CUSTOM*FLEX*® ARTIFICIAL*IRIS*

Patient Information

WHAT YOU NEED TO KNOW ABOUT THE CUSTOM*FLEX*® ARTIFICIAL*IRIS*

A CUSTOM-MADE IMPLANT TO TREAT FULL AND PARTIAL IRIS DEFECTS

Patient Information Brochure

CAUTION: U.S. Federal law restricts this device to sale by or on the order of a physician.

CAUTION: U.S. Federal law restricts this device to practitioners who have been trained and have experience in the surgical management and treatment of aniridia.

This brochure has been provided to assist you in your understanding of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* procedure. Read the brochure in full and discuss the benefits and risks with your eye care provider. Prior to any type of surgery, it is important to make sure all your questions are addressed.

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Table of Contents

List of Figures:

2 Glossary

Albinism	Inherited condition present at birth, characterized by a lack of pigment that normally gives color to the skin, hair and eyes.
Aniridia	An eye disorder characterized by a complete or partial absence of the iris
Anterior Chamber	The fluid-filled space inside the eye between the iris and the cornea's innermost surface, the endothelium.
Antibiotic Eye Drops	Medication used to prevent or treat infections of the eye.
Anti-inflammatory Eye Drops	Medication used to prevent or treat inflammation of the eye.
Aqueous Humor	The clear fluid filling the anterior chamber.
Best Corrected Visual Acuity	The best vision that can be obtained with glasses.
Cataract	Clouding of the lens inside the eye that may cause loss of vision.
Cones	Photoreceptors in the retina responsible for vision at high light levels.
Congenital	Present at birth.
Contraindications	Specific situation in which a drug, device, procedure or surgery should not be used because it may be harmful to the person.
Cornea	The clear front surface of the eye, which bends rays of light to focus an image of objects on the retina.
Custom-Made	Made specifically for an individual patient
Diabetic retinopathy	Disease of the retina caused by diabetes that involves damage to the tiny blood vessels in the back of the eye.
Epithelial Ingrowth	A condition in which cells from the surface of the **cornea** (the corneal epithelium) start growing underneath the corneal flap that's produced in the LASIK procedure.
FDA	Food and Drug Administration. This is the governmental agency that approves medical technology for use in the U.S.A.
Foreign body sensation	Feeling of grittiness or something in the eye.
Glare	Scatter from bright light that decreases vision.
Glaucoma	A group of diseases that cause increased pressure in the eye, and can result in vision loss by damaging the optic nerve.

Halo	Circular flares of light around bright lights in dim lighting conditions.
Haze	Cloudiness of the cornea.
ICE Syndrome	Iridocorneal endothelial syndrome (ICE) is a group of conditions related to changes in corneal cells and the iris.
Inflammation	The body's reaction to trauma, infection, or a foreign substance, often associated with pain, redness, swelling, and/or loss of function.
Iris reconstruction	Repair of the shape and appearance of the iris using sutures.
Intraocular lens	An artificial lens surgically implanted into the eye with cataract or other surgeries.
Intraocular Pressure	Fluid pressure inside the eye.
Iridectomy	A surgical procedure to remove part of the iris.
Iridocyclitis	Inflammation of the iris and the muscles and tissues involved in focusing the eye.
Iris	The colored part of the eye between the cornea and the lens that controls the amount of light reaching the retina by changing the size of the pupil.
Keratitis	Inflammation of the cornea.
Lens	A clear structure behind the iris that helps focus rays of light, or an image, on the retina.
Macula	The central part of the retina responsible for sharp, detailed and color vision.
Microphthalmus	One or both eyes are abnormally small and have anatomically malformations.
Mydriasis	Dilation of the pupil of the eye.
Optic nerve	Connects the eye to the brain, carrying light impulses formed by the retina.
Pathology	Any deviation from a healthy, normal or efficient condition.
Photophobia	Painful sensitivity to bright light.
Photosensitivity	Uncomfortable sensitivity to day or night-time lighting.
Punctal plug	A small medical device that is inserted into the tear duct of an eye to block the duct.
Pupil	The opening in the center of the iris. The iris changes the size of the pupil and controls how much light enters the eye.

Retina	The membrane in the eye that receives the images you see and sends them to your brain.
Retinal detachment	Retina separates from its connection at the back of the eye.
Rods	Photoreceptors in the retina responsible for vision at low light levels.
Sequelae	A condition that is the consequence of a previous disease or injury.
Starbursts	Troublesome, bright circles of light that surround headlights and other light sources.
Stargardt's retinopathy	Inherited disease that causes cells in the main focusing area of the retina to deteriorate.
Steroids	Medications used to reduce inflammation or the body's healing response after injury or disease.
Uncorrected visual acuity	Vision that can be obtained without glasses or contact lenses.
Visual Acuity	The measurement of your vision on an eye chart.
Vitreous	Gel-like fluid that fills the inside of the eye.

3 Introduction

This booklet has important information to help you decide whether to have CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery to repair your **iris** defect and improve the quality and quantity of your daily living.

Please read this brochure completely and discuss the risks and benefits with your eye care professional. Your doctor can help you decide if the CUSTOM*FLEX*® ARTIFICIAL*IRIS* is suitable for you. Discuss the content of this booklet and any questions you may have with your doctor. Check with your doctor if any of the possible **contraindications**, precautions and warnings may apply to you. Make sure your doctor answers all your questions to your satisfaction before you agree to have the CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment.

