SUBJECT INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Research Study/ Protocol Title: A randomized, double-blind, placebo-controlled study to assess the effect of MT-8554 on the frequency and severity of vasomotor symptoms in postmenopausal women

Study Sponsor: Mitsubishi Tanabe Pharma Development America, Inc.
525 Washington Boulevard, Suite 400
Jersey City, NJ 07310

Protocol Number: MT-8554-A01

Study Doctor Name: **Michael L Twede MD, FACOG**

Research Site Address(es):

Physicians Research Options LLC /Clinical Research Company
11724 S State St Ste 201
Draper UT 84020

Daytime Telephone Number(s): 801-576-2050

24-hour Contact Number(s): 801-576-2050

INTRODUCTION

You have been asked to volunteer for a clinical research study involving an experimental drug named MT-8554 for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause, as further described herein (this "Research Study")**.**

The purpose of this Subject Informed Consent Form and HIPAA Authorization is to give you information about this Research Study. If signed, you will give your permission to take part in this Research Study. To make an informed decision, you should know the purpose, the procedures, how your participation may help you, the benefits and risks, the discomforts, the precautions taken, and what is expected of you during this Research Study. This process is called "informed consent". Please take the time to read the following information carefully and discuss it with others.

Your Study Doctor (or Study Staff) will go over this Informed Consent Form with you and answer any questions you have regarding this Research Study. This Informed Consent Form may contain words you do not understand. Before you agree to volunteer for this study, please be sure to ask your Study Doctor or Study Staff to explain any words or information you do not clearly understand. If you agree to volunteer, you will be asked to sign and date this Informed Consent Form. You will be given a signed and dated copy that you may keep.

No one can force you to take part in this Research Study. Even if you agree to participate now, you are free to change your mind and stop at any time without penalty or loss of benefits to which you would otherwise be entitled.

You do not have to take part in this Research Study to receive treatment for your condition. You may choose not to participate. There may be other procedures that your doctor can use to treat your condition. Your doctor should discuss alternative treatments with you.

Some insurance companies require people who are renewing a policy or getting a new policy to tell them about participating in a clinical study. You should check with your insurer to determine if taking part in this Research Study will affect your existing insurance policy.

Your Study Doctor will be paid by the Study Sponsor to conduct this Research Study.

PURPOSES OF THIS RESEARCH STUDY

You are being asked to take part in this Research Study because you have experienced symptoms such as hot flashes, flushes, or night sweats, which may occur after menstruation stops, or after the removal of the ovaries and Fallopian tubes, otherwise known as menopause. The symptoms are referred to as "VMS" (vasomotor symptoms) and this is the main focus of the research study.

The main purpose of this Research Study is to test whether an experimental medication called MT-8554 could work to reduce the frequency and severity of VMS in postmenopausal women.

"Experimental" in this context means that the drug is currently being tested. It has not been approved by the U.S. Food and Drug Administration ("FDA") in the United States. Studies like this Research Study are used to determine whether an experimental drug is effective and safe in humans.

If you agree to take part, your Study Doctor will determine if you meet other specific eligibility requirements to enroll in this Research Study.

DESIGN OF THIS RESEARCH STUDY

Approximately 364 subjects who are postmenopausal and have the condition VMS will be enrolled in this study.

This is a double-blind placebo controlled Research Study. Double-blind means you and your Study Doctor will not know what Research Study drug you will receive—although if your Study Doctor needs to find out he/she can do so.

This is also a randomized Research Study, which means you will be selected by chance (like drawing straws) to receive an "active" form of medicine or an inactive form. Active means the pill will contain the experimental medicine and "inactive" form also referred to placebo acts like a sugar pill and contains no medication. In this study, three out of every 4 participants will receive active medicine (75% chance) and 1 out of 4 will receive placebo (25% chance).

You will be responsible for taking two (2) capsules once every night from the blister card provided to you by the study doctor or nurse.

The term "study drug" refers to both MT-8554 and placebo in this form.

DURATION OF THE STUDY

If you agree to take part in this Research Study, you will first sign this Informed Consent Form before any Research Study-related procedures are performed. There are 3 phases related to your study participation lasting approximately 20 weeks including:

SCREENING PHASE: This 2 week period consists of a clinic visit that includes tests and assessments to determine whether you meet the criteria to participate in the study. You will be taught how to complete an electronic diary for tracking the symptoms related to your VMS symptoms.

