INFORMATION AND CONSENT FORM

For Parents/Guardians/Participants 18+

Study Title: Collagen Crosslinking with Ultraviolet-A in Asymmetric Corneas

Study #: CXL-1

Sponsor: CXLUSA

Study Doctor: Daniel F. Goodman MD

Daniel F. Goodman, MD, A Medical Group, Inc.
2211 Bush St., 2nd Fl.
San Francisco, CA 94115

Telephone Number: (415) 474-3333

After Office Hours: (415) 474-3333

For California participants: Before you read this consent form, you should read and sign a copy of the California Experimental Subject's Bill of Rights. Ask the study staff for a copy of this document if you haven't already received one.

The study doctor wants to know if you would like to be part of a research study. This form describes the study in order to help you decide if you want to participate. This form will tell you what you will have to do during the study and the risks and benefits of the study.

You are being asked to read the following material to help ensure that you are informed of the nature of this research study and of how you will participate in it, if you consent to do so. Signing this form will indicate that you have read this form and that you give your consent to participate in the study. Federal regulations require written informed consent prior to participation in any research study so that you can read about the nature and the risks of your participation as described in the consent form, and can decide to participate or not participate in a free and informed manner.

If you have any questions about or do not understand something in this form, you should ask the study doctor or study staff. Discuss your participation with anyone you choose in order to better understand this study and your options. Do not sign this form unless the study doctor or study staff has answered your questions and you decide that you want to be part of this study.

Participating in a research study is not the same as getting regular medical care. The purpose of regular medical care is to improve your health. The purpose of a research study is to gather information. Being in this study does not replace your regular medical care.

When reading this form, please note that the words "you" and "your" refer to the person in the study rather than to a parent or guardian who might sign this form on behalf of the person in the study.

PURPOSE

You have corneal weakness caused by keratoconus or another condition affecting the cornea of your eye (the clear, front part of your eye). You are being invited to participate voluntarily in a research study to evaluate the effectiveness of an investigational procedure that uses ultraviolet-A (UVA) light-induced cross-linking of corneal collagen (CXL) on people with corneal conditions that affect their vision and/or the health of their eyes. An "investigational procedure" is a procedure that is being tested and is not approved for use as a treatment in the United States by the U.S. Food and Drug Administration (FDA).

The study doctor is doing the CXL procedure to see if it strengthens the structure of participants' corneas to increase the stability of the cornea. It is hoped that the UVA light procedure will improve the shape of the cornea and reduce astigmatism in participants. There is no guarantee that being in this study will help you.

In this study, the study doctor will be using a device that emits UV light which is critical to the cross-linking procedure. This light source is being used because this UV light device has been adapted to emit the correct type and amount of UV light for corneal collagen cross-linking. In this study, participants will also be given vitamin eye drops (vitamin B2, also called riboflavin) during the study procedure to enhance the strengthening of their cornea. Riboflavin solution will be given every 30 seconds to 5 minutes for 15 to 30 minutes. The cornea will then be exposed to ultraviolet light at a wavelength of 340 to 400 nm, and energy per area of approximately 2.7 J/cm^2 to 5.4 J/cm^2 for 15 to 30 minutes.

Be aware that this form refers to the CXL procedure performed in this study as the "study procedure."

HOW DO I KNOW IF I CAN BE IN THIS STUDY?

The first part of the study is called a screening period. During this time, the study doctor will decide if you qualify to be in the main part of the study.

NUMBER OF SUBJECTS AND DURATION OF PARTICIPATION

It is planned that about 1500 to 2000 participants, age 12 and above, will be enrolled in this study. One or both of each participant's eyes may receive the study procedure.

If you decide to be in this study and the study doctor says you can be in the study, your participation in this study will be up to nine months. You will have to come to the study center about 6 times during the study. The study staff will tell you when to come in for your study visits. You should ask the study staff how long your visits will last.

PROCEDURES

If you decide to be in this study and you wear contact lenses, you might have to stop using your regular contact lenses on some days during the study. If you stop wearing your regular contact lenses during the study, your vision may be unclear in certain situations.

Before you can start the study, the study doctor or study staff will talk to you about the study. Then you have to read and sign this consent form before the study doctor or study staff can begin the screening period to see if you qualify to be in the main part of the study. Please note that if you are the parent or guardian of a child in the study, your child may have to sign a separate assent form before the study doctor or study staff can begin the screening procedures.

