Main Master Informed Consent Form (Stage 2)
And
Authorization To Use And Disclose Protected Health Information

Sponsor / Study Title:	**Oculis Operations Sàrl / "A Phase 2/3 Double-Masked, Randomized, 2-stage, Multicenter Study of the Efficacy and Safety of OCS-01 Eye Drops in Subjects With Diabetic Macular Edema"**
Protocol Number:	**DX219**
Principal Investigator: (Study Doctor)	**Eric Chin, MD**
Telephone:	**(909) 335-8940 (24 Hours)**
Address:	**Retina Consultants of Southern Ca** **1895 Orange Tree Lane** **Suite 204** **Redlands, CA 92374**

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. When the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing and dating this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired.

You are invited to take part in a research study because you have diabetic macular edema (DME). DME is a swelling of the light-sensitive layer at the back of the eye called the macula and is a condition that affects some people with diabetes. Your participation is voluntary and requires your written consent. If you decide not to take part in this study, you can continue with your current medical care.

This study involves research. Participating in a research study is not the same as getting regular medical care. The purpose of a research study is to collect information about a new study treatment; the purpose of regular medical care is to improve your health. Being in this study does not replace your regular medical care, but you may have other tests or changes in your treatments during the study.

Oculis Operations Sàrl (Oculis) is sponsoring this study of an experimental drug (not yet approved for sale by the government). The study will consist of 2 stages. Stage 1 was already completed and this stage (Stage 2) will take place in approximately 92 centers in approximately 10 countries with about 350 people with DME participating .

The study has received favorable/positive opinion and an authorization from the applicable competent authorities (government) Food and Drug Administration according to the laws in force. This means that your local government and your country's government have reviewed this study and believe that it is safe for its subjects.

Before agreeing to participate in this study, it is important that you read and understand this form. It explains the purpose, procedures, benefits, risks, discomforts, and safeguards of the study. It also explains the different choices that are available to you and your right to withdraw from the study at any time. Please read this information carefully and ask the study doctor or study staff for an explanation if you have any questions. You may take home an unsigned copy of this informed consent form to think about it or to talk about it with your partner, family, or friends before deciding whether or not to take part in the study.

If you choose to participate in this study, you will be asked to sign and date this consent document. You will receive a copy of this form to keep.

1. Why is this study being done?

Oculis has begun a study of an investigational drug called OCS-01 as a possible treatment for DME. An investigational drug is one that has not been approved by regulatory agencies, such as the United States (US) Food and Drug Administration (FDA), European Medicines Agency (EMA), or others.

The active ingredient in OCS-01, dexamethasone, is a corticosteroid currently approved as an intravitreal (inside of the eye) implant for the treatment of DME in the US; however, the eye drop formula containing OCS-01 in this study is not currently approved. OCS-01 is thought to work by improving the concentration of dexamethasone in the posterior (back) part of the eye, thereby decreasing eye inflammation and possibly improving DME.

The main goal of this study is to learn how well OCS-01 works and how safe OCS-01 is compared with placebo. A placebo is an inactive material that looks like OCS-01 but does not have any OCS-01. Researchers use a placebo to see if OCS-01 works better or is safer than taking nothing.

2. How long will my participation in this study last?

You will be in this study for up to 57 weeks, and you will need to come to the study center at least 12 times over this period.

3. What will happen during this study?

The study is divided into 2 periods: a screening period and a study treatment period. During the screening period, you will have **1 screening visit** and during the study treatment period, you will have **11 study treatment visits** with your study doctor at the center.

Visit 1 (Days -28 to -3; Screening Visit): It may last about 3.5- 4 hours.

Visit 2 (Day 1): It may last about 2.5 - 3 hours.

Visit 3 (Week 1): It may last about 2.5 - 3 hours.
Visit 4 (Week 6): It may last about 2.5 - 3 hours.
Visit 5 (Week 12): It may last about 2.5 - 3 hours.
Visit 6 (Week 18): It may last about 2.5 - 3 hours.
Visit 7 (Week 24): It may last about 2.5 - 3 hours.
Visit 8 (Week 30): It may last about 2.5 - 3 hours.
Visit 9 (Week 36): It may last about 2.5 - 3 hours.
Visit 10 (Week 42): It may last about 2.5 - 3 hours.
Visit 11 (Week 48): It may last about 2.5 - 3 hours.
Visit 12 (Week 52; End of Study): It may last about 3.5 - 4 hours.