STUDY DRUG TREATMENT PHASE: This period lasts 14-weeks and includes 6 visits (Visits 2-7). You will receive study drug and be required to take it every day as instructed by the study doctor or nurse. You will also be asked to enter information

related to your illness into the electronic diary on a daily basis. There are other procedures performed and they are described in more detail later in this document.

SAFETY FOLLOW UP: This period of time occurs over 4 weeks after your final visit where no study medication will be taken and no visits at the clinic are required; however, the study doctor or nurse will phone you and the end of the 4 weeks to ask you about your health status.

RESEARCH STUDY PROCEDURES

SCREENING PROCEDURES

After you have signed, dated and received a copy of this Informed Consent Form you will be asked to participate in "screening tests and procedures" to help the Study Doctor decide if you are eligible to take part in this Research Study. Any tests and procedures will only be performed after you sign this Informed Consent Form.

RESPONSIBILITIES

If you are enrolled in this study you will have the following responsibilities during the study:

- Go to all scheduled visits;
- Take the study drug as directed. You will receive a 14-capsule blister card after of study medication to be taken only at night. You will follow all directions for use and storage of the Study Drug;
- Return all unused study drugs and return drug packaging at all in-clinic visits following screening;
- Follow the study doctor's directions about the study;
- Tell the study doctor about any medications or illness you have had;
- Discuss any plan to take new medications or supplements with the study doctor. This is important for your safety as several medications and supplements may interact with the study drug;
- Tell the doctor of any injuries, visits to the hospital, or medical procedures you have had or plan to have during the study. It is crucial that you report these events as quickly as possible to your study staff;
- Tell the study doctor about any side effects or problems that occur;
- Follow the diet and exercise recommendations from the study;
- You will receive a daily diary device (similar to a cell phone) and the site staff will provide instructions on how to use it. You will need to enter total number of hot flash events you had every day. Even if you had 0 hot flashes, you need to enter that 0 hot flashes occurred on that day. A paper diary will be provided to you after screening and should only be used on days when the device could not be used or was not working.
- You need to bring the diary device and paper diary to all clinic visits. You must return the device to the clinic at your final visit.

- Complete multiple questionnaires provided to you during the study visits. You provide answers to questionnaire aimed at assessing various aspects of the health including general health, mental status and sleep quality.

COLLECTION OF BLOOD SAMPLES

During your participation blood will be taken at 7 visits during the first 16 weeks for laboratory testing to monitor your health. The staff will need to stick you 7 times and take approximately 2-3 teaspoons or about 1 tablespoon of blood for each visit. The total volume of blood collected is estimated to be approximately 7 tablespoons.

LIST OF PROCEDURES TO BE PERFORMED AT EACH VISIT

Below is a list of the procedures to be performed during the Screening Phase, Study Drug Treatment Phase, and Follow-up Phase.

If you choose to participate and you have signed and dated the Informed Consent Form, the following procedures will occur over the 20 week duration.

Screening Phase (2 Week Period) Visit 1

Once your study doctor finds you eligible to proceed, Visit 1 will be scheduled within 3 weeks of the initial screening visit. The following procedures will occur;

- The study staff will collect information including;
    - Your date of birth, sex, height, weight, and race;
    - Information related to your current and past health status including: medical history, VMS history, doctor visits conducted in the last six (6) months, past participation in research studies within the last 12 months, and alcohol/drug/tobacco use;
    - You will be asked about any medications you are taking or have taken;
- You will have a complete physical examination including a breast exam
- Urine will be collected for testing related to your general health;
- Vital signs will be taken (this includes temperature, blood pressure and heart rate)
- Blood will be collected for study related laboratory testing (to assess general health status and study related tests such as hormone levels);
- An ECG will be performed to test for heart abnormalities;
- If you have a uterus, a Transvaginal Ultrasound will be performed;
- If you have a uterus an Endometrial Biopsy will be performed;
- You will be given a written questionnaire to assess whether you have a sleep condition known as sleep apnea;
- If you meet all criteria specified above, you will be given a VMS (hot flash) Diary in which to record the frequency and severity of VMS (hot flash) for 14 days. Instructions will be given.