After you sign this form, the study doctor or study staff will do the things listed below when you come in for study visits. If you would like more information about the tests and procedures done at each study visit, ask the study doctor or study staff.

If you choose to participate in the study and the study doctor says you can be in the study, the following procedures will be performed:

Visit 1 (Preoperative): After you review and sign this consent form, your medical and contact lens history will be recorded. You will have tests performed to measure your vision with and without the use of your glasses or contact lenses (uncorrected visual acuity and best corrected visual acuity tests). You will take a vision test that determines how well you see with the best possible correction of the eye (manifest refraction). You will take a test that measures the thickness of your cornea (pachymetry).Your eyes will be scanned with a camera to map the surface of your cornea (topography). You will have a high magnification examination of your eyes (slit lamp examination). Your retina (the light sensitive part inside the inner layer of your eye) will be examined (undilated or dilated fundus exam). You will have an intraocular pressure (IOP) test done to check the fluid pressure inside the eye. You may also fill out a quality of life and/or comfort survey. Ask the study doctor if you have questions about what will be asked on the surveys in this study.

Visit 2 (Day of CXL Study Procedure): You will have the collagen cross-linking study procedure performed on the cornea of your eye(s) according to your study doctor's standard procedure. You may have the study procedure performed on one or both eyes on the same day or on different days.

After the study procedure, your cornea will be rinsed with saline solution or artificial tears, your eye will receive drops of antibiotic and anti-inflammatory, and your eye may be dilated. The study doctor will tell you what times during the day to use the eye drops and how many drops to put in your eye(s). The study doctor will also talk to you about things you can do if you have pain or discomfort after the study procedure.

A bandage contact lens may be placed on your eye(s) at the end of the procedure to help with healing of the cornea. In most cases, this will be removed at Study Visit 3 or 4, when the study doctor will examine your eye and see how it is healing.

The study doctor may insert a small punctal plug into your tear duct to help keep tears in your eye.

You may also fill out a quality of life and/or comfort survey.

If you have the study procedure performed on both eyes, the study doctor may perform some of the procedures on one eye and then the other, or to both eyes at the same time. Ask the study doctor if you have questions about the procedures included in the cornea cross-linking procedure.

Visit 3 (1 day after the procedure): On the day following the CXL procedure, you will come to the study center to have a test performed to measure your vision without the use of your glasses or contact lenses (uncorrected visual acuity). You will have a high magnification examination of your eyes (slit lamp examination). You may also fill out a quality of life and/or comfort survey.

Visit 4 (3 to 7days after the procedure): You will have an uncorrected visual acuity test. You will have a slit lamp examination. The contact lens bandage (if one was placed) may be removed. You may also fill out a quality of life and/or comfort survey.

Visit 5 (3 months after the procedure): You will have uncorrected visual acuity and best corrected visual acuity tests. You will take a manifest refraction test. You may have a pachymetry test. You will have a topography scan performed. You will have a slit lamp examination. Your medical and contact lens history will be recorded. You will have an IOP test. You may also fill out a quality of life and/or comfort survey.

Visit 6 (6 to 9 months after the procedure): You will have uncorrected visual acuity and best corrected visual acuity tests. You will take a manifest refraction test. You will have a pachymetry test. You will have a topography scan. You will have a slit lamp examination. Your medical and contact lens history will be recorded. You will have an IOP test done. You may also fill out a quality of life and/or comfort survey.

You will then exit the study.

Early Termination: Your study doctor may stop your participation in the study at any time and may stop the study at any time for reasons he/she determines are appropriate. You may need to exit the study for some reason before the final visit even if you do not want to.

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for all visits with the study doctor.
- Tell the study doctor or study staff about any changes in your health or the way you feel.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

Ask the study doctor for the estimated recovery time of your participation in this study.

Your regular medical care might include some of the tests and procedures that are required for participation in the study. The study doctor or member of the study staff can answer any questions you may have about the tests and procedures that are not part of your regular medical care.

After the study is over, you should talk to the study doctor about your future treatment of your eye(s).

RISKS

What can happen if I have the CXL procedure?

All medical procedures carry a risk of side effects.

Ask the study doctor if you have questions about the signs or symptoms of any side effects you read about in this consent form.