All terms printed in bold can be found in the glossary at the beginning of this booklet. The glossary defines each of these terms for you.

4 How Does the Eye Work?

The main parts of the eye are the **cornea**, **iris**, **lens** and **retina**, shown below in Figure 1.

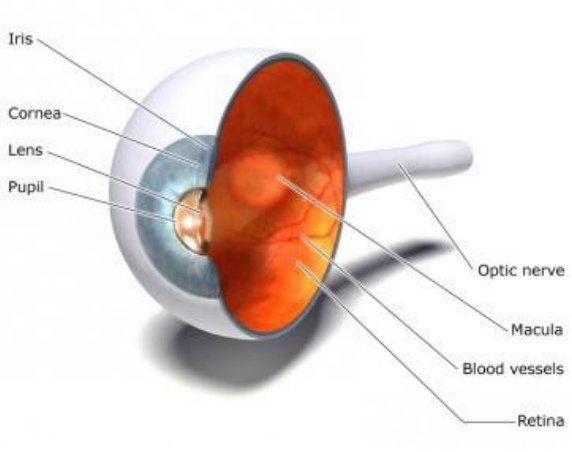

Figure 1: Main Parts of the Eye[1]

The main parts of the eye work together like a camera. Light enters the eye through the **cornea** (clear front covering of the eye) and the **pupil** (opening of the eye in the center of the **iris**) and then passes through the **lens.** The **cornea** and **lens** work together to bend rays of light and focus an image on the **retina**, the back surface of the eye, in the same way that a camera **lens** focuses light to form a clear image onto film. For our brain to be able to create an image of our surroundings, special sensory cells within the **retina** convert light into electrical signals called nerve impulses. These nerve impulses then travel to the brain along the **optic nerve**.

The **iris** is the colored part of your eye and contains a ring of muscles within it that can expand and contract. The **iris** controls the size of the **pupil** and the amount of light that enters the eye by changing the size of the **pupil** in response to light. If you are in bright light, the **iris** expands (gets bigger) to make the **pupil** smaller and allows less light to enter. When in darkness, the **iris** contracts to make the **pupil** bigger to allow as much light as possible to enter the eye so you can see.

The space between the **cornea** and the **lens** is filled with a liquid called **aqueous humor**. This space is known as the **anterior chamber** or front part of the eye. The space between the **lens** and the **retina** is filled with a gel called the **vitreous**.

The **retina** is a membrane that lines the back part of the eye and contains cells that are sensitive to light. These special sensory cells are of two types: **rods** allow black and white vision at twilight and at night; **cones** allow us to see color. The cones are most densely located at the center of the **retina**, called the **macula**. Thus, the **macula** helps us see in bright light and is the central area of sharpest vision.

[11] How does the eye work. Informed Health Online [Internet] - Institute for Quality and Efficiency in Health Care (IQWiG) Version: January 7, 2015 PMHID: PMH0072432 https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0072432/

5 What is Aniridia?

Aniridia is an eye disorder characterized by a complete or partial absence of the **iris**. **Aniridia** can be **congenital** (present at birth) or acquired as the result of an accident or some other type of trauma or injury to the eye. Full or partial aniridia is also associated with conditions such as ocular or oculocutaneous albinism and **iridocorneal endothelial (ICE) syndrome**, and iris coloboma.

Congenital aniridia is a rare genetic disorder that affects 1 in 50,000 to 1 in 100,000 newborns in the United States. The condition primarily arises when an abnormal PAX 6 gene, that controls the normal development of the eye, is either inherited from one or both parents or spontaneously becomes abnormal (mutates) during development before birth. Congenital aniridia may also be associated with other disorders including Wilm's tumor, Rieger syndrome, and juvenile glaucoma.

The PAX 6 gene produces a protein that moderates limbal stem cells, which control how, when and where different parts of the eye are produced during development before birth. Congenital aniridics are born with either a deficiency or absence of this protein and, as a result, different parts of the eye are incomplete or malformed at birth. While the **iris** defect is the most striking hallmark of the disorder, multiple structures in the eye such as the **cornea**, crystalline lens, retina and **optic nerve** may be affected and are often not fully developed. The PAX6 protein also has an active role in the maintenance and repair of healthy eyes after birth and during adulthood. Unlike normal eyes, those eyes with a PAX 6 deficiency do not have the ability to heal well after surgery or injury due to the lack of functional stem cells and may lead to progressive changes in corneal structure and function that require eventual limbal stem cell or corneal transplant. As a result, **aniridia** is a complex syndrome that encompasses many other conditions that are present at birth or emerge throughout early childhood and later in adult life.

The **iris** deficiency associated with **aniridia** results in visual symptoms that are often debilitating. Patients with **aniridia** commonly suffer from decreased **visual acuity** ranging from functional to legally blind or worse from refractive errors or malformation of the **retina** or **optic nerve**, extreme **light sensitivity** in daylight and at night (**photosensitivity**), **glare**, **halos**, amblyopia (lazy eye), ptosis (droopy eyelids), nystagmus, poor depth of field or vision in dim light, lens displacement from weak internal structures, **cataracts**, **retinal detachment**, eye dryness, corneal degeneration, fibrosis, **glaucoma** and other visual disturbances. These symptoms or conditions are responsible for the progressive loss of vision that occurs in adolescence and adulthood and can be so severe that the person's activities of daily living are significantly impacted.

