INFORMED CONSENT FORM
FOR
ADULT SUBJECTS, SUBJECTS WHO TURN AGE OF MAJORITY AND PARENTAL/LEGAL GUARDIAN PERMISSION

Sponsor / Study Title:	**EYENOVIA, INC. / "A Multi-center, Double-masked, Placebo-controlled, Phase 3 Study of the Safety and Efficacy of Fixed Combination Phenylephrine 2.5%-Tropicamide 1% Ophthalmic Solution Administered with a Microdose Dispenser for Dilation of the Pupil (The MIST-2 Study)"**
Protocol Number:	**EYN-MYD-TP-32**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Additional Contact(s): (Study Staff)	**«AdditionalStaffMemberContacts»**
Address:	**«PiLocations»**

INTRODUCTION

You are invited to take part in a research study. This study is to test phenylephrine 2.5%-tropicamide 1% ophthalmic solution for dilating the pupil at the time of eye examinations. Eyenovia, Inc. is sponsoring this research study.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

If you are the parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When "you" appears in this form, it may refer to you or your child; "we" means the study doctors and study staff.

BACKGROUND AND PURPOSE

You are being asked to take part in this research study as a volunteer. The study will evaluate an investigational drug for dilation of the pupil. Dilation of the pupil means to increase the size of the black circle in the center of the colored part (the iris) of the eye.

The purpose of this research study is to test the safety and effectiveness of the study drug, phenylephrine 2.5%-tropicamide 1% ophthalmic solution.

The study drug is a fixed combination of the 2 drugs, phenylephrine 2.5% and tropicamide 1%. Each of these drugs is currently marketed as an eyedrop for pupil dilation. The fixed combination study drug is administered as a spray mist, and the amount of drug delivered to the eye is much less than the amount of drug contained in an eyedrop.

The fixed combination study drug is "investigational" because the United States Food and Drug Administration (FDA) has not approved this formulation and dosage of the drug for sale or for use in dilating the pupil.

In this study, the safety and pupil dilation performance of the fixed combination study drug will be compared versus a placebo that has no therapeutic effect (a placebo looks like study drug, but contains no active drug). Both the study drug and the placebo will be sprayed as a mist to the eye by Eyenovia's dispenser, which has been designed to deliver precise low-volume drug doses. You will receive either study drug or placebo at each study treatment visit.

About 90 subjects will take part in this study.

WHAT WILL HAPPEN DURING THE STUDY

Your time in this study will last approximately 3 weeks. You will need to come to the study center for 4 scheduled visits.

Screening:

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

- You will be asked to provide information about yourself, including your date of birth, gender, race, ethnic origin, and personal data (information).
- You will be asked about your current overall health and the condition of both eyes. You will also be asked about any previous conditions or treatments you have had. You must be honest in providing information about your eyes and your overall health. Giving false or incomplete information could have serious health consequences.
- A list of the drugs you are taking now and have taken in the past will be recorded.
- If you are female and able to become pregnant, you will need to have a urine pregnancy test.
- Your vision in both eyes will be checked.

- You will be asked to focus on a target and a bright light will be shone into each eye while a special instrument called a pupillometer measures the size of your pupil. For younger pediatric subjects, the pupil diameter may be measured using a ruler or pupil gage.
- The front part of each eye will be examined using a bright light and a special microscope called a slit lamp. Photographs of your eyes may be taken during this examination. For pediatric subjects who cannot cooperate with a traditional slit lamp examination, a portable slit lamp model may be used.
- Numbing drops will be put in your eyes and your eye pressure will be measured by touching an instrument called a tonometer to your cornea (the clear front window of your eye). Because your eyes are numb, you should feel no discomfort during this procedure.
- Dilating drops will be put in your eyes to make your pupils large. The study doctor will use a magnifying lens and a bright light to examine your retina, which is the back of your eye. The effect of these eye drops will last approximately 4 – 5 hours. During that time, you should not drive a car or operate machinery. You may also need to wear sunglasses outside to reduce light sensitivity.

Note: Younger pediatric subjects who are unable to perform certain testing may have eye pressure and uncorrected visual acuity evaluated using an age-appropriate testing method.