Study Drug Treatment Phase (14 Week Period) 6 Clinic Visits 2-7

At Visit 2

- You will be asked about your medical, drug, smoking, alcohol, and surgical history;
- You will be asked about your any medical issues, surgeries, or medications taken since the last visit;
- You will be asked about any recent drug, smoking, or alcohol use;
- You will be asked about any medications you are currently taking;
- Your vital signs will be taken;
- Blood and urine will be collected for laboratory testing;
- Routine physical exam which includes abdominal, breast, cardiovascular, general appearance, and respiratory exams will be performed;
- If you have a uterus, a Transvaginal Ultrasound will be performed (if not done during at the previous visit);
- If you have a uterus an Endometrial Biopsy will be performed (if not done at the previous visit);
- Your VMS Diary will be reviewed;
- You will be asked about any unusual, unpleasant, or untoward medical occurrence or possible side effects;
- You will be asked to complete multiple (Est. 7) questionnaires aimed at assessing your symptoms as well as some related to general health, mental health and sleep quality;
- You will receive a 14-day blister pack of Study Drug and instructions for its use and your next appointment will be scheduled.

At Visit 3:

- The study staff will confirm you are still eligible to participate in the study;
- Your recent medical history, drug/smoking/alcohol and surgical history will be recorded;
- A routine physical examination and breast exam will be performed;
- Urine and blood will be collected for study related laboratory testing;
- Your vital signs will be checked;
- You will undergo an ECG;
- You will receive a new 14-day blister pack of the Study Drug (as previously described);
- You will return the used Study Drug blister card, whether or not you have any remaining Study Drug;
- Your VMS Diary information will be reviewed;
- You will complete study questionnaires;
- You will be assessed for any side effects of the study medication;
- You will be asked about any study medications you have taken since the last visit;
- You will be provided with instructional materials on what to do if you experience symptom related to body temperature such as feeling cold

At Visit 4, 5, and 6:
The following procedures will be done for the next 3 visits:

- A routine physical examination will be performed;
- Your vital signs will be checked;
- Urine and blood will be collected for study related laboratory testing
- You will complete questionnaires;
- You will receive the Study Drug as previously described;
- You will return the used Study Drug blister card, whether or not you have remaining Study Drug;
- Your VMS Diary information will be reviewed;
- You will be assessed for side effects ;
- Your medications, other than Study Drug, will be reviewed;
- You will receive phone calls from the site staff on weeks where no in clinic visit is occurring to remind you to monitor your temperature if you feel cold or experience certain symptoms. You will be also asked about any side effects since the last visit. The clinic staff may call you to remind you to complete the VMS (hot flash) diary entry each day if they see you have missed days.

Visit 7 (Week 16)
- Weight will be collected;
- A routine physical examination and breast exam will be performed;
- Your vital signs will be checked;
- An ECG will be performed to check for heart abnormalities;
- If you have a uterus, a Transvaginal Ultrasound will be performed;
- If you have a uterus an Endometrial Biopsy will be performed;
- Blood and urine will be collected for study related laboratory testing;
- Your VMS diary device and/or card diary will be collected;
- You will complete various study related questionnaires (approximately 7) to assess your health status;
- You will return the Study Drug blister card, whether or not you have any remaining Study Drug;
- You will be assessed for any side effects; and
- You will be asked about any study medications you have taken since the last visit.

Safety Follow-up Visit 8 (Week 20);
- You will receive a phone call to assessed for any side effects;
- Your medications will be reviewed.

RISKS, SIDE EFFECT AND/OR DISCOMFORTS
It is possible that your VMS may not improve during this Research Study or may even worsen.

If you agree to take part in this research study, you may experience (have) one or more common side effects related to the study medication. In previous studies involving a small number of healthy volunteers and post-menopausal women, the majority of side effects were mild and most were not considered serious. This means the side effects did not interfere with day-to-day activities and were temporary. All potential side effects of drug MT-8554 are not known; such side effects may impact your health in future.

