FDA Briefing Document

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Joint Meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee and Ophthalmic Device Panel of the Medical Devices Advisory Committee

NDA 203324
Photrexa Viscous and Photrexa (riboflavin ophthalmic solution)
and KXL System (UVA light source)
Avedro, Inc.

Division of Transplant and Ophthalmology Products
Office of Antimicrobial Drugs
Center for Drug Evaluation and Research (CDER)

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1 Introduction

1.1 Application

Avedro, Inc. submitted a new drug application (NDA 203324) for a combination product (21 CFR Part 3). The proposed indications are the treatment of progressive keratoconus and the treatment of corneal ectasia following refractive surgery. This proposed treatment uses Photrexa Viscous (riboflavin ophthalmic solution) with dextran and Photrexa without dextran in certain patients, and KXL-System (the UVA light source) for corneal collagen cross-linking. (See Section 4.1)

The proposed dose of Photrexa Viscous, or Photrexa in patients with corneal thickness < 400 nm, is 1 drop applied topically on the eye every 2 minutes for 30 minutes. Before drug dosing, patients undergo epithelial removal / debridement.

The proposed application of light from the KXL system is with a 365 nm wavelength at an intensity of 3 mW/cm^2 for 30 minutes, following riboflavin treatment.

See Section 3 for information on the collagen-cross linking procedure, drug and device constituent parts.

1.2 Description of Diseases

Keratoconus is a naturally-occurring ocular condition characterized by progressive thinning and protrusion of the cornea, resulting in corneal optical irregularities with increasing myopia, irregular astigmatism, and consequential loss of best corrected visual acuity (BCVA). The prevalence of keratoconus is often reported as 1 per 2000 people in the general population. Onset of keratoconus generally occurs during puberty or early adulthood and the disease generally progresses over the next ten to twenty years until the progression gradually stops. The rate of progression is variable. The disease process results in mild to marked impairment of visual function that initially managed with glasses and contact lenses. But sometimes, with further progression, impairment may eventually result in the need for corneal transplantation.
Corneal ectasia is reported following some refractive surgical procedures. Similar to keratoconus, postoperative corneal ectasia is characterized by progressive thinning and protrusion of the cornea, resulting in corneal optical irregularities and loss of both uncorrected visual acuity (UCVA) and BCVA.

1.3 Available Therapies

There is currently no FDA-approved drug in the United States (US) for the treatment of keratoconus or corneal ectasia following refractive surgery.

One device has labeling for use in patients with keratoconus (KC), INTACS.[1]

Based on literature publications, presentations at scientific meetings and information on the internet, FDA is aware that there is the practice of medicine use or study of other products that are not approved for these uses.

2 Summary of Presubmission Regulatory Activity Related to Submission

As noted in section 1.1, this is a combination product submitted under NDA 203324, which was studied under two INDs.

IND 78,933 was first opened in August 16, 2007, by a single investigator. The IND included Protocol UVX-001 for the study of patients with progressive keratoconus and corneal ectasia following refractive surgery.[2]

IND 77,882 was submitted as an IND on November 7, 2007, after having submitted a Pre-IND on July 11, 2007. Protocol UVX-002 (progressive keratoconus) and UVX-003 (corneal ectasia) were submitted to IND 77,882.

The Agency provided comments on Protocol UVX-001 on September 11, 2007, and subsequently held a teleconference with these IND holders[3] to discuss potential modifications to Protocol UVX-001, including timing of the primary endpoint. Protocol UVX-001 was amended on September 14, 2007, and October 12, 2007,[4] to become a randomized, one year study. The applicant declined to follow the Agency's, recommendations to evaluate the primary endpoint at one year, but did agree to extend the follow-up evaluations through one year, including both a Month 6 and Month 12 evaluation.

Sponsorship of IND 77,882 was transferred to Avedro, Inc. on May 7, 2010. Avedro, Inc. received orphan-drug designation "for corneal cross-linking for the treatment of keratonus (sic)" on September 2, 2011, and "treatment of corneal ectasia following refractive surgery" on December 2, 2011.