Based on the information gathered from these tests and activities, the study doctor will determine if you meet the requirements for receipt of the study drugs to be administered in the study. If you are qualified to continue, you will be scheduled to return for 3 Study Treatment Visits after your Screening Visit. These visits will occur 2-7 days apart and require that you be available for 3 – 4 hours.

This study will use competitive enrollment. This means that when the designated number of subjects begin drug administration, all further enrollment will be closed. Therefore, it is possible that you could be in the screening phase, ready to begin the study, and be discontinued without your consent if the target number of subjects has already begun the study.

Study Treatment:
The study drugs will be put in your eyes only when you come for your clinic visits. The study drugs will be given as a mist that is sprayed in your eyes by trained study staff. The mist will be sprayed 2 times in each eye over a period of about 5 minutes.

You will receive either the study drug or the placebo at each clinic visit. At the end of the study, you will have received either the placebo twice and the study drug once, or the study drug twice and the placebo once. Neither you nor the person who examines you will know which drug you receive at each visit. In case of an emergency, however, the study doctor can get this information.

The following tests and activities will be performed:

At Study Treatment Visit – Day 1:
- Your vision in both eyes will be checked.

- The size of each of your pupils will be measured in the same way as at the Screening Visit. Your pupillary light reflex, which is how quickly your pupil gets smaller in the presence of a bright light, will also be evaluated.
- The front part of each eye will be examined with a slit lamp in the same way as at the Screening Visit.
- Numbing drops will be put into both eyes and your eye pressures will be measured.
- One of the study drugs will be put into each eye and a video recording of the study drug administration may be made.
- At about 20 minutes, 35 minutes, 50 minutes, 65 minutes, 80 minutes and 120 minutes after study treatment, the size of each pupil will be measured. Your pupillary light reflex will also be periodically evaluated. You will be asked if you are feeling differently since receiving study treatment.
  - About 65 minutes after study treatment, numbing drops will be put into both eyes and your eye pressures will be measured.
- At about 180 minutes after study treatment, your vision will be checked, the size of your pupils will be measured, your pupillary light reflex will be evaluated, and the front part of each eye will be examined with a slit lamp. Photographs of your eyes may also be taken. You will be asked if you are feeling differently since receiving the study treatment.

Note: Younger pediatric subjects who are unable to perform certain testing may have eye pressure and uncorrected visual acuity evaluated using an age-appropriate testing method.

At Study Treatment Visit - Days 2 and 3:

- You will be asked how you are feeling and if you have had any changes in your health or drugs you have taken since your last visit.
- Your vision in both eyes will again be checked.
- The size of each of your pupils will again be measured in the same way as at the Screening Visit.
- The front part of each eye will again be examined with a slit lamp in the same way as at the Screening Visit.
- Numbing drops will be put into both eyes and your eye pressures will again be measured.
- One of the study drugs will be put into each eye and a video recording of the study drug administration may be made.
- At approximately 20 minutes, 35 minutes, 50 minutes, 65 minutes, 80 minutes and 120 minutes after study treatment, the size of each pupil will be measured and your pupillary light reflex will also be periodically evaluated. You will be asked if you are feeling differently since receiving study treatment.
  - About 65 minutes after study treatments, numbing drops will be put into both eyes and your eye pressures will be measured again.
- At approximately 180 minutes after study treatment, your vision will be checked, the size of your pupils will be measured, your pupillary light reflex will be evaluated, and the front part of each eye will be examined with a slit lamp. Photographs of your eyes may also be taken. You will be asked if you are feeling differently since receiving study treatment.

Note: Younger pediatric subjects who are unable to perform certain testing may have eye pressure and uncorrected visual acuity evaluated using an age-appropriate testing method.

After Study Treatment:
The study drugs will be given to you only during the study and not after the study is over. If your pupil diameter is larger than baseline (screening) at the time of study exit, you may be asked if you would be willing to stay at the clinic for additional measurements of your pupil during the remainder of the day. These additional measurements help determine how long the study drug works. You are not required to stay for these additional measurements if you do not wish to.

If you have a problem with your eyes related to the study drug and the problem continues after the end of the study, you may need to return to the clinic for additional follow-up.