Before any study-related tests and procedures can be done, you will be asked to read and sign and date this informed consent form. After you sign and date this informed consent form, the study will begin with a screening visit. The goal of the screening visit is to decide whether or not you meet the requirements to take part in this study. If you do not meet the requirements, you will not be able to participate in this study, and the study doctor will explain why and will discuss other treatment options with you.

If the study doctor decides that you meet all of the requirements to be in this study, you will be randomly assigned (like flipping a coin) to receive 1 of the following:

- OCS-01
- Placebo

You will have a 50% (1 in 2) chance of receiving OCS-01 and a 50% (1 in 2) chance of receiving placebo. You will not be told if you are receiving OCS-01 or placebo. The study doctor and any other people involved in the study will not know whether you are receiving OCS-01 or placebo. However, this information will be given to the study doctor if it becomes necessary for your safety.

The study doctor or study staff will give you instructions on how to apply the study eye drops, when you are outside the study center (at home for example). You will be given enough OCS-01 or placebo eye drops to last until the next scheduled visit.

Description of the procedures and assessments

- **Eye Assessments:** Several tests will be done to check your eyes.
    - Visual acuity: Your vision will be tested using an eye chart.
    - Slit lamp examination: Your eyes will be examined with a special magnifying microscope (called a slit lamp).
    - Lens clarity: The clarity of your study eye lens will be assessed using a scale from 1 to 8.
    - Intraocular pressure: You will receive numbing eye drops before your eye pressure is measured with a device.

  - Dilated indirect ophthalmoscopy: The study staff will shine a bright light into your eyes to check the back of your eyes (retina). **This assessment requires dilation (widening) of the pupils.**
  - SD-Optical coherence tomography (SD-OCT): You will look at a light while a safe laser scans the back of your eyes to see the retinal layers.
  - Fundus photography: A specialized camera with a microscope will be used to photograph the back of your eyes.
  - Fluorescein angiography: A dye will be injected into your vein. As the dye passes through your body and reaches your retina, a special camera will take pictures of the back of your study eye.
  - Specular microscopy: A specialized camera with a microscope will be used to look at the size and shape of cells in the posterior (back) layer of the cornea in your eye.
- **Demographics:** Questions about your race and ethnicity.
- **Medical history and previous therapy:** Includes questions about your health and DME. You will also be asked about any medicines and any treatments for DME you have used in the past.
- **Vital signs:** Your blood pressure will be measured.
- **Laboratory tests:** Blood and urine (if applicable) sample(s) will be collected.
  - If you are a woman able to become pregnant, a urine sample will be collected before you receive/apply the study eye drops at screening (Visit 1) and at the end of the study treatment period (Visit 12) to make sure you are not pregnant. Pregnant women are not allowed in the study.
  - Blood will be taken during the study. The blood will be taken from a vein in your arm for the following:
    - Between 6-8 mL (a little over 1.5 teaspoons at each scheduled visit where blood is drawn per the Study Procedures table below) for different blood tests to check the cells and chemicals in your blood.
    - If you are a woman able to become pregnant and your urine pregnancy test result is positive, a blood sample will be collected to confirm whether or not you are pregnant.
- **OCS-01 or placebo administration:** OCS-01 and placebo come in the form of study eye drops, which you will apply directly into your study eye.
  - Each study eye drop container (vial) should only be used once.
  - You will be trained by the study staff on how to apply and store the study eye drops when you receive your first dose at the study center.
  - You will apply the study eye drops 6 times a day for the first 6 weeks and then 3 times a day for the remaining 46 weeks.

The table below shows which procedures and assessments will occur at which visit(s).

In addition to the visits described below, the study doctor may ask you to come in for extra visits, if necessary for your safety.