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[1] INTACS prescription inserts are intended for the reduction or elimination of myopia and astigmatism in patients with KC, who are no longer able to achieve adequate vision with their contact lenses or spectacles, so that their functional vision may be restored and the need for a corneal transplant procedure may potentially be deferred.

[2] The single investigator provided right of reference for IND 78,933 to IND 77,882.

[3] Avedro, Inc. the current sponsor for IND 77,882 and applicant for NDA 203324 acquired rights to these applications in April 2010.

[4] Dates listed on this page represent the document dates, not necessary the dates that the revised protocols were submitted to the IND.

A pre-NDA Meeting was held on September 21, 2011. CMC indicated that the briefing document was inadequate and requested additional information on the composition of the material used for the Phase 3 studies and the composition of the proposed commercial formulation. Clinical staff stated it was not possible to determine whether the clinical program will be sufficient to support approval based on the information previously submitted and would need to review the final study reports for studies UVX-001, -002 and -003 to determine whether it is appropriate to combine patients from -001 into - 002 and -003. The Division further commented that "The lack of statistical significance between groups in the patients treated for keratoconus at Month 3 was noted as potentially problematic."

The final Statistical Analysis Plan (SAP) for Progressive Keratoconus was dated December 16, 2011. The SAP described changes from the planned analyses in the protocol. These changes were:

1. Efficacy data would be summarized in 3 ways: (1) the UVX-001 keratoconus data pooled with the UVX-002, (2) the UVX-001 keratoconus data alone and (3) the UVX-002 data alone.

2. The original protocol defined Month 3 as the primary time point for analysis of improvement in Kmax. The final SAP extended the primary time point for analysis to Month 12, and a last observation carried forward analysis strategy was added.

3. Although no formal interim analysis was planned, the SAP incorporated an adjustment to the alpha-level to account for the analyses at Month 3 and Month 12.

The final SAP for Corneal Ectasia was dated January 18, 2012. The statistical analysis plan described changes from the planned analyses in the original protocol. With the exception that the pooled analyses included UVX-001 corneal ectasia data and UVX-003 data, changes were identical to those described above in the SAP for Progressive Keratoconus.

The applicant provided the following explanation for the change in the primary endpoint:

> "At the time the study was initially planned, a review of the existing literature suggested that the primary efficacy endpoint could be analyzed at 3 months post-procedure. However, subsequent additional literature suggested that later time points are better suited for evaluating the long-term clinical significance of the CXL procedure because the corneal stromal remodeling associated with the healing response following CXL requires 6 to 12 months to stabilize. This is consistent with the FDA's previous comments to the Sponsor whereby the FDA strongly recommended that the Sponsor evaluate later time points. Based on the findings of this additional literature, and consistent with FDA's recommendations, the Sponsor

> decided to extend the time point of the primary efficacy endpoint analysis to 12 months. The definition of clinically meaningful benefit, as previously agreed to with the FDA, did not change and continued to be a ≥1D difference in the mean change in Kmax between the CXL treatment group and the control group. This extension of the primary efficacy endpoint analysis to 12 months occurred after all subjects have any impact on conduct of the study. Because the study design allowed subjects in the control group to cross over to receive the CXL treatment after Month 3, the imputation of data (last observation carried forward [LOCF]) was necessary to allow comparisons between the treatment and control groups at later time points."

NDA 203324 for the Photrexa Viscous /Photrexa/KXL-System was submitted September 16, 2013. Avedro was issued a Complete Response letter on March 14, 2014, and asked to provide additional information on the drug constituent part, the drug facility inspections, the device constituent part, clinical/statistical information, clinical site inspections and other comments. On August 6, 2014, Avedro met with FDA to go over their proposed responses to the outstanding items and submitted a complete response to the NDA on September 29, 2014.