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

- Tell the truth about your medical history, current conditions and any prescription or over-the-counter drugs or supplements you are taking.
- Tell the study doctor if you have been in a research study during the past 1 month or are in another research study now. You will not be able to enroll in any other clinical study of an investigational drug or device until you have completed participation in this study.
- Go to all your scheduled study visits.
- Follow all instructions given by the study doctor and study staff.
- Tell the study doctor or study staff about any changes in your health or the way you feel.
- If you typically wear contact lenses, on the days the study drug is given, you may not wear your contact lenses until after you have completed all study tests and activities. Instead, you may need to use your eyeglasses during this time.
- If you are female and able to become pregnant, you will be asked to use medically acceptable birth control to prevent pregnancy.

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS
As with any drug, there are risks that side effects may occur. While each individual drug in the fixed combination solution is currently marketed in the United States as eyedrops for dilation of the pupil, the United States Food and Drug Administration (FDA) has not approved this formulation and dosage of the drug for sale or for use in dilating the pupil. The fixed combination phenylephrine 2.5%-tropicamide 1% ophthalmic solution has not been evaluated by the FDA.

After each drug is given, your vision may be blurry. You should not drive until your vision returns to normal. You may also need to wear sunglasses when outside if you experience light sensitivity. The following side effects have been reported with use of phenylephrine and tropicamide in the eye. You may experience some or all these side effects listed below:

Likely

- Temporary blurred vision
- Temporary light sensitivity

- Eye stinging at the time of drug administration

Less Frequent

- Itching, burning, stinging or foreign body sensation in the eye after drug administration
- Increased pressure in the eye
- Dryness in the eye
- Increased tearing in the eye
- Rash or allergic skin reaction
- Blood pressure increase or decrease, which may result in fainting
- Abnormally fast, slow, or irregular heart beat
- Headache
- Dryness of the mouth
- Nausea and vomiting
- Unhealthy skin appearance around the eye
- Excitability, behavioral disturbances, or psychotic reactions

RISKS OF STUDY PROCEDURES

- Eye Pressure Measurement: There is a slight risk that you may receive a minor scratch to your cornea from the instrument that measures eye pressure. Minor scratches of this nature usually heal within 24-72 hours.
- Retina Exam: The eyedrops used to make your pupil large so the study doctor can see your retina may cause blurred vision or temporary glare. The eyedrops could also make your eye pressure go up. You may also have an allergic reaction to these drops.

UNFORESEEN RISKS

There may be other risks or side effects that are currently unknown. Allergic reactions can occur with any drug. 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. It is important to tell the study doctor if you start to experience any new symptoms after the study drug is administered. Your study doctor will monitor you for side effects throughout this study.

Also, there may be unknown risks to a pregnancy, embryo, or fetus if you become pregnant.

BIRTH CONTROL RESTRICTIONS

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

To reduce the risk of pregnancy, you should use an effective method of birth control while you are participating in this study. Acceptable methods of birth control are intrauterine devices (IUDs), hormonal drugs, barrier devices and abstinence. The Investigator or study staff will discuss this with you.

If you become pregnant while you are participating in this study or within the 4 weeks after the last study treatment visit, tell your Investigator or the study staff immediately. The drug will not be given again and your participation in this study will be ended.

ALTERNATIVES TO PARTICIPATION
This study is for research purposes only. The only alternative is to not take part in this study.

NEW FINDINGS
Any new important information that is discovered during the study that may influence your willingness to continue participation will be provided to you.

BENEFITS
This study is for research purposes only. There is no direct benefit to you from your taking part in the study. Information learned from the study may help other people in the future.

COMPENSATION FOR PARTICIPATION
You will be paid up to a total of $xx.xx if you complete this study. You will be paid for the visits you complete according to the following schedule:

Visit	Payment
Screening Visit	
Study Treatment Visit - Day 1	
Study Treatment Visit – Day 2	
Study Treatment Visit – Day 3	
Study Treatment Day 3 – Post 180 Minutes (optional)	

If you do not complete the study for any reason, you will be paid for each study visit you do complete. If you do not complete an entire study visit, you will not receive payment for that visit. You will be paid _____ ***'after each visit', 'annually', 'bi-weekly', etc.***

If you have any questions regarding your compensation for participation, please contact the study staff.