Study Procedures	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**
	Screening (Day -28 to Day -3)	**Baseline Day 1**	**Week 1 ±2 days**	**Week 6 ±2 days**	**Week 12 ±3 days**	**Week 18 ±7 days**	**Week 24 ±7 days**	**Week 30 ±7 days**	**Week 36 ±7 days**	**Week 42 ±7 days**	**Week 48 ±7 days**	**Week 52 ±7 days**
Sign and date informed consent form and HIPPA document; review demographic data; and questions about your medical history (including eye health and past surgeries).	X											
Questions about other medicines you are taking or have taken	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test for women who are able to have children (urine)[1]	X											X
Eye assessments (visual acuity, slit lamp biomicroscopy, and eye pressure)	X	X	X	X	X	X	X	X	X	X	X	X
Eye assessments (lens clarity and dilated indirect ophthalmoscopy) and measure your eye blood pressure	X	X	X	X	X	X	X	X	X	X	X	X
Eye assessments (color fundus photography and fluorescein angiography)	X											X
Eye assessment (SD-OCT)	X	X	X	X	X	X	X	X	X	X	X	X
Blood samples for safety tests	X						X					X

Study Procedures	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**
	Screening (Day -28 to Day -3)	**Baseline Day 1**	**Week 1 ±2 days**	**Week 6 ±2 days**	**Week 12 ±3 days**	**Week 18 ±7 days**	**Week 24 ±7 days**	**Week 30 ±7 days**	**Week 36 ±7 days**	**Week 42 ±7 days**	**Week 48 ±7 days**	**Week 52 ±7 days**
Blood sample to check if your diabetes is progressing	X			X		X		X		X		X
Eye assessment (specular microscopy)[2]		X										X
Questions about how you are feeling (side effects)	X	X	X	X	X	X	X	X	X	X	X	X
Receive study eye drops		X	X	X	X	X	X	X	X	X	X	
Return unused study eye drops and empty vials			X	X	X	X	X	X	X	X	X	X
Exit from study												X

[1] - A positive urine pregnancy test will be confirmed by a serum (blood) pregnancy test.

2 - Will be done at selected sites only.

4. What do I have to do?

During the study, you will have the following responsibilities:

- Tell your study doctor if you have any allergies, including drug allergies. If you are not sure, ask your family/personal doctor.
- Attend all scheduled visits.
- You cannot use contact lenses in the study eye (including cosmetic contact lenses) for the duration of your participation in the study.
- Apply the study eye drops as directed.
- Return any unused and/or empty single dose study eye drop containers as instructed by the study staff.
- Follow the study doctor's instructions about whether or not you may continue to take your regular prescribed medications and/or over-the-counter medicines during the study period.
- Tell the study doctor of any changes to your current medications, illnesses or injuries, unexpected or troublesome side effects, or problems that occur during the study.
- Tell the study doctor if you plan to have an elective surgery or any other medical treatment or procedure.
- For 2 to 3 hours after study visits that require your pupils to be dilated, you should not perform activities that require visual alertness, judgment, or physical coordination such as driving or operating machinery.
- You should continue to make regular visits to your family/personal doctor or any other special doctors you were seeing before starting the study because being in the study does not replace regular medical care.
- Make sure that the study eye drops are kept out of the reach of children and people who have a limited capacity to read or understand. You are the only person who should use the study eye drops.
- Store the study eye drops at room temperature.
- Contact the study doctor if you find you have any questions about the study after you sign and date this informed consent form.

5. What are the risks and possible discomforts?

Any study has risks, which may include things that could make you sick, make you feel uncomfortable, or harm you. You might experience side effects related to OCS-01 while participating in the study. All subjects in the study will be watched carefully for any side effects; however, the study staff does not know all the side effects that OCS-01 may have on you. The study staff may give you medicines to help reduce side effects. These side effects may be mild or serious. In some cases, these side effects might be long lasting or permanent and may even be life threatening.

Taking part in this study involves some risks and possible discomfort to you.

Possible risks/side effects associated with OCS-01:

- If you are assigned to take placebo or if OCS-01 does not work for you, you may see an increase in your diabetic macular edema or diabetic retinopathy symptoms.
- OCS-01 may cause unpleasant side effects or reactions. OCS-01 has been tested in animals and in a limited number of people. In other clinical studies in which a similar

dose of OCS-01 was given to people, the most common side effects were cataract formation or progression, infection, eye irritation, and increased pressure in the eye. A single serious side effect of endophthalmitis (inflammation of the inside of the eye) was reported in 1 subject being treated for pain and inflammation after cataract surgery. Cataract surgery is an intraocular (inside the eye) procedure, which is not planned as part of this study. In Stage 1 of this study there was 1 single serious side effect of intraocular bleeding (Vitreous hemorrhage), observed in 1 subject who received OCS-01.