3 Product Overview

3.1 Corneal Crosslinking Mechanism of Action Goal

The intent of corneal collagen crosslinking is to biomechanically strengthen and stabilize the cornea to delay progression of the deformation associated with keratoconus and postoperative corneal ectasia.

Collagen cross-linking occurs when the Photrexa Viscous or Photrexa solutions are exposed to the KXL UVA light and the drug product emits a singlet oxygen species. The singlet oxygen forms intermolecular bonds to cross-link the corneal collagen.

In addition there is literature information to suggest that riboflavin is absorbed into the corneal stroma, the absorption spectrum provides a degree of protection to structures interior to the stroma, corneal endothelium, lens and retina.

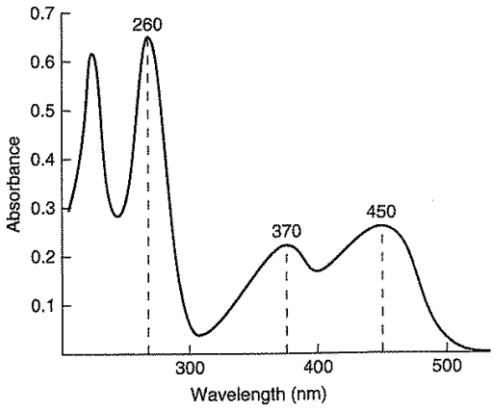


Figure 1-1 Absorption spectrum of riboflavin (22 μM in 0.1 M sodium phosphate, pH 7.06, in 1-cm light path).

Basic Techniques in Experimental Biochemistry, Chapter 1, Photometry
www.chem.uky.edu/courses/che554/2.../Photometry_Chpt1.pdf

3.2 Product Overview – Drug Constituent - Riboflavin Ophthalmic Solutions

Photrexa Viscous (riboflavin ophthalmic solution) is a clear yellow solution containing 0.12% riboflavin 5'-phosphate sodium and 20% dextran (b) (4) in phosphate buffered saline, adjusted to a pH of 7.0, viscosity of 146-188 cP.

Photrexa (riboflavin ophthalmic solution) is a clear yellow solution containing 0.12% riboflavin 5'-phosphate sodium in phosphate buffered saline, adjusted to a pH of 7.0, viscosity of < 5 cP. Photrexa, unlike Photrexa Viscous, does not contain dextran.

Table 1: Composition of Photrexa and Photrexa Viscous (3 mL)

Ingredient	Photrexa Viscous	Photrexa	Function	Quality Standard
	Amount per Syringe (w/w)	Amount per Syringe (w/w)		
Riboflavin 5'-Phosphate Sodium	0.12%	0.12%	Active Ingredient	USP; EP
Dextran (b) (4)	20%	--	(b) (4)	USP; EP
Sodium Chloride	0.31%	0.31%	Buffer	USP; EP; JP
Sodium Phosphate, Monobasic	0.02%	0.02%	Buffer	USP; EP
Sodium Phosphate, Dibasic	0.38%	0.38%	Buffer	USP; EP
Sterile Water for Injection	~79%	~99%	Diluent	USP

Source: 3.2.P.1

Photrexa Viscous and Photrexa are aseptically filled into 3 mL (b) (4), multi-compendial (USP/NF and EP), clear glass syringes with (b) (4) rigid tip cap and stoppered with a (b) (4) stopper.

3.3 Product Overview - Device Constituent- KXL System

The KXL System is an electronic medical device that delivers ultraviolet light (365 nm wavelength) in a circular pattern onto the cornea after application of Photrexa or Photrexa Viscous (riboflavin ophthalmic solution). UVA flux and irradiation time (that is, fluence) at the cornea are controlled by an onboard computer system. Figure 1 provides an illustration of the KXL System.

