with you in more detail. Subjects who are abstinent (not sexually active) must agree to use an acceptable method of birth control if they become sexually active.

Since the effects of the study drug on sperm are unknown, males are required to use a barrier birth control method, such as a condom with or without a spermicide, while being in this study.

If you are a female and become pregnant during the study, you will be withdrawn from the study. If you think you or your partner might be pregnant at any time during the study, please inform the study doctor right away. A member of the research team will follow up on you throughout the pregnancy in order to collect information on the outcome of the pregnancy and development of the child after birth. Female subjects should not breast-feed during or for two months after the last study drug administration.

Placebo Risks

The placebo is a pharmacologically inactive product which contains the same ingredients as the study drug (with exception of main active ingredient), including dimethyl sulfoxide (DMSO). DMSO is a medicine and dietary supplement which is also used as solvent. Some data indicate potential side effects of DMSO on eyes. For this

reason, an ophthalmological examination will be performed at screening and at visit 14 (Day 85).

Please keep in mind that placebo is not a treatment for your disease. If your study doctor thinks you need a treatment, you will be discontinued from the study and will receive the required treatment.

New Findings

Your study doctor will tell you of any information learned during the course of the study that might cause you to change your mind about taking part in the study. You may contact the study doctor at any time after your participation ends to find out if any new information about this study has become available.

Possible Benefits

Your symptoms of schizophrenia may improve while participating in this study. Your participation in the study will contribute to information about the study drug and may benefit other patients in the future.

Costs

Being in this study will not cost you or your insurance company. Laboratorios Farmacéuticos ROVI, S.A. will pay for all charges for the study drugs. It will also pay for all study-related procedures, like lab tests and ECGs.

Alternative Treatments

You do not have to take part in this study to receive treatment for your condition. If you decide not to take part in this study, there are other treatments for schizophrenia available to you. Your doctor will discuss alternative treatments with you and their benefits and risks.

Confidentiality and Data Protection

This section provides information about how your medical records and health information (together, your "records") will be used and disclosed in the clinical study referenced above. Your records may include information about your blood samples, physical examinations, medical history, and any other data collected or reviewed during the course of the study as described in the consent form for the study. By signing this form, you authorize the study doctor identified in the consent form and the study staff to use your records to carry out the study described in the consent form. If you do not sign this form, you cannot participate in the study.

Personal Data which will include the following general categories: name, contact details, date of birth age, marital status; and the following sensitive categories: initials, gender, race, ethnic origin, health, sex life will be collected from you during the study and recorded in your medical notes by the Principal Investigator and/or the hospital/clinic staff.

For most purposes, your personal data will be coded and Study records will identify you only by number, not by name. This coded personal data will be processed electronically by INC Research on behalf of the Study Sponsor. INC Research is a contract research organization specialized in organization and management of clinical studies which has been contracted by the Sponsor to conduct this project. The Investigator is responsible for keeping the code list which makes it possible to link your assigned unique number to your name. This will be kept in a safe place to ensure that in case of an emergency you can be identified and contacted. The code list may be retained until 15 years after the end of the research or 2 years after the treatment has received its last authorisation for sale or development has discontinued or as required by applicable law, whichever is longer. The information in your medical records, and the information you give to us, will be kept confidential (private) to the extent allowed by law. If any information from this study is published, your identity will not be disclosed, nor will your name be used in any way. Only coding or initials will appear on any records used.

In addition, qualified representatives of (i) the Study Sponsor and its worldwide affiliates; and/or (ii) INC Research and its worldwide affiliates; and/or (iii) the Food and Drug Administration (FDA); and/or (iv) independent auditors; and/or (v) national and foreign regulatory authorities (including the European Medicines Agency and the Ethics Committee) may look at your medical notes (including uncoded personal data) if necessary for data analysis. If your personal data is transferred outside the country the Sponsor of the Study is responsible for taking appropriate steps to protect your personal data and keep it secure.

With respect to data stored or processed in the United States by INC Research, INC Research will process personal data originating from Europe according to the relevant Safe Harbor Principles. INC Research subscribes to the "Safe Harbor Principles" issued by the U.S. Commerce Department on July 21, 2000. You can view INC Research's certification of compliance with the Safe Harbor Principles at https://safeharbor.export.gov/list.aspx.

By signing this form, you are consenting that the Principal Investigator and hospital/clinic staff can use your personal data for purposes of carrying out the Study, and can transfer and disclose your personal data to other members of the research team, as listed above.

With your permission your general practitioner will also be informed of your participation in this Study.

You have the right to access and correct the information collected about you during the Study and submit any queries or concerns about the collection or processing of your personal data by contacting the Principal Investigator at the address listed on page one of this document or INC Research's Global Privacy Officer at data.privacy@incresearch.com.

If you have personal insurance (eg, life insurance) your participation in this study may affect your policy. If necessary, before agreeing to take part in this study, you need to check this to ensure that your taking part does not affect your medical insurance or other personal insurance.