You will be monitored for the duration of your time in the study and you should tell your study doctor about any changes in your health while taking part in the study.

Because OCS-01 is investigational, there may be risks and side effects that are unknown. All drugs have a possible risk of an allergic reaction. Some symptoms of allergic reactions are rash, wheezing and difficulty breathing, dizziness and fainting, swelling around the mouth, throat or eyes, a fast pulse or sweating. Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms, or any other side effects, during the study.

Possible discomforts and risks associated with the study procedures:

- Blood samples: Taking blood from your arm may cause faintness and/or swelling, pain, redness, bruising, bleeding, or infection (infection rarely happens) at the site where the needle is inserted.
- Eye assessments: Eye assessments that require your eyes to be dilated may cause stinging, your vision to be blurry and your eyes to be more light sensitive for a few hours. You may experience eyelid swelling from the mild pressure put on your eye during the examinations.
- Fluorescein angiography: This procedure involves administration of a contrast dye into a vein. You may experience a reaction (mild, moderate, or severe) from the contrast dye that is used. The most common reactions associated with the fluorescein dye are:
    - Nausea
    - Vomiting
    - Hives
    - Dry mouth
    - A metallic taste
    - Increased production of saliva
    - Sneezing
    - An increased heart rate.

      Severe complications can occur but are very rare. **PLEASE TELL YOUR STUDY DOCTOR IF YOU HAVE A KNOWN ALLERGY TO FLUORESCEIN.**

6. What about birth control, pregnancy, and breastfeeding?

Taking OCS-01 may involve unknown risks to a pregnant woman, an embryo, a fetus (unborn baby), or a breastfeeding infant.

Women

If you are pregnant, planning to become pregnant, or breastfeeding a child, you cannot take part in this study. Before entering the study, a pregnancy test will be done for all women able to become pregnant. This test might not detect an early pregnancy. Pregnancy tests will be done at the screening visit and at the end of study treatment visit.

You are considered able to become pregnant after menarche (first period) until becoming postmenopausal (no period for at least 12 months without another cause). Female subjects should be compliant with a highly effective and acceptable birth control method throughout the study. Highly effective methods of birth control include:

- Combined (containing estrogen and progestogen) hormonal pills, ring, or patch
- Progestogen-only hormonal birth control associated with preventing ovulation (pills, injection, or implant)
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal ligation or occlusion (similar to having your tubes tied)
- Vasectomized partner (with a negative semen analysis)
- Sexual abstinence (not have sex with a man able to father children), if in line with your preferred and usual lifestyle.

If during the study you become pregnant, you should tell the study doctor as soon as possible. The study eye drops will be stopped, and you will be asked to complete any final assessments. The Sponsor may want to receive updates on the progress of the pregnancy and its outcome. By signing this consent form, you agree to allow the Sponsor to follow your pregnancy and its outcome. The study doctor will request copies of all related medical reports from you and/or your physician during your pregnancy.

Men

Male subjects and their female partners of childbearing potential should be use a highly effective and acceptable birth control method (described above under "Women" section). If your partner is planning to become pregnant, you should discuss this with your study doctor. You should discuss the unknown risks to a pregnant woman, an embryo, a fetus (unborn baby), or a breastfeeding infant with your partner.

If your partner becomes pregnant the Sponsor may want to receive updates on the progress of the pregnancy and its outcome. If you agree to this, your pregnant partner will be asked to sign and date a separate informed consent form.

7. What are the benefits of being in this study?

There is no guarantee that you will receive any benefits. However, you will be helping others by contributing to medical research. You may feel that you are benefiting in the following ways:

- Your condition will be checked as long as your participation in the study lasts. However, services provided and evaluations carried out as part of the study should not be seen as a substitute for a careful evaluation, ongoing medical care, or follow up by your family/personal doctor.

You have the right to be informed of the overall results of the study.

8. What other options are available if I do not take part in this study?

You do not have to take part in the study to treat your DME. There are other options of therapies, such as tight blood sugar control, medications such as anti-VEGF treatments, and/or laser surgery.

Your family/personal doctor or the study doctor can answer any questions that you have about other treatments or other research currently being done in the treatment of DME.