Figure 1: Overview Illustration of the KXL System

The KXL System is portable with an articulating arm to allow movement of the system for alignment of the UV Beam to the patient's cornea. An internal battery powers the system; the battery is recharged by a system internal charger from any standard AC outlet. The treatment parameters (induction period, UV power and UV energy) are selected through the user interface touch screen computer.

The KXL System includes a Radio Frequency Identification (RFID) reader and RFID activation card. The RFID activation cards are supplied with Photrexa Viscous or Photrexa (riboflavin ophthalmic solution). The software allows treatment only if a valid RFID activation card has been identified by the RFID reader of the system console. For the KXL System, software lock-out provides the maximum allowable treatment parameters will be limited to 3mW/cm^2 for 30 minutes and a maximum energy density of 5.4 J/cm^2.

The user will not be able to change the induction, power and treatment time.

The following treatment parameters provided by the RFID activation card

- Induction Period: 1 – 30 minutes
- Irradiance: 3 mW/cm2
- Total Energy: 5.4 J/cm^2
- Exposure Time: 30 minutes

Table 1 shows excerpts from the KXL System specifications.

Table 1: KXL System Specifications

Specification	Description
Electrical	Battery Powered: (b) (4) Line voltages 100-240 volts AC, (b) (4) Current 2A (b) (4) (b) (4), 50/60 Hz, (b) (4) (b) (4)
User accessible Fuses	250 V~ T2AL
Energy Delivery	UV Radiation 3 mW/cm2 365 nm
External Interfaces	(b) (4)
Battery Life (normal operating conditions)	16 hours

The Optics Head houses the UVA irradiation mechanism. UVA radiation is generated by a single Nichia UV LED. The LED is manufactured to emit UVA radiation at a wavelength of 365 nm. The LED output is coupled into a homogenizer (hexagonal mixing rod) that is positioned closely to the LED output window. Spillover UV that does not couple into the homogenizer is picked up by a photodiode and used to measure and control UV output.

The homogenizer creates a uniform intensity profile by superimposing a multitude of images of the LED die through total internal reflections. A fixed aperture mounted in the UVA irradiation beam path is used to produce a uniform circular area of irradiation at the treatment plane with an approximate diameter of 9 mm.

To correctly position the UV beam onto the cornea, two targeting lasers are used. The first targeting laser is a red (650nm) laser with crosshair beam-forming optics. The laser cross is collinearly coupled into the UV path with a dichroic beam combiner. The second is a green (532nm) laser that is positioned at an oblique angle such that its beam centrally intersects the crosshair at the focal distance of the UV. Both lasers are controlled by the microcontroller.

3.3.1 Device Constituent Part Difference: Clinical trial device vs. the proposed for market device

The device used in the three Phase 3 trials differed from the device proposed for approval in this NDA (Avedro KXL) as summarized in the table below. The KXL-System was not used in the three Phase 3 trials. Table 5 summarizes the device similarities followed by the differences.

Table 5: Similarities and Differences between the UVX and Avedro KXL Devices

Parameter	Clinical trial device (used in UVX-001, UVX-002 and UVX-003)	Avedro KXL System (device to be marketed)	Comparison Comment
Patient Contact	Non-contacting	Non-contacting	Same
UV Source	LED Illumination Source	LED Illumination Source	Same
UV Irradiance	3.0 ± 0.3 mW/cm2	3.0 ± 0.3 mW/cm2	Same
UV Exposure Time	30 minutes	30 minutes	Same
UV Wavelength	365 nm (nominal)	365 nm (nominal)	Same
UV Emission	Continuous	Continuous	Same
Operating	+10C - +40C 30-75% RH, non-condensing 700-1060 mbar	+10C - +40C 30-75% RH, non-condensing 700-1060 mbar	Same
EMI/EMC per IEC 60601-1-2 FCC Part 15	Class B	Class B, 3rd Ed.	Same
Safety Classification	Class II Equipment Type B Applied Part	Class II Equipment (IEC60601-1, 3rd Ed.) Type B Applied Part	Same