Although this procedure has been used for more than 10 years, there may still be some risks or side-effects that are not known yet.

The risks that are known are divided into sections below:

Removing the Outer Tissue of the Eye

The most common side effects of epithelial (outer layer of the eye) removal include moderate pain, and blurred vision that typically lasts up to 5 days. There is also risk of infection, corneal inflammation, corneal haze, dry eye, and delays in epithelial healing.

Riboflavin Drops

The most common side effects from using riboflavin drops are blurred vision, and mild redness or stinging in the eyes. Uncommon allergic side effects (discussed below) can also occur.

UV-A Light

The most common side effects of the UV-A light source include blurred vision, mild redness, or stinging in the eyes. Another side effect of the UV-A light source is if too much UV light is absorbed, eye structures such as the cornea, the lens and the retina can be damaged. This can lead to temporary loss of vision for 24 to 48 hours. It may also lead to additional surgery. You should ask the study doctor what kind of surgery may need to be performed if damage to your eye occurs. An uncommon side effect may be changes to other layers of your cornea.

Antibiotics

The most common side effects of topical antibiotic eye drops include: ocular irritation (pain, swelling, burning, dryness, or itchiness of the eye).

Other risks

There may be side effects or discomforts from the medications or study procedure that are not yet known.

Eye drops used to dilate your eyes can cause blurred vision and sensitivity to light. You should not drive for at least 4 hours (and sometimes longer) after this procedure.

Although very unlikely, a serious infection or inflammation can lead to permanent loss of vision, or even loss of the eye. Additional surgery may rarely be needed.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these problems are related to the study procedure.

You should ask the study doctor about the risks of using medication you receive to help treat or prevent pain, discomfort or inflammation following the study procedure.

There is a risk of loss of confidentiality of your information that is used in this study. You will read more about the protection of your information later in this form. Please ask the study doctor if you would like to know more about how your information will be protected while you are in this study.

Could I have an allergic reaction?

Sometimes people have allergic reactions to drugs or product ingredients. Some things that happen during an allergic reaction are:

- a rash
- having a hard time breathing
- wheezing
- a sudden drop in blood pressure (making you feel dizzy or lightheaded)
- swelling around the mouth, throat, or eyes
- a fast pulse
- sweating
- itching of the eye
- redness to the eye
- swelling/redness to the eyelids

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

If I stop my regular corrective contact lenses what are the risks?
If you stop your regular corrective contact lenses to be in the study, your vision might be impaired, which could make you uncomfortable. Please tell the study doctor or study staff right away if you have problems when you stop using your regular corrective contact lenses.

Could I have any other problems with my health if I do this research study?

It is possible that receiving the procedures and drugs in this study with your regular medications or supplements may change how these procedures and drugs, your regular medications, or your regular supplements work. It is very important that you tell the study doctor about all medications or supplements you are taking during the study.

If the study doctor learns any new information about the collagen cross-linking procedure that might change your mind about continuing in the study, the study doctor or study staff will tell you about it. The study doctor will also tell you if new treatments become available for your condition.

Are there risks if I am pregnant or nursing a child during the study?

A woman cannot be in this study if she is:

- pregnant
- planning to become pregnant during the study
- nursing a child

If you are pregnant or nursing a child while receiving the study procedure, there may be risks to your unborn baby or nursing child. Nobody knows what these risks are right now.

If you think you are pregnant during the study, you must tell the study doctor immediately. Women who become pregnant during the study may have to leave the study. The study doctor may ask for information about the pregnancy and the birth of the baby. The study doctor may share this information with the sponsor and Quorum Review, a group of people who review research studies to help protect the rights and welfare of research participants.

COST OF BEING IN THE STUDY

While you are in the study, you still need to get regular medical care. You (and/or your health care payer) will still have to pay for the costs of your regular medical care that are not a part of this study.

You (and/or your health care payer) will be charged for the procedure. You and/or your health care payer will have to pay for all medications and supplies (including antibiotics, anesthetics, analgesics, eye drops), procedures, tests, and study visits during the study. **Before you agree to be in this study, you should contact your health care payer to see if your plan will cover the costs required as part of your participation.** To find out more about costs, you can ask the study doctor or study staff.