Common Side Effects

- feelings of being hot (67.6%)
- sensation of tingling or pricking (29.1%)
- reduction of sensation in the mouth (25.0%)
- tingling or pricking in the mouth (20.9%)
- feelings of being cold (12.8%)
- abnormality in sense of taste (11.5%)
- mild reduced sense of touch or sensation (11.5%)
- dizziness (6.8%)
- feeling of being cold in hands and feet (6.8%)

You will be provided with an ear-based temperature monitor at Visit 2 to use during the study. Should you feel your body's temperature is changing, such as feeling cold/hot, or other unusual symptoms as listed above, you should measure your body temperature with a thermometer every 30 minutes while the symptoms are occurring. If there is a fall or drop in your temperature reading of below 95^{o} F (35^{o} C) and you confirm it with repeat reading after at least 30 minutes, then stop taking your medication and call your Study Doctor/study staff to inform them about this event. Likewise, if you have symptoms of coldness lasting for some time (few hours), you should stop your medication and call your Study Doctor/study staff to inform them of that this has occurred. Your doctor may ask you to come to the clinic within 3 days to be examined. You may need to stop taking study medication permanently if the doctor believes it is necessary. During any instances of feeling cold, be sure to prevent further heat loss by layering your clothes, drinking hot beverages and avoiding alcohol. In case you are unable to use the ear thermometer provided to you and you choose to use a mouth thermometer, wait at least 20 minutes after drinking any beverage before checking your temperature by mouth.

You will be given an instructional card that outlines this information and you will receive reminder phone calls from your study site to ensure you remember these important instructions.

RISKS RELATED TO STUDY PROCEDURES

Endometrial Biopsy

An endometrial biopsy is a procedure where a small tissue sample is taken from the lining of the uterus (endometrium) for study. The procedure last approximately 5-15 minutes in duration. Some possible risks may include bleeding, pelvic infection, and puncture of the uterine wall with the biopsy device, which is rare. The procedure may cause some cramping and pain. There may be other risks based on your condition. Be

sure to talk about any concerns with your healthcare provider before the procedure. Certain things may interfere with an endometrial biopsy including vaginal or cervical infections. If you are allergic to or sensitive to medicines, iodine, or latex tell your healthcare provider.

Transvaginal Ultrasound Scan
A transvaginal ultrasound is a test where a probe like wand is inserted into the vagina used to look at a woman's uterus, ovaries, tubes, cervix and pelvic area. The process takes approximately 30 minutes. There are no known harmful effects of transvaginal ultrasound on humans. The test is most often painless, although some women may have mild discomfort from the pressure of the probe.

Blood Draws
You will be required to provide blood samples at all study visits except the last telephone call visit. You will experience needle pricks 7 times and it is possible that the process may be associated with localized discomfort or pain, bleeding, bruising, occasional lightheadedness, and/or fainting, and, very rarely, infection at the site of the needle puncture.

ECG
You will undergo an ECG 3 times during the Research Study, and ECGs are associated with mild irritation, slight redness, and itching at the places on the skin where the recording patches or gel are placed. You may have to have your chest shaved for this procedure.

Unknown Risks and Discomforts
In addition to the side effects listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of the Study Drug, including the potential risk for allergic reactions which may also be severe or life-threatening. There is also the potential for interactions between Study Drugs or interactions with another medication. You will be informed in a timely manner, both verbally and in writing of any new information, findings or changes to the way the research will be done that might influence your willingness to continue your participation in this Research Study.

PREGNANCY AND BREAST FEEDING
Currently, we are not fully aware of the effects of the Study Drug on the effect of MT-8554 on developing embryo, fetus (unborn baby), pregnancy or breast feeding.

Because the full effects of MT-8554 on a developing embryo, fetus (unborn baby) or a nursing infant are not known, any female who is pregnant or breast feeding an infant will not be enrolled in this study.

If you are pregnant, or may become pregnant (less than 2 years post-menopausal or not surgically sterile), the Study Drug may lead to new, previously unknown, side effects and this may involve risks to you or your unborn baby. If you become pregnant or suspect that you have become pregnant while in this Research Study, you must stop

taking all Study Drugs and notify your Study Doctor immediately. You will be discontinued from the study drug. This is important as the Study Drug could have harmful effects on an embryo, fetus (unborn child) or a pregnant woman.