9. What if I get harmed or injured during the study?

The Sponsor has taken out an insurance policy for the study. If you are injured as a direct result of taking the eye drops, Oculis will pay for reasonable and routine costs to treat the injury, if the following conditions are met:

- The injury was a result of taking part in the study.
- The cost of treatment or any part of the cost is not covered by any other health insurance, government health program, or other institutions providing coverage for health care.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare. If you believe you have experienced a research-related injury, please contact the study doctor using the contact information at the beginning of this document.

You will not lose any of your legal rights or release Oculis, the study doctor, the study staff, or study site from liability for mistakes by signing and dating this consent document.

10. What are the costs for participation and will I be paid?

This study is being funded by Oculis, who appreciates your involvement in the study. You will receive no direct payment for taking part. However, you will be compensated up to$75for each completed visit for transportation or parking payments related to visiting the study center. You will be reimbursed following each completed visit after you submit your travel receipts to the study staff.

The study eye drops will be given at no cost to you, and you will not be charged for any study doctor visits, laboratory work, tests, or procedures needed for the study. There will be no cost to you to participate in this study.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your condition while in this study, including the cost of tests, procedures, or medicines as part of your standard of care.

Before you decide to be in the study, you should check with your health plan/insurance company to find out exactly what they will pay for. Examples of procedures and drugs that may be billed include the following: standard of care costs (including routine clinic visits, routine laboratory

tests, routine imaging, infusion intravenous and injection administration) that are not research-related procedures associated with this study.

The study doctor will be paid for his or her work in this study.

11. May I or someone else stop my participation after the study has begun?

Taking part in this study is voluntary, and you can leave the study at any time for any reason. A decision to stop study participation will not impact your regular medical care or benefits to which you are entitled.

If you are considering or have already decided to leave the study, you should contact the study doctor to discuss the safest way to leave the study. This may involve completing some final tests and examinations. You should also contact your primary/family doctor so he or she can provide you with the best course of continuing care.

You will not take part in the study after withdrawal.

If new findings that would affect your safety and willingness to participate in the study are identified while you are in the study, you will be told as soon as possible, so you can decide whether to leave the study or continue. **If you decide to continue, you will be required to sign and date a new version of this informed consent form.**

Premature Discontinuation from the Study

Your study doctor may decide that you should no longer take part in the study if you do not follow the instructions you receive for taking part in the study. The Sponsor, Institutional Review Board (IRB) or Regulatory Authority may also decide to stop the study at any time for any reason.

Premature Discontinuation of Study Drug

Sometimes the study doctor or Oculis may decide it is best for you to stop taking the study drug (even if you do not agree). He or she will discuss this with you. Possible reasons for doing so include the following:

- It is in your best interest.
- You have a side effect that requires stopping the research study.
- You need a treatment not allowed in this research study.
- You become pregnant.
- The research is canceled by the FDA or the Sponsor for any reason.
- You are unable to take the research medication.
- You are unable to keep your scheduled appointments.

If you discontinue study drug for any of the reasons above, you will not be discontinued from the study and will be asked to attend all subsequent visits until Visit 12 for completion of the safety and efficacy assessments as described in the table above.

12. What medical care will I receive when my participation in this study stops?

When you leave the study, you will be under the care of your regular health care provider, who will decide the best way to treat your DME. The study eye drops will no longer be available to you.

13. What will happen to the samples that I provide?

The blood samples that you give will be sent to a central laboratory (ICON Laboratory Service, 123 Smith Street, Farmingdale, NY 11735, USA) to be analyzed. They will be used only for the tests specified in the table and discarded 14 days post analysis.

14. What happens with my data and other personal information?

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

A description of what will happen to your health data and other personal information is included in the Authorization to Use and Disclose Protected Health Information located in Appendix 1 (below) that you should read and agree to be able to participate in this study.

If the results of the study are published, your identity will remain confidential.

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.

With your permission, your primary/family doctor will be informed of your participation in this research study.

15. Whom to contact about this study?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00055506.

Consent to Participate

By signing and dating this informed consent form, I agree to the following:

- I have read and I understand this informed consent form.
- I have been given the chance to ask any questions that I had about the study, and all questions that I asked were answered to my satisfaction.
- I understand the risks of taking part in this study as described in this informed consent form.
- I freely consent to receive OCS-01 under the study doctor's care. I understand that there is no guarantee that I will receive any benefits from taking part in this study.
- I understand that I am free to withdraw from the study at any time for any reason. I will tell the study doctor if I decide to withdraw so that my participation may end in an orderly manner and my future care can be discussed. I understand that my study doctor can stop my participation in the study at any time.
- I understand that I will be told of any new information that might relate to my willingness to continue in the study.
- I understand that I cannot participate in another research study while taking part in this study.
- I understand that I will receive a signed and dated copy of this informed consent form for my records.