Sports and recreation related eye injuries are the most common cause of eye injuries in youth, the majority of which are blunt eye injuries that may require partial or full **iris** repair. Acquired **aniridia** also can result from trauma during eye surgery, **iris** defects from removal of **iris** tumors, or **iris** defects resulting from **epithelial ingrowth** after ocular surgery. Eyes with acquired aniridia suffer visual symptoms that are similar in nature and severity as congenital aniridics but without the complications associated with the PAX6 genetic deficiency.

6 Treating Aniridia

Treatment of **aniridia** is aimed at preservation of vision, reduction of symptoms, and management of co-existing conditions. Implantation of an artificial iris, such as the CUSTOM*FLEX*® ARTIFICIAL*IRIS*, is one possible treatment for **aniridia** and is an elective surgical procedure. Other possible alternative treatments for **aniridia** include:

- **Tinted Glasses:** Patients may benefit from wearing prescription or non-prescription filter lens or sunglasses, to help with glare and sensitivity to light (common symptoms associated with the large **pupils** and corneal changes).
- **Iris Reconstruction**: Surgery many be performed using sutures to repair the shape of the iris to improve vision and the overall look of the eye without implanting an artificial **iris** device.
- **Colored Contact Lenses**: Colored contact lenses are a medical device which requires a valid prescription to purchase them. Most colored contact lenses are designed to mimic the natural look of the **iris**. Since this area is made up of colorful shapes and lines, some colored contacts feature a series of tiny colored dots and radially arranged colored lines and shapes to help the lenses look more natural on the eye. These lenses are often used as fashion or costume accessories and carry the same health risks as corrective contact lenses when used incorrectly. Extra care should be used when wearing contact lenses if corneal abnormalities also exist.
- **Corneal tattooing**: Reasons for corneal tattooing include improvement of cosmetic appearance and the improvement of sight. Corneal tattooing is also performed on patients who still have vision to reduce symptomatic **glare** associated with large **iridectomies** or traumatic **iris** loss. Complications, risks and disadvantages include **keratitis**, toxic reaction, **iridocyclitis**, persistent corneal epithelial defects, corneal ulceration, loss of sight, fading of color and reduction in the size of the tattoo.

7 What is the CUSTOM*FLEX*® ARTIFICIAL*IRIS*?

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* device is a foldable iris prosthesis that is **custom-made** for each individual patient, as shown below in Figure 2. The device is manufactured using medical- grade colorized silicone of the type that is used in other eye devices, such as **intraocular lenses** (IOLs). During manufacturing, the silicone is applied by hand as either a single color or as an individually selected color pattern to match the coloring of the natural **iris**. This is done by matching the color of a photograph printout of the patient's existing **iris** (or a selected template photo), producing nearly an exact match.

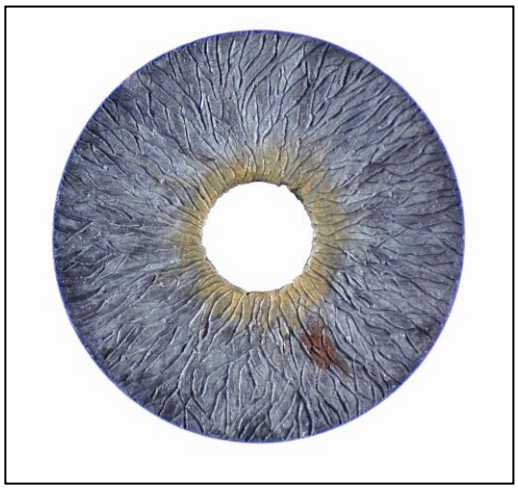

Figure 2: CUSTOM*FLEX*® ARTIFICIAL*IRIS*

8 When is the CUSTOM*FLEX*® ARTIFICIAL*IRIS* Device Used?

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* is intended for use as an **iris** prosthesis for the treatment of iris defects. The CUSTOM*FLEX*® ARTIFICIAL*IRIS* is indicated for use in children and adults for the treatment of full or partial **aniridia** resulting from **congenital aniridia,** acquired defects, or other conditions associated with full or partial aniridia.

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* for the treatment of full **aniridia** is shown below in Figure 3. When implanted, the artificial **iris** mimics the natural **iris** and produces an improvement in the visual symptoms associated with **aniridia** that most affect the patient's quality of life. These symptoms include a reduction in severity of light sensitivity day and night, difficulty night driving, reading difficulty, **glare** and **halos** day and night, and **starbursts**.