BENEFITS OF BEING IN THE STUDY

There is no guarantee or promise that you will receive any clinical benefits from this study. The study procedure may help the condition of your cornea, but there is no guarantee that being in this study will help you. Your optical health/vision might not get better or may even get worse while you are in this study. Information from this study might help researchers to come up with new tests or procedures to help others in the future.

However, clinical studies have shown over the past 10 years that the cross-linking procedure stops the progression of the condition in the majority of cases. As well, many people also experience an improvement in their uncorrected and best-corrected vision.

ALTERNATIVE TREATMENTS

You do not have to be in this study to get help for your corneal condition. Your eyes could be treated with other medications or you could use (or continue to use) corrective glasses or contact lenses. You could have a surgical procedure such as a corneal transplant or placement of intracorneal rings in order to improve your vision.

The study doctor will talk to you about other things you can do to treat your corneal condition, including the important risks and benefits.

FINANCIAL DISCLOSURES

A company called CXLUSA, the sponsor of the study, is paying for IRB review and paying Innovative Medical Data, Inc. to run the study. The study doctor is not being paid by CXLUSA to participate in this study.

CONFIDENTIALITY

A report of the results of this study may be published or sent to the appropriate health authorities in any country in which the study procedure is marketed, but your name or other information that could be used to identify you will not be disclosed in these documents. Your name may be disclosed to the governing health authorities, or the U.S. Food and Drug Administration (FDA), if they inspect your medical records. If the FDA inspects the study records, information such as names, medical records and other personal information may be reviewed by the FDA. By participating in this research study your study records will become part of the research database and you cannot prevent the FDA from having access to your study records and results of your study participation. This information may be used in a submission to the FDA at some point in the future.

Appropriate precautions will be taken to maintain confidentiality of medical records and personal information, as described in this form.

The following people will have access to the data:

- The study doctors and study staff
- The sponsor, CXLUSA.

- Innovative Medical Data, Inc. (an agent for the sponsor)

And may be inspected and/or copied by:

- The Food and Drug Administration (FDA)
- Department of Health and Human Services Agencies (DHHS)
- Governmental agencies in other countries
- Quorum Review
- Innovative Medical and Epidemiologic Data Solutions (IMEDS), an agent for the sponsor

The study doctor or sponsor may use some facts about your being in this study in books, magazines, journals, and scientific meetings. If this happens, no one will use your name or other information that could be used to identify you.

Please note that the study doctor or study staff may also share personal information about you if required by law (for example, if the study doctor or study staff suspects that you are going to harm someone or yourself). If you have questions about this, please ask the study doctor.

COMPENSATION FOR INJURY

The sponsor does not plan to reimburse you for expenses for medical treatment if you get hurt or sick as a direct result of the CXL procedure being administered in this study. Appropriate medical treatment will be available, if required. The sponsor does not plan to provide any compensation.

Participation in this research study may put you at risk for injury. In the event of an injury, treatment will be billed to you or your health care payer. This treatment may be provided by your study doctor or another physician. You are not waiving any legal rights by signing this document, nor are you releasing the sponsor from liability for negligence. To ask questions about this, talk to the study doctor or study staff.

Be aware that your health care payer might not cover the costs of study-related injuries or illnesses.

WILL I GET PAID?

You will not get paid for being in this study.

WHO CAN I TALK TO ABOUT THIS STUDY?

In the event of an emergency, dial 911 immediately.

If you require emergency care, be sure to tell the emergency care provider about your participation in this study. Contact the study doctor as soon as possible.

You can ask questions about the study at any time. You can call the study doctor at any time if you have any concerns or complaints. You should call the study doctor at the phone number

listed on page 1 of this form if you have questions about the study procedures, study costs (if any), study payment (if any), or if you get hurt or sick during the study.

Quorum Review reviewed this study. Quorum Review is a group of people who review research studies to protect the rights and welfare of research participants. Review by Quorum Review does not mean that the study is without risks. If you have questions about your rights as a research participant, if you are not able to resolve your concerns with the study doctor, if you have a complaint, or if you have general questions about what it means to be in a research study, you can call Quorum Review or visit the Quorum Review website at www.quorumreview.com.

Quorum Review is located in Seattle, Washington.
Office hours are 8:00 AM to 5:00 PM Pacific Time, Monday through Friday.
Ask to speak with a Research Participant Liaison at 888-776-9115 (toll free).