CONFIDENTIALITY
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 Investigator, the Sponsor (or persons working on behalf of the Sponsor), and under certain circumstances, the United States FDA and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records that 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 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.

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should tell the healthcare professional treating you that you are taking part in this study. If you tell the study staff that you think you have been injured, they will help you get the care you need.

If you are injured as a result of taking the study drug(s) or from procedures done for this study, the Sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. You will not lose any of your legal rights or release the Sponsor, the Investigator, the study staff, or study site from liability for their mistakes by signing this consent document.

To pay medical expenses, the Sponsor will need to know some information about you, such as your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the Sponsor must check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

COSTS

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

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 Investigator 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 taking part in this study.

An 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 Advisor
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00029864.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to take part in this study is voluntary. You may choose to not take part, or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

If you are an employee of this study center or a family member of someone who is an employee at this center and you decide to take part in this study, you may leave the study at any time for any reason without penalty or prejudice.

If you decide not to take part in the study or to withdraw after it has started, this decision will have no effect on employee performance evaluations, job advancement or current employment status. No action will be taken against an employee based on information the study doctor obtains due to their study participation.

The Investigator or the Sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the Investigator may ask you to have some end-of-study tests for your safety.

Primary Health Care Provider Notification Option

I consent to having my family doctor or primary health care provider notified by the study center of my participation in this study and/or any significant findings related to my health (please check yes or no).

❒Yes (If yes, please complete the information below)
❒No

Name and address of family doctor or primary health care provider:	Name: Address:
Telephone and Fax Number:	Tel: Fax:

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

STATEMENT OF PARENTAL / LEGAL GUARDIAN PERMISSION

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree for my child to participate in this study until I decide otherwise. I do not give up any of my or my child's legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____ ____/____/____
Signature of Parent/Legal Guardian (if subject is under age of majority) Date

_____
Printed Name of Parent/Legal Guardian (if subject is under age of majority)

_____
Printed Name of Second Parent

_____ _____/____/_____
Second Parent Signature Date

Second parent permission not documented, reason (person obtaining consent will initial and check all that apply):

Initials of person obtaining consent

☐2nd Parent is deceased: _____
☐2nd Parent is unknown: _____
☐2nd Parent is incompetent: _____
☐2nd Parent does not have legal custody: _____
☐2nd Parent "Not Reasonably Available": _____
- ☐ 2nd Parent Not available by telephone
- ☐ 2nd Parent Not available by email
- ☐ 2nd Parent Not available by mail
- ☐ 2nd Parent Not available by fax

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

FOR CHILDREN WHO BECOME AGE OF MAJORITY DURING THE STUDY

I have been told that my parents/legal guardian agreed for me to participate in this research study as a minor. I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all my questions have been answered to my satisfaction. I voluntarily agree to continue to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____

Printed Name of Impartial Witness

_____ _____

Signature of Impartial Witness Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include

- Representatives of Eyenovia, Inc.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this research, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe.
- To compare the study drug performance to that of phenylephrine 2.5% and tropicamide 1%.
- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

STATEMENT OF PARENTAL / LEGAL GUARDIAN PERMISSION

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree for my child to participate in this study until I decide otherwise. I do not give up any of my or my child's legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____ ____/____/____
Signature of Parent/Legal Guardian Date
(if subject is under age of majority)

_____
Printed Name of Parent/Legal Guardian (if subject is under age of majority)

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date

FOR CHILDREN WHO BECOME AGE OF MAJORITY DURING THE STUDY

I have been told that my parents/legal guardian agreed to the use and disclosure of my Protected Health Information as outlined in this document. I have read and understand the information in this authorization. I have had an opportunity to ask questions and all my questions have been answered to my satisfaction. I continue to authorize the use and disclosure of my Protected Health Information. I will receive a copy of this signed and dated authorization.

_____

Subject's Printed Name

_____ _____

Subject's Signature Date

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. This Authorization document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____

Printed Name of Impartial Witness

_____ _____

Signature of Impartial Witness Date