My consent to participate in this study does not take away any legal rights in the case of negligence (carelessness) or other legal fault of anyone who is involved with this study.

_____
Name of subject (print)

_____ _____
Signature of subject Date (dd/Mmm/yyyy)

I confirm that all the contents of this informed consent form were discussed and that any questions have been answered.

_____
Name of study doctor or person administering consent (print)

_____ _____
Signature of study doctor or person administering consent Date (dd/Mmm/yyyy)

Legally Authorized Representative Consent

As the legally authorized representative for _____, I have read this informed consent form. I have been given the chance to ask any and all questions that I had about the study, and all the questions that I asked were answered to my satisfaction. I understand the risks and benefits of taking part in the study, as described in this informed consent form. I affirm that I have the legal right to sign and date this form on behalf of

_____.

I give my consent for _____to take part in this study under the conditions stated above.

_____
Name of legally authorized representative (print)

_____ _____
Signature of legally authorized representative Date (dd/Mmm/yyyy)

_____
Authority of legally authorized representative to act on behalf of the Subject

Impartial Witness

I am an impartial witness and I confirm I was present during the entire informed consent discussion. I attest that the information in this informed consent form was accurately explained, apparently understood, and that the consent to participate was given freely.

_____
Name of subject (print)

_____
Name of impartial witness (print)

_____ _____
Signature of impartial witness Date (dd/Mmm/yyyy)

Appendix 1: AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information in your study-related records (that we will refer to as "your study records"). In addition, the study doctor may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI"). The PHI gathered in this study includes your medical history, medications you may be taking, any problems you have during the study and information related to your use of the study drug or gathered by the study device.

Under federal law (the "Privacy Rule"), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization." Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing and dating this Authorization. By signing and dating, you are agreeing to allow the study doctor and study staff to use your PHI to conduct this study.

By signing and dating this Authorization, you also are agreeing to allow the study doctor to disclose PHI as described below:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study (referred to as "the sponsor"). The sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.

- The Institutional Review Board ("IRB") may have access to your PHI in relation to its responsibilities as an Institutional Review Board.
- Your information may be audited by agents of the Sponsor, the IRB, or the government to determine compliance with applicable regulations and the validity of the study data.

The study doctor or sponsor may disclose your PHI to the United States Food and Drug Administration ("FDA") or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. You are agreeing, however, by signing and dating this document, not to see or copy some or all of your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records**.**

According to legal requirements, your personal data will be stored in the study databases and/or paper files for whichever time period is longer, as required by applicable laws:

- At least 25 years after the study ends, OR
- At least 2 years after the drug being studied has received its last approval for sale, OR
- At least 2 years after the study drug’s development has stopped.

This Authorization will expire 50 years from the date you sign and date it unless you revoke (cancel or withdraw) it sooner.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to complete analysis and reports for this research. To revoke your

Authorization, you must write to the study doctor, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed and dated it.

_____
Name of subject (print)

_____ _____
Signature of subject Date (dd/Mmm/yyyy)

Legally Authorized Representative Consent
As the legally authorized representative for _____, I have read this authorization form. I have been given the chance to ask any and all questions that I had about the authorization, and all the questions that I asked were answered to my satisfaction. I will receive a copy of this Authorization after I have signed and dated it.

_____
Name of legally authorized representative (print)

_____ _____
Signature of legally authorized representative Date (dd/Mmm/yyyy)

_____
Authority of legally authorized representative to act on behalf of the Subject

Impartial Witness

I am an impartial witness and I confirm I was present during the entire authorization discussion. I attest that the information in this authorization form was accurately explained, apparently understood, and that the authorization was given freely.

_____
Name of subject (print)

_____
Name of impartial witness (print)

_____ _____
Signature of impartial witness Date (dd/Mmm/yyyy)

_____
Printed Name of the Person Obtaining the Authorization

_____ _____ _____
Signature of the Person Obtaining the Authorization Date Time