POSSIBLE BENEFITS OF THE STUDY

If you receive MT-8554 and it is effective, your VMS such as hot flashes, flushes, or night sweats may improve while taking part in this Research Study. The information we get from this Research Study may help us to provide future better therapies for postmenopausal women suffering from vasomotor symptoms. While there is no guarantee that you will receive personal benefit from participating in this Research Study, and while the Study Drugs are not expected to cure you of VMS, clinical research studies such as this Research Study are a way for doctors to determine if a drug is useful in fighting a disease.

TREATMENT OPTIONS

You have the option to discuss with your Study Doctor not to have treatment or to choose other drugs such as estrogens or anti-depressants to treat your disease. These medicines include commercially available medicines. Your Study Doctor will discuss appropriate alternative treatment options with you.

WHAT IF NEW INFORMATION ABOUT THE STUDY DRUG BECOMES AVAILABLE?

Sometimes new information about the Study Drug is received. You will be made aware of any relevant new findings that become available during the course of this Research Study that may affect your willingness to continue taking part. If this happens, your Study Doctor will contact you as soon as possible, and will discuss whether you should continue in this Research Study. If you decide not to stay in this Research Study, your Study Doctor will make arrangements for your care to continue. If you decide to continue in the study, you may be asked to sign a new consent form.

Also, if new information becomes available, your Study Doctor may stop your participation even without your consent, as further described in the section below entitled Withdrawal from Study and Refusal to Participate. If this happens, the reasons will be explained and arrangements will be made for your care to continue.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE

Your participation in this Research Study is voluntary and you can refuse to participate or stop at any time without stating a reason. Your withdrawal will not affect your access to other medical care to which you would otherwise be entitled.

You may withdraw from the Research Study at any time or choose to not take part. Your decision will not result in any penalty or affect any benefits to which you are entitled.

If you decide to withdraw before the end of the Research Study you will be asked to return to the Study Center for an end-of-study assessment and to return all unused Study Drugs and your diary device. You may also be asked for permission to be

contacted at a later date by your Study Doctor to collect minimum additional data about your health status and physical condition.

Your doctor, Study Doctor, the Sponsor, or the FDA (or other appropriate regulatory agencies) has the right to stop your participation in this Research Study at any time, with or without your consent. Some reasons may include a) if you have an adverse event b) if you need a treatment not allowed in this Research Study, c) if you did not provide correct information related to your medical history, do not keep appointments, follow instructions, or take the Study Drug as instructed, e) if you become pregnant, or f) If it is considered important for your medical safety.

The Sponsor or the FDA may decide to stop this Research Study even if the Study Drug appears to be safe and effective.

Special care will need to be taken when determining if you need to stop study drug. Your Study Doctor will supervise any discontinuation of the study drug with your health as the first priority.

COST OF TREATMENT

The Study Drug used in this Research Study will be given to you free of charge. All clinic, professional, diagnostic, and laboratory fees for tests and procedures that are part of this Research Study will be provided at no cost to you. You and/or your usual health care payer will be responsible for any other health care costs.

PAYMENT FOR PARTICIPATION

You will be reimbursed for your participation in this study. You will receive $54.00 according to the following visit schedule: Screen, Run in visit 2, V3D1, V4, V5, V6, V7/Early Termination. You will be paid following each visit via check request with payment mailed via US mail. Payment arrival can take up 14 or so days.

MEDICAL TREATMENT AND COMPENSATION FOR STUDY-RELATED INJURY

If you become sick or injured as a direct result of taking the Study Drug and/or following the Study procedures (that has been used as described in the Study protocol), The research site will provide you with medical treatment. The Sponsor will reimburse you or the research site for the reasonable and necessary costs of such medical treatment, *provided* that you have followed the instructions of the Study Doctor. The Sponsor has taken out an insurance policy to cover compensation for any personal injury resulting from your taking the Study Drug, provided such personal injury is not due to fault or negligence of the Study Doctor or his Study Staff and team. The Sponsor will not compensate you where the injury has happened because a procedure has been carried out that is not in line with the Study protocol or where the Study Doctor has acted negligently. Any compensation payable for any injury caused to you by taking part in this Research Study will be in line with local guidelines. No other form of reimbursement for study-related injury or illness is offered by the Sponsor. If you have medical insurance, please check with your insurance company to ensure that taking part in this study will not affect your policy. You do not give up any legal rights by signing this

Informed Consent Form. You should immediately contact your Study Doctor at the contact information shown on the first page of this form in the event you experience any Study-related illness or injury.