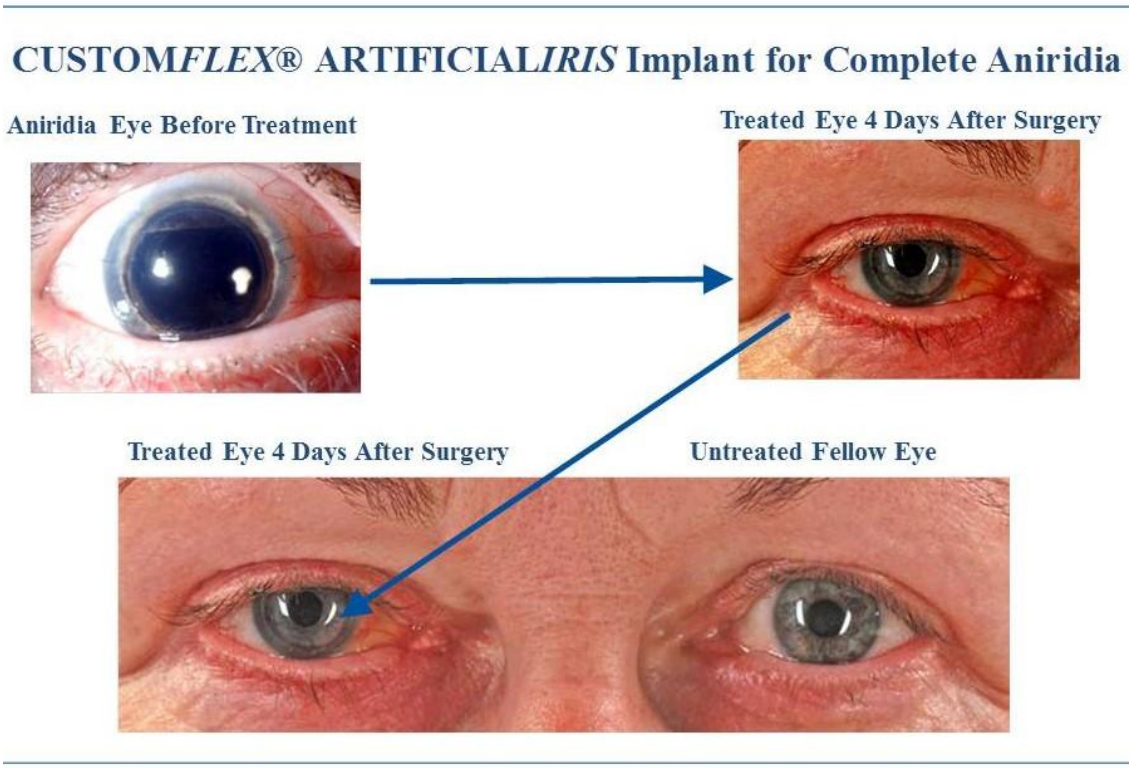

Figure 3: CUSTOM*FLEX*® ARTIFICIAL*IRIS* for the Treatment of Complete Aniridia

9 Are You a Good Candidate for the CUSTOM*FLEX*® ARTIFICIAL*IRIS*

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* is surgically implanted for the treatment of **aniridia** in children and adults who are born with **aniridia** or have **iris** defects that occur as the result of injuries or other conditions in which the **iris** becomes damaged or non-functional. You may be a good candidate for CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment if:

- You are an adult or a child at least 3 years of age or older -- there is no upper age limit for treatment
- You have a diagnosis of congenital or acquired full or partial **iris** defect in the eye to be treated, such as:
    - An **iris** defect resulting from injury or trauma to the eye
    - An **iris** that does not react to light and the pupil remains large (traumatic **mydriasis)**
    - An **iris** that is damaged or does not function properly because of an inflammatory condition
    - An **iris** defect resulting from removal of an **iris** tumor or cyst
    - An **iris** defect resulting from an eye surgery
    - **Albinism**
    - An eye condition that results in a distortion or abnormality of the pupil, such as Chandler's syndrome or **ICE syndrome**
    - An **iris** that becomes separated or torn away from the structures holding it in place within the eye (iridodialysis)
- You have symptoms of light sensitivity, **photophobia**, and/or **glare** in the eye to be treated or other medically necessary indication for treatment -- the CUSTOM*FLEX*® ARTIFICIAL*IRIS* can NOT be used if the only reason is to change the color of your eyes
- Your eye to be treated either already has an IOL in place, has no **lens**, or is scheduled to undergo **cataract** extraction before or concurrently with the artificial iris surgical procedure
- Your eye has no other condition for which the implantation of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* is **contraindicated** or not recommended

The information presented in the following sections of this booklet will help you determine if CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery is advisable for you. It reviews the probable risks and benefits of the procedures, reports the outcomes of the clinical study that was completed to evaluate the CUSTOM*FLEX*® ARTIFICIAL*IRIS*, and describes what to expect if you decide to

undergo surgery and have the CUSTOM*FLEX*® ARTIFICIAL*IRIS* implanted.

Surgical alternatives to CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery include **iris reconstruction** in which sutures are used to repair the shape and appearance of the **iris**. Iris reconstruction surgery is used to repair damaged eye tissue and restore vision when the iris becomes injured from trauma or a surgical complication. It cannot repair an **iris** that is missing at birth. Ask your physician whether you might be a better candidate for iris reconstruction surgery than CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment.

10 What to Expect with the CUSTOM*FLEX*® ARTIFICIAL*IRIS* Procedure

10.1 Before the Procedure

Your doctor will perform a complete eye exam to help determine whether you may be a good candidate for the CUSTOM*FLEX*® ARTIFICIAL*IRIS***.** Your doctor will assess your general health and consider any medications you are taking. Make sure you tell your eye care professional about all medical and eye conditions that you have, and all medications you are taking, including over-the- counter items like vitamins and supplements.

If you decide to move forward with the CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment, your eye care provider will photograph your eyes for ordering the artificial iris implant.

10.2 Choosing Your CUSTOM*FLEX*® ARTIFICIAL*IRIS* Implant

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* is **custom-made** for each individual patient. To order a color- matched device, you will have photos taken of your eyes. You and your doctor should select the hardcopy photo printout that is the best match to your existing **iris** as the target color. This will be used as the template to custom-manufacture the artificial iris. **Aniridia** patients who have no natural **iris** available to use as a template will submit the photo of another person's eye (e.g., family, friends) to use as the template photo. Photos from magazines or other digital sources are not acceptable. The photo that is to be used for production must be signed and dated by you and your doctor to verify that you both agree on the photo you selected.