If you decide that you no longer wish to have your personal data shared:

- You must provide a written request to the Principal Investigator at the address listed on page one of this document and tell him or her that you no longer want to share your personal data.
- To ensure that the scientific integrity of the trial is not compromised, the research team may continue to process any of the personal data that they already have collected up until the date that you withdrew your consent. However, going forward, no additional personal data from you will be collected.
- You will no longer be able to take part in this Study.
- Your personal data may still be shared in accordance with applicable law if: (i) you have a bad reaction from the Study drug or device; and/or (ii) collection or further use of your personal is necessary to protect your vital interests; and/or it is legally required.

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

Your doctor, the sponsor company, or the regulatory authorities that have reviewed and approved the study has the right to stop your participation in the study at any time, with or without your consent, for any of the following reasons if:

- you have an adverse effect from the study drugs
- you need a treatment not allowed in this study
- your study doctor thinks that it is in your best interest not to take part any longer in the study
- you do not follow your study doctor's instructions, and you do not take the study drug as instructed
- you are a female and become pregnant
- or the study is canceled by the regulatory authorities or the sponsor company

If this happens, the reason will be explained to you.

This authorization for use of your personal data will not expire until the end of the trial and the final results are obtained, but you may revoke your authorization at any time, by writing to the Principal Investigator.

Compensation

If you take part in this study, you will not be paid or rewarded in any way but your travelling expenses due to your participation in the study and after providing receipts for expenses encountered like travel, parking and meals, will be reimbursed with a maximum. Your study doctor can give you the details about how to get reimbursed. [If the volunteer is to be reimbursed, clearly state the total amount to be paid, conditions for the payment(s) and when the payment(s) will be made.] You will not be charged for the study drug or for any of the procedures connected with your participation in the study.

If you become ill or are injured as a direct result of being in this study, necessary and associated professional medical care will be provided at no cost to you.

The sponsors of this study Laboratorios Farmacéuticos ROVI, S.A will pay (name of hospital department or research fund) for including you in this study. This payment represents a compensation for study-related tests and procedures completed, as required by the protocol.

Contact Persons

If you have any questions about this study, or about what to do if you become ill while in the study, please call Dr. [name of principal investigator] at [phone number] or [name of sub-investigator, research nurse etc.] at [phone number].

If you have any questions about your rights as a study subject, please call [subject representative, ombudsman local EC etc.] at [phone number].

Insurance

In accordance with country regulation, the sponsor of the research has subscribed an insurance guaranteeing its civil liability, like that of the study doctors taking part in this research. A contract (enter policy number) was issued with the company
Name and address of the insurance company: .....
Policy number: .....

If you experience any unexpected symptoms or injury, and if emergency medical treatment is required, please report immediately to your study doctor.

Additional information

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov* as required by the U.S. Law and on https://www.clinicaltrialsregister.eu/ in agreement with the Declaration of Helsinki that recommends public registry of clinical trials [*add also any country specific public registry if applicable*]. These web sites 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.

INFORMED CONSENT FORM TEMPLATE

Title: Multicenter, Randomized, Double-Blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Intramuscular Injections of Risperidone ISM® in Patients with Acute Exacerbation of Schizophrenia (PRISMA-3)

Protocol number: ROV-RISP-2016-01
EudraCT number: (applicable to EU countries only)

Sponsor name: Laboratorios Farmacéuticos ROVI, S.A.
Address of Sponsor: C/ Julián Camarillo, 35. 28037 Madrid, Spain

Principal Investigator: Insert Name, affiliation, location
Telephone number
Daytime:
After Office Hours:

Please initial each box to indicate your agreement

1. I confirm that I have read and understand the information sheet for the above study. I confirm that the study has been explained to me and I have had the opportunity to ask questions and ample time to decide whether to participate. I know who to contact if I have any further questions.	
2. I confirm that I voluntarily agree to participate in this study, that I am aware of the conditions of participation and withdrawal and that I am free to leave the study at any time without giving a reason. I understand that I do not give up any of my legal rights by signing this Informed Consent Form.	
3. I understand that sections of my medical notes will be reviewed by representatives of INC Research, auditors and national and foreign regulatory authorities where it is relevant to my taking part in the study. I give permission for these individuals to have access to my medical records.	
4. I agree to the collection and transfer of my personal coded data including sensitive data initials, gender, race, ethnic origin, health, sex life, to Laboratorios Farmacéuticos ROVI, S.A. and to regulatory authorities both within and outside (insert country name), including to countries that may not have the same level of data protection as (insert country name),	
5. I agree that my personal coded data can be archived.	
6. I agree that my biological materials (blood, urine, etc.) collected from me can be used for the purposes of this study.	
7. My consent does not discharge the sponsor and the study doctor for their responsibilities.	

8. I agree to take part in this study.	

Do you agree to have your general practitioner informed about your participation in this study? ☐ Yes ☐ No

An original or copy of the information sheet and signed consent form will be given to you to keep and an original will be placed in your subject's file at site.

Read and understood:

_____	_____	_____	_____
Patient's first and last Name	Signature	Date	Time

Are you willing to participate in a sub-study for PK analysis? ☐ Yes ☐ No
If yes, please confirm by signature:

_____
Signature

_____	_____	_____	_____
First and last Name of Investigator conducting consent	Signature	Date	Time