What if I have questions?

You will be under the care of the study doctor, for the duration of this Research Study. If you have a question, concern, or complaint about any part of this Research Study or if you feel that you have experienced a Study-related injury or reaction to the Study Drug, contact your Study Doctor by using the contact information listed above on the first page.

This Research Study and this Informed Consent Form have been approved by an Independent Institutional Review Board (IRB). The IRB is a group of scientific and non-scientific people who watch over research involving humans by following the guidelines and rules of the FDA. They perform the initial and ongoing ethical review of this Research Study with the study subjects' rights and welfare in mind. You may talk to them at (888)-303-2224, irb@cgirb.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.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Your privacy and your personal information will be protected using measures that follow the requirements applicable in your country for the protection of your personal information. Any information about you that is collected during this Research Study will remain confidential. Your records will be identified by your study subject number (in line with local law). These records will not include your full name or any address details. The information from this Research Study may be published or sent to regulatory authorities or health insurers in your country or other countries where regulatory approval or payment for MT-8554 is required. Your identity will not be released except with your permission, unless necessary for the vital interests of your safety.

The Sponsor and its representatives, monitors, auditors, the FDA, and Copernicus Group Independent Review Board (CGIRB) will be entitled to review your medical files at the hospital (or Study Doctor's office) to check this Research Study's procedures and information, without breaking your confidentiality.

By signing this Informed Consent Form, you are giving permission for the processing and use of your personal information for this Research Study. You are also giving permission for processing of your coded personal information in a database and transferring of the same or any part of it to people and organizations outside your country, where personal data protection laws may be less strict. You may use your

rights under your local data protection laws to access and correct your personal information or ask for it to be deleted. You can object to any further processing of your information by applying to your Study Doctor.

Your Study Doctor may tell your doctor about you taking part in this Research Study and ask them for medical information about you.

There is a risk of loss of confidentiality in research studies. Every effort will be made to protect you and your health information to the extent possible.

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.

HIPAA AUTHORIZATION

If you do not sign the HIPAA Authorization at the end of this document, you cannot participate in this Research Study or receive Study-related treatment.

AGREEMENT TO BE IN THIS RESEARCH STUDY

This Informed Consent Form contains important information to help you decide if you want to be in this Research Study. If you have questions that are not answered in this Informed Consent Form, please ask the Study Doctor or one of the Study Staff. Please answer the following questions by placing your **initials** in the line for **"Yes"** or **"No"**.

1.	Have you understood this Informed Consent Form?	_____ Yes _____ No
2.	Have you had the opportunity to ask questions and discuss this Research Study?	_____ Yes _____ No
3.	Have you received answers you find acceptable to all of your questions?	_____ Yes _____ No
4.	Have you received enough information about this Research Study to make an informed decision?	_____ Yes _____ No
5.	Do you understand you are free to stop the study at any time without having to give a reason and without affecting your medical care to which you would otherwise be entitled?	_____ Yes _____ No
6.	Do you understand your historical medical records may be reviewed and how the information contained in them will be used?	_____ Yes _____ No
7.	Do you agree to have your personal information, medical data, biological samples and laboratory test results collected or learned about you from this Research Study ("Study Information") used in possible future scientific research of Sponsor relating to VMS.	_____ Yes _____ No
8.	Do you understand that the research done with your Study Information may generally help the Sponsor develop new commercial drugs or new treatments for diseases and that you will not receive any direct benefit or compensation if this occurs?	_____ Yes _____ No
9.	Do you understand that you must notify your Study Doctor immediately if you suspect that you may be pregnant?	_____ Yes _____ No
10.	Do you understand that you must notify the Study Doctor if there is any change in the medication prescribed for you by doctors outside this Research Study or if you take any medicines bought without a prescription?	_____ Yes _____ No

If you answered NO to any of the questions listed above you should not sign this form.

Once you have had all your questions answered and you are comfortable participating in this Research Study, please sign in the space indicated below.

By signing this Informed Consent Form I agree that I am freely consenting to be in this Research Study and I agree to all of the conditions of this Research Study described in

this Informed Consent Form and agree to follow the instructions of the Study Doctor and Study Stuff.