Once the photos are selected, your doctor will order the CUSTOM*FLEX*® ARTIFICIAL*IRIS* from the manufacturer. It takes 8 to 12 weeks for the device to be **custom-made**. The manufacturer will let your doctor know when the device is expected to be delivered so that you can schedule the date for your surgery.

10.3 During the Procedure

You will be positioned to make you comfortable for the surgery, and the operated eye will be prepped and draped in the surgeon's usual sterile fashion for ophthalmic surgery. Eye drops to help control infection, swelling, and numbing will be put into your eye. Your doctor will select the surgical technique based on the CUSTOM*FLEX*® ARTIFICIAL*IRIS* device ordered and your eye's anatomy and **pathology**. A small incision is made, and the artificial **iris** is folded and inserted through the incision. The **iris** device is unfolded, and the edges are smoothed out using surgical instruments. If sutures are required, they are tied with only enough tension to prevent movement. The incision is sealed and secured according to your doctor's preference.

If your eye is undergoing a **cataract** procedure to place an IOL, the IOL surgery may be

performed at the same time as the artificial **iris** surgery. Depending on your eye's conditions, other surgical procedures may need to be performed as part of the same surgery experience. You should discuss the surgery procedure in detail with your doctor to assure you understand all the procedures that will occur and the risks of the surgical procedures and any special instructions you need to follow before, during, or after the surgery.

10.4 After the Procedure

Right after surgery you should remain in the recovery area for a short time. You should make plans to have someone else drive you home. You will be given written instructions about what you can do and how often to use eye drops. You can then go home, but someone will need to drive you because your vision will be blurry. You can expect your eye to be uncomfortable for a few days after the surgery. You will be given a prescription for pain medication that you can take if you need it.

You should avoid rubbing your eyes, wearing eye make-up, playing contact sports, exercise, swimming, gardening, smoking, and being in dusty environments for at least the first week after surgery. Please check with your eye care provider for when you can resume these and other activities your doctor may have asked you to stop after surgery.

If you feel any pain, see any discharge or redness in the eye with the CUSTOM*FLEX*® ARTIFICIAL*IRIS* device, or have a sudden decrease in your vision or flashing lights or floating spots, then call your eye care provider immediately.

You will typically see your eye care provider the day after the procedure and at frequent visits for the first 12 months. Your doctor will determine the exact schedule based on your condition and ability to return for follow-up visits. After that, you should be seen for an annual eye exam each year, at minimum, or sooner if you experience any problems in the implanted eye.

Most health insurance policies do not cover the CUSTOM*FLEX*® ARTIFICIAL*IRIS* procedure.

11 What are the Risks of CUSTOM*FLEX*® ARTIFICIAL*IRIS* Surgery?

Risks

You should consider the risks as well as the benefits of having your **aniridia** treated with the CUSTOM*FLEX*® ARTIFICIAL*IRIS*. There are risks and possible complications of artificial iris implantation. Complications could be minor or temporary, or could permanently affect your vision. The frequency of complications is low relative to the cause of aniridia. Complications may include those that occur as a result of the artificial iris or IOL that is implanted, the surgical procedure to implant these devices, or from other eye conditions that are unrelated to the CUSTOM*FLEX*® ARTIFICIAL*IRIS*, IOL or surgical procedure.

Contact your eye doctor right away if you have any of the following symptoms after surgery: itching, pain, flashing lights or "floaters", redness, severe headache, nausea/vomiting, sensitivity to light or watery eyes.

- **Vision and Eye Symptoms**: CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery improves symptoms related to photosensitivity and vision, including **glare**, **halos**, blurred vision, double vision, fluctuation of vision, dryness, **foreign body sensation** and pain. However, these symptoms may worsen in some patients and may not resolve, even with treatment.
- **Eye Infection or Inflammation**: As with any surgery in the eye, there is a risk of infection and/or **inflammation** to the front part of the eye or the back part of the eye.
- **Lens Removal**: Because the CUSTOM*FLEX*® ARTIFICIAL*IRIS* is a permanent implant, it may have to be removed if surgery to the lens or back of the eye is required at a later time. For this reason, if your eye has its natural lens in place, the natural lens must be removed before or at the same time as the artificial iris surgery and an IOL will be implanted.
- **Decreased Uncorrected or Best Corrected Distance Vision**: As with any eye surgery, there is a risk that you may lose some distance vision in the implanted eye. This could result from complications of the eye surgery, or if your doctor selects the wrong correction of IOL to implant in your eye.
- **Increased Eye Pressure**: There is a probable risk for eye pressure to increase as a result of the surgery, the artificial iris or IOL devices, or from using steroid eye drops (**steroids**) needed to suppress **inflammation** from the implantation of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* and any concurrently placed IOL. Inflammation is the body's natural reaction to surgery. If you have glaucoma before the surgery, your glaucoma may be at increased risk for episodes of worsening glaucoma after the surgery. If your pressure increases, your doctor will treat it by prescribing oral medications or eye drops to decrease the eye pressure. In some cases your doctor may need to perform a procedure to relieve the pressure. This will usually control the eye pressure; but in some cases, further treatment may be needed. In many cases, treatment to lower eye pressure

is no longer needed once the episode of pressure increase returns to normal. In other cases, long- term treatment for high eye pressure may be needed, even after the steroids are stopped.