VOLUNTARY PARTICIPATION IN THE STUDY

Your participation in this study is voluntary. You can decide not to be in the study and you can change your mind about being in the study at any time. There will be no penalty to you, and you won't lose any benefits. If you want to stop being in the study, tell the study doctor or study staff.

If you stop being in the study early, the study doctor or study staff may ask you some questions about being in the study. To help you leave the study safely, the study doctor may ask you to participate in more tests.

The study doctor or sponsor can remove you from the study at any time, even if you want to stay in the study. This could happen if:

- The study doctor believes it is best for you to stop being in the study.
- You do not follow directions about the study.
- The sponsor stops the study for any reason.

If you stop being in the study early, the study doctor or study staff may ask you some questions about being in the study. To help you leave the study safely, the study doctor may ask you to participate in more tests.

WHO WILL USE AND SHARE INFORMATION ABOUT MY BEING IN THIS STUDY?

This section explains who will use and share your study-related health information if you agree to be in this study. If you do not sign this form, you cannot be in the study.

During the study, the study doctor and study staff will use, collect, and record health information about you (your "records"). Your records will include any information about you that the study doctor needs to do the

study, including information from the tests described above. Your records also will include other identifying information about you, such as your name and address.

If you sign this form:

- You allow the study doctor and study staff to use your records to carry out this study.
- You allow the study doctor to share your records with the sponsor, CXLUSA; people who work with or for the sponsor; and other researchers involved in this study. These people will use your records to review the study and to check the safety and results of the study.
- You allow the study doctor to share all of your records and this signed consent form with the FDA and other government agencies in the United States and other countries. The study doctor may also share your records with Quorum Review, a research ethics board that reviews this study. These agencies may use your records to check the study information, how researchers are doing the study, participants' safety, and the results of the study.
- You allow the study doctor to share your records with your health care payer to resolve your claim if you are hurt because of being in this study. If this happens, the study doctor or the sponsor may share your records with their insurance carriers to resolve your insurance claim, and the study doctor may also request medical records from your other health care providers to learn more about your condition.
- You allow the study doctor to share your records with your health care payer in order to collect payment for study costs (even if your health care payer does not cover those costs).

There are national and state laws that make the study doctor protect the privacy of your records. However, you do not have a guarantee of absolute privacy because of the need to share your information. After the study doctor shares your records with the sponsor and others, the laws may no longer protect the privacy of your records. The sponsor or others may share your records with other people who do not have to protect the privacy of your records.

You may or may not have the right to see and copy your health records related to this research. You might not be able to see or copy some of your records until after all participants finish the study.

You can cancel this consent to use and share your records at any time. If you want to cancel your consent, you must write a letter to the study doctor. If you cancel your consent you will not be able to continue in the study.

Even if you cancel your consent and leave the study early, the study doctor and study staff will still be able to use and share your records that they have already collected as described above.

This consent to use and share your records expires in 50 years.

You will receive a signed copy of this form for your records.

Indicate your agreement to the use and sharing of your records by checking the box below and signing:

☐ I agree to the use and sharing of my records related to this study as described above.

_____ _____

Signature of Parent/Guardian/Participant 18+ Date

AUTHORIZATION

I have read about the methods, inconveniences, risks, and benefits of this research study described in this form. This study has been explained to me and my questions have been answered. I may ask questions at any time during the study, and I can withdraw from the study at any time without penalty or loss of benefits.

New information developed during the course of this study that may affect my willingness to continue in this research project will be given to me as it becomes available. I voluntarily agree to be in this study.

I do not give up any of my legal rights by signing this form. A copy of this signed consent form will be given to me.

Name of Participant (Print)	Date of Birth
Signature of Participant (if age 18+)	Date

If participant does not have the legal capacity to consent to their participation:
I certify that under state law I am the parent/guardian of the participant named above and that I am authorized to sign this consent to his/her participation in the research study described above.

Name of Parent/Guardian (Print)	Relationship to Participant
Signature of Parent/Guardian	Date

I attest that the participant and/or parent/guardian named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

Name of Person Explaining Consent (Print)	
Signature of Person Explaining Consent	Date

I attest that I or my representative discussed this study with the participant and/or parent/guardian named above.

_____

Signature of Principal Investigator or Sub-Investigator