OPTION:
I acknowledge that I have read, or had explained to me in language I understand, this consent document and that the study doctor and/or study staff has explained to me the nature and purpose of this Research Study. This explanation included a description of the parts of this Research Study that are experimental, the possible discomforts, symptoms, side effects and risks that I might reasonably expect, and the possible complications, if any, that I might reasonably experience from both known and unknown causes as a result of my participation. I have had the opportunity to ask questions I had about this Research Study and all of the questions I asked were answered to my satisfaction.

I understand that I am free to withdraw this authorization and to discontinue my participation in this Research Study any time. The consequences and risks, if any, of withdrawing from this Research Study while it is ongoing have been explained to me. I understand that such withdrawal will not affect my ability to receive medical care to which I might otherwise be entitled.

I confirm that I have read, or had read to me, this entire Informed Consent Form and all questions answered before I signed this Informed Consent Form.

I will receive a copy of this signed and dated consent form.

Thank you for reading this, and for considering if you will take part in this Research Study.

Printed Name of Subject

Signature of Subject **Date**

The information about the study was described to the subject in language he/she understood.

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent **Date**

Statement of the Witness (when applicable*)
The information in the consent form was accurately explained to, and appeared to be understood by the subject. Informed consent was freely given.

Printed Name of Impartial Witness

Signature of Impartial Witness **Date**

*Impartial Witness: If the subject cannot read, the signature of an Impartial Witness is needed.

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the informed consent process, and
- who reads the informed consent form and any other written information supplied to the subject.

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 ("HIPAA" or the "Privacy Rule"). The Privacy Rule is designed to protect the confidentiality of your personal health information. The document you are reading, called an "Authorization," describes your rights and explains how your health information will be used and disclosed (shared).

In working with the Sponsor, the Study Doctor will use and share personal health information about you. 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.

This includes information in your medical record and information created or collected during this Research Study. This information may include your medical history, physical exam and laboratory test results. Some of these tests may have been done as part of your regular care. The Study Doctor will use this information about you to complete this Research Study.

In most cases, the Study Doctor will use your initials and assign a code number to your information that is shared with the Sponsor. The Sponsor and its representatives may review or copy your personal health information at the Study Site. Regulatory authorities, such as the FDA and the Copernicus Group Independent Review Board (CGIRB) may also review or copy your information to make sure that the Research Study is done properly or for other purposes required by law.

By signing this Authorization, you allow the Study Doctor to use your personal health information to carry out and evaluate this Research Study. You also allow the Study Doctor to share your personal health information with:

- the Sponsor and its representatives
- the IRB
- the U.S. Food and Drug Administration ("FDA")
- other regulatory agencies

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

You have the right to see and get a copy of your records related to this Research Study for as long as the Study Doctor has this information. However, by signing this Authorization you agree that you might not be able to review or receive some of your records related to this Research Study until after this Research Study has been completed. You may choose to withdraw this Authorization at any time, but you must notify the Study Doctor in writing.

If you withdraw from this Research Study and withdraw your Authorization, no new information will be collected for this Research Study's purposes unless the information concerns an adverse event (a bad effect) related to this Research Study. If an adverse event occurs, your entire medical record may be reviewed. All information that has already been collected for this Research Study's purposes, and any new information about an adverse event related to this Research Study, will be sent to the Sponsor.

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

If you do not withdraw this Authorization, it will remain in effect.

If the research site is located in California, Delaware, Illinois, Indiana, Washington, or Wisconsin this authorization will expire on 31Dec2060.

There is no expiration of this authorization except for research conducted in the states listed above.

Your Study Doctor will keep this Authorization for at least 6 years. If you do not sign this Authorization, you cannot participate in this Research Study or receive Study-related treatment. If you withdraw this Authorization in the future, you will no longer be able to participate in this Research Study. 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
I authorize the release of my medical records and personal health information related to this Research Study to the Sponsor and its representatives, the IRB, the FDA, and other regulatory agencies as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

Printed Name of Subject

Signature of Subject **Date**

Statement of the Witness (when applicable*)
The information in the authorization was accurately explained to, and appeared to be understood by the subject. Informed consent was freely given.

Printed Name of Impartial Witness

Signature of Impartial Witness **Date**

*Impartial Witness: If the subject cannot read, the signature of an Impartial Witness is needed.

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the informed consent process, and
- who reads the informed consent form and any other written information