- **Changes to Device Position:** After CUSTOM*FLEX*® ARTIFICIAL*IRIS* implantation, the device may not be perfectly centered or may move slightly and become off-center or dislocated. This may or may not require additional surgery to reposition the device.
- **Need for Device Removal or Additional Surgery**: After CUSTOM*FLEX*® ARTIFICIAL*IRIS* implantation, more surgery may be needed to reposition the device, exchange the artificial iris for a new one, or permanently remove the device in order to treat a complication. Other types of surgery may also be needed to treat complications. Each additional surgery has its own risks, and may or may not completely resolve the problem.

12 Contraindications, Warnings and Precautions

Discuss with your doctor if you have any of the following conditions to determine if CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery is right for you.

12.1 Contraindications - When it is NOT Advisable to have CUSTOM*FLEX*® ARTIFICIAL*IRIS* Surgery?

You should NOT have CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery if you have any of the following situations or conditions, because the risk is greater than the benefit:

- Have an active eye infection or uncontrolled **inflammation** of the eye (such as acute or severe chronic uveitis)
- Were born with an eye disorder (other than **aniridia**) that causes the eye to be abnormal in size, shape or function (such as **microphthalmus** or rubella cataract)
- Have an untreated eye disorder that is potentially vision-threatening (such as an untreated **retinal detachment** or untreated chronic **glaucoma**)
- Have a disease process in which new blood vessels grow abnormally on the **iris** (rubeosis of the **iris**)
- Have a complication of diabetes in which new blood vessels grow on the surface of the
- **retina** or elsewhere (proliferative diabetic retinopathy)
- Have an inherited disease that causes cells in the main focusing area of the **retina** to deteriorate (**Stargardt's retinopathy**)
- Are pregnant because the medications that are given to you during the surgery and after the surgery may not be safe for your unborn child

12.2 MRI Safety Information

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* implant is MR Unsafe. You may not receive an MRI scan with the CUSTOM*FLEX*® ARTIFICIAL*IRIS* implant. If you receive an MRI scan while the implant is in place, it may cause injury to your eye or adjacent tissues.

12.3 Warnings - What Other Information Do You Need to Know About?

Discuss with your doctor if you have any of the following conditions. You may be able to have CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery if your doctor evaluates the seriousness of your condition and believes the benefit of having the surgery is greater than the risk.

- Children who are less than 3 years of age because their eyes are still in a stage of major growth development that would be disrupted by ocular surgery
- The **intraocular pressure** (IOP) in your eye is above 21 mm Hg and does not respond to pressure-lowering medication, unless the IOP above 21 mm Hg is due to a known underlying condition (such as **glaucoma**) that is stable and well-controlled with **glaucoma** treatment.
- You have a disease of the **cornea** that causes it to swell and be cloudy (severe endothelial corneal dystrophy). Potential surgical trauma associated with implantation of this device may lead to damage of your cornea such that the potential benefits of implantation do not outweigh the risks
- You have no useful vision or vision potential in your eye that will NOT be treated which could cause you to be visually impaired if something happened to your "good" eye that is undergoing the artificial iris surgery unless your **aniridia** symptoms are so debilitating that the probable benefits of receiving the CUSTOM*FLEX*® ARTIFICIAL*IRIS* clearly outweigh the risks
- Presence of a condition or finding in your opposite eye that is not undergoing the artificial iris surgery that would make it unsafe to implant a CUSTOM*FLEX*® ARTIFICIAL*IRIS* in the eye to be treated
- You are allergic to any of the planned postoperative antibiotic or anti-inflammatory medications, unless a suitable alternative medication can be prescribed
- Implantation for cosmetic color changes of the iris
- You are nursing or lactating and any of the medications you will need to take before or after the surgery can pass into your breast milk and are unsafe for your child
- You have gastric ulcers or diabetes mellitus and will need to take high doses of orally administered **steroids** after the surgery
- Any other current condition that would interfere with the planned surgical procedure to implant the artificial iris

12.4 Precautions

If you have any of the conditions below, talk to your doctor before you decide to have the CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery, as the risks of having the CUSTOM*FLEX*® ARTIFICIAL*IRIS* are higher in patients who have any of the following conditions.

- If your eye has its natural **lens** in place, the natural **lens** must be removed and an IOL will be implanted along with the CUSTOM*FLEX*® ARTIFICIAL*IRIS* procedure. The IOL procedure must be performed even if no **cataract** is apparent.
- The visual potential of your opposite eye that is not undergoing the artificial iris surgery cannot be evaluated (e.g., poor vision in the eye due to **cataract**)

- The IOP in your eye is above 21 mm Hg and is known to be stable and well controlled with **glaucoma** treatment (e.g., medication, tubes or shunts)
- Presence of any other medical condition that might be expected to make you an unsuitable candidate for CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment of **aniridia**
- Surgical difficulty of the planned surgery, which might increase the potential for complications
- Implantation in the fellow eye before stabilization of the first implanted eye (typically 1 month or more)

Safety and effectiveness of intraocular lenses has not been established in pediatric patients in the U.S.

The opening in the middle of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* is fixed at 3.35 mm. In the event that a future surgical procedure must be performed through an opening that is larger than 3.5 mm, your surgeon may need to remove the CUSTOM*FLEX*® ARTIFICIAL*IRIS* to perform the surgery and implant a new CUSTOM*FLEX*® ARTIFICIAL*IRIS* device during the surgery or as a separate procedure.

13 Clinical Study

A clinical study was done to evaluate the safety and effectiveness of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* for the treatment of congenital and acquired aniridia in children and adults. The study included 447 eyes that had the CUSTOM*FLEX*® ARTIFICIAL*IRIS* implanted. At the time the patients were enrolled in the study, the youngest patient was 6 years old and the oldest patient was 94 years old. Of the 447 eyes treated in the study, 44 eyes were in pediatric patients (less than 22 years of age).

For your information, a summary of the results from the clinical study is provided below.

13.1 What are the Probable Benefits of CUSTOM*FLEX*® ARTIFICIAL*IRIS*?

One of the probable benefits of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment is that your symptoms related to light sensitivity and vision may improve. You may also be able to function better and more easily perform normal activities that require useful vision. At 12 months after the patients in the clinical trial underwent the CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery:

- There was a decrease in the severity of day-time symptoms of light sensitivity, **glare** and **halos:**
  - 14.2% (48/339) of the eyes had symptoms of light sensitivity during the day that were marked or severe after the artificial iris surgery compared to 73.8% (327/443) of eyes before the surgery
  - 11.2% (38/339) of the eyes had symptoms of **glare** during the day that were marked or severe after the artificial iris surgery compared to 64.3% (285/443) of eyes before the surgery
  - 2.7% (9/339) of the eyes had symptoms of **halos** during the day that were marked or severe after the artificial iris surgery compared to 22.3% (99/443) of eyes before the surgery
- There was a decrease in the severity of night-time symptoms of light sensitivity, **glare**, **halos** and **starbursts**:
  - 6.8% (23/339) of the eyes had symptoms of light sensitivity at night that were marked or severe after the artificial iris surgery compared to 48.3% (214/443) of eyes before the surgery
  - 9.1% (31/339) of the eyes had symptoms of glare at night that were marked or severe after the artificial iris surgery compared to 57.6% (255/443) of eyes before the surgery
  - 7.7% (26/339) of the eyes had symptoms of halos at night that were marked or severe after the artificial iris surgery compared to 38.1% (169/443) of eyes before the surgery
  - 6.5% (22/339) of the eyes had symptoms of **starbursts** at night that were marked or severe after the artificial iris surgery compared to 30.9% (137/443) of eyes before

the surgery

- Reading was improved with 26.3% (89/339) of eyes having marked to severe reading difficulty after CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment compared to 64.8% (287/443) before the treatment.
- Difficulty driving at night also improved with 14.2% (48/339) of subjects who were driving reporting marked to severe difficulty driving after CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment compared to 43.8% (194/443) who had marked to severe difficulty driving before the treatment.
- There was a three-fold improvement in the patients' ability to complete normal vision-related activities of daily living, as measured by a standardized health related quality of life questionnaire. The mean score on the questionnaire before CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery was 66.7 compared to 15.4 after the surgery, where a lower score indicates improvement in health related quality of life and less dysfunction.
- Satisfaction with the cosmetic appearance was high, with 93.8% (318/339) of patients rating their appearance as improved to very much improved after implantation of the CUSTOM*FLEX*® ARTIFICIAL*IRIS*.
- Although the CUSTOM*FLEX*® ARTIFICIAL*IRIS* is not designed to improve vision, 67.2% (170/253) of the eyes had better **uncorrected visual acuity** (vision without glasses or contact lenses) after the artificial iris surgery; and, 27.7% (70/253) of the eyes had uncorrected vision that was unchanged.

13.2 What are the Risks of CUSTOM*FLEX*® ARTIFICIAL*IRIS*

The doctors in the clinical study evaluated the risks of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* by measuring **best corrected visual acuity** (BCVA; vision with glasses or contact lenses) before and after the CUSTOM*FLEX*® ARTIFICIAL*IRIS* treatment. The doctors also performed other safety measurements, such as measuring IOP, evaluated adverse events, and the position of the artificial iris after the surgery. After the CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery:

- None of the eyes (0%) had a clinically significant loss of more than 2 lines on the eye chart of BCVA at 12 months postoperatively that was caused by the CUSTOM*FLEX*® ARTIFICIAL*IRIS*.
    - 5.5% (18/330) of the eyes did lose more than 2 lines of BCVA at 12 months postoperatively, but this loss was related to other conditions.
    - 1.7% (6/447) of the eyes lost more than 2 lines of BCVA at 3 months or later after implantation of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* that was related to the surgical procedure to implant the device.
- Increases in IOP > 30 mm Hg were the most common adverse event reported in the study. Throughout the 12 months after CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery:
    - 7.8% (35/447) of the eyes had one or more spikes of IOP > 30 mm Hg as a result of the surgical procedure.

- 0.2% (1/447) had an episode of an elevated IOP > 30 mm Hg that was caused by the CUSTOM*FLEX*® ARTIFICIAL*IRIS*.
- There were no reports (0/447) of increased IOP > 30 mm Hg that was caused by the IOL that was surgically implanted along with the artificial iris.
- Episodes of IOP > 30 mm Hg related to patients' other eye conditions occurred in 9.4% (42/447) of the eyes.
- Steroid drops administered after the artificial iris surgery resulted in episodes of IOP > 30 mm Hg in 6.0% (27/447) of the eyes.

- The CUSTOM*FLEX*® ARTIFICIAL*IRIS* implant remained in its intended position in the majority of eyes throughout the 12 month study; secondary surgeries could be performed when needed to reposition the device:
  - The artificial iris device was observed to be decentered (not perfectly centered) tilted or dislocated (not in its intended position) in 4.2% (19/447) of the eyes.
  - A second surgery to reposition the CUSTOM*FLEX*® ARTIFICIAL*IRIS* was performed in 2.2% (10/447) of the eyes; and, all surgical repositions were performed successfully.
  - The CUSTOM*FLEX*® ARTIFICIAL*IRIS* had to be removed and replaced with the backup device in 0.2% (1/447)of the eyes.
  - There were no circumstances in which the CUSTOM*FLEX*® ARTIFICIAL*IRIS* had to be permanently removed in any the eyes.
- **Inflammation** (iritis) occurring at 1 month or later after the surgery:
  - Was related to the CUSTOM*FLEX*® ARTIFICIAL*IRIS* device in 0.7% of the eyes;
  - Was related in to the surgical procedure in 3.4% of the eyes, and was chronic (present at all postoperative visits) in 1.8% (5/447) of the eyes; and ,
  - Was related to other eye conditions in 3.4% of the eyes, and chronic in 0.2% of eyes.
  - Adverse events related to the surgical procedure to implant the artificial iris and any concurrently implanted IOLs that occurred in 2% or more of the eyes were:
    - Cystoid macular edema (2.9%; 13/447)
    - Corneal edema at 1 month or later (2.5%)
    - Iritis at 1 month or later (3.4%; 15/447)
    - IOP > 30 mm Hg (7.8%; 35/447)
    - Hemorrhage into the vitreous (4.3%; 19/447)
    - Hyphema (4.0%; 18/447)
  - Adverse events related to the CUSTOM*FLEX*® ARTIFICIAL*IRIS* device that occurred in 2% or more of the eyes were all related to the implant's position:
    - Device dislocation (2.5%; 11/447)

- Secondary surgery to reposition the device (2.2%; 10/447)

- Adverse events related to the other eye conditions and that were unrelated to the study devices or study procedures and occurred in 2% or more of the eyes were:
  - BCVA loss of more than 2 lines on the eye chart at 3 months or later (2.5%; 11/447)
  - Corneal edema at 1 month or later (3.1%; 14/447)
  - Cystoid macular edema (3.4%; 15/447)
  - Hypotony (3.6%; 16/447)
  - IOP > 30 mm Hg (9.4%; 42/447)
  - Iritis at 1 month or later (3.4%; 15/447)
  - Drug induced IOP > 30 mm Hg (6.0%; 27/447)

14 Summary of Important Information

- The CUSTOM*FLEX*® ARTIFICIAL*IRIS* procedure is not risk-free. Read this entire booklet, most importantly the section on Risks, before you elect to have this procedure.
- Implantation of the CUSTOM*FLEX*® ARTIFICIAL*IRIS* device has the potential to cause:
  - Increased eye pressure
  - The need for another surgery, such as removal or replacement of the device, or another treatment.
- You should not have the CUSTOM*FLEX*® ARTIFICIAL*IRIS* implanted if you:
  - Have an active eye infection or uncontrolled inflammation of the eye (such as acute or severe chronic uveitis)
  - Were born with an eye disorder (other than aniridia) that causes the eye to be abnormal in size, shape or function (such as microphthalmus or rubella cataract)
  - Have an untreated eye disorder that is potentially vision-threatening (such as an untreated **retinal detachment** or untreated chronic **glaucoma**)
  - Have a disease process in which new blood vessels grow abnormally on the iris (rubeosis of the **iris**)
  - Have a complication of diabetes in which new blood vessels grow on the surface of the **retina** or elsewhere (proliferative **diabetic retinopathy**)
  - Have an inherited disease that causes cells in the main focusing area of the **retina**
  - to deteriorate (**Stargardt's retinopathy**).
- If your eye still has its natural **lens**, you will need to have the **lens** removed and have an IOL placed in the eye (same procedure as a cataract surgery).
- There are non-surgical alternatives to the CUSTOM*FLEX*® ARTIFICIAL*IRIS* device, which include tinted glasses, iris reconstruction surgery with suturing, colored "**iris**" contact lenses, or corneal tattooing.
- Before having the CUSTOM*FLEX*® ARTIFICIAL*IRIS* procedure, you should:
  - Have a complete eye examination.
  - Talk with your eye care provider about alternative treatments, probable benefits, complications, risks, healing time, and any other concerns you have about having the surgery.
  - Be able to complete your follow-up visits and use the eye drops prescribed for you after the surgery.

What this Means to You

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* device has advantages and disadvantages. You should evaluate the factors in this brochure as they relate to your vision and your quality of life. We recommend that you ask your eye care provider to assist you in this evaluation.

The CUSTOM*FLEX*® ARTIFICIAL*IRIS* has been well studied in the U.S.A. In the clinical study, 94% (318/339) of patients rated their postoperative appearance as improved after receiving the CUSTOM*FLEX*® ARTIFICIAL*IRIS*. If you decide to have the CUSTOM*FLEX*® ARTIFICIAL*IRIS* surgery, we hope that you are satisfied and have great pleasure in your improved quality of life.

15 Where Can I Obtain More Information?

- **Primary Eye Care Professional:**

  Name**:**

  Address: Phone: Email:

- **CUSTOM*FLEX*® ARTIFICIAL*IRIS* Physician**

  Doctor:

  Name:

  Address: Phone: Email:

- **Treatment Location**:

  Name:

  Address: Phone:

- **CUSTOM*FLEX*® ARTIFICIAL*IRIS* Manufacturer:** [2]

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