Parameter	Clinical trial device (used in UVX-001, UVX-002 and UVX-003)	Avedro KXL System (device to be marketed)	Comparison Comment
Patient Position	Supine or Sitting	Supine Only	The Clinical Trial Device allows UV delivery for treatment in a sitting or supine position while the KXL System is used only in the supine position. However, the UVX-001, UVX-002 and UVX-003 clinical protocols all specified treatments were performed in the supine position.
Available UV Beam (Ø)	7.5 mm 9.5 mm 11.5 mm	9.0 mm	The Clinical Trial Device had three available beam diameters while the KXL System only includes the 9 mm setting.
Power Monitoring	Stand-alone commercial power meter, used at start-up.	Continuous, on-board monitoring using two independent dedicated UV photodiodes	The Clinical Trial Device requires the user to strap the power meter sensor to the treatment head to obtain a power reading prior to treatment. In the KXL System, power monitoring is integrated in the system, is automated and continuous. The automated, continuous power monitoring provided in the KXL System does not require the user to manually check calibration prior to treatment.
UV Light Emission	Initiated via a manual switch	Initiated via touch-screen menus and a valid RFID card must be detected to allow UV treatments	Different methodologies are used for initiating UV light treatment.

Parameter	Clinical trial device (used in UVX-001, UVX-002 and UVX-003)	Avedro KXL System (device to be marketed)	Comparison Comment
UV Focal Alignment	User observes the riboflavin fluorescence to gauge beam shape to determine proper alignment.	Two visible aiming lasers provide direct alignment confirmation in x, y, and z directions.	The KXL System alignment system should be easier for users to correctly align the system compared to the more subjective process with the Clinical Trial Device.
UV Focal Plane (working distance – instrument exit to patient corneal apex)	50 mm nominal	150 mm nominal	The working distances differ between the two systems; both systems have methods for the user to determine the correct focal plane for treatment.
Software	Controlled by internal microprocessor which controls the electrical current used to drive the UV-LEDs	Controlled by software which is responsible for handling the user interface, UV delivery, alignment lasers, and wireless	Both systems' UV output is software controlled and both systems include software that was verified and validated before use.
Device Dimensions	32x5x5 cm	60x60x150 cm, maximum extended position.	The dimensions of the two systems differ.
Device Weight	<10 kg	45 kg	The weights of the two systems differ.

Parameter	Clinical trial device (used in UVX-001, UVX-002 and UVX-003)	Avedro KXL System (device to be marketed)	Comparison Comment
Power Supply	External, commercial, DC supply Input: 100-240VAC; 1A max; 50/60 Hz Output: 9VDC, 1.7A	Internal. 100-240VAC; 2A max;50/60 Hz	The power supplies differ.

The procedure using the clinical trial device is summarized in Section 6.1.2 Investigational Products

4 Cross-linking Procedure Proposed for Market: Photrexa Viscous and Photrexa and KXL System

4.1 Drug selection and dosing:

The selection of Photrexa Viscous or Photrexa is based on the corneal thickness.

- Using topical anesthesia, debride the epithelium using standard aseptic technique. Post epithelial debridement, instill 1 drop of Photrexa Viscous topically on the eye every 2 minutes for 30 minutes.

- At the end of the 30 minute soaking period, examine the eye under the slit lamp for the presence of a yellow flare in the anterior chamber. If the yellow flare is not detected, instill 1 drop of Photrexa Viscous every 2 minutes for an additional 2 to 3 drops and recheck for the presence of a yellow flare. This process can be repeated as necessary.

- Once the yellow flare is observed, perform ultrasound pachymetry.

- If corneal thickness is less than 400 microns as measured by an ultrasound pachymeter, instill 2 drops of Photrexa every 5 to 10 seconds until the corneal thickness increases to at least 400 microns. Irradiation should not be performed unless this 400 micron threshold is met.

- Irradiate the eye for 30 minutes at 3mW/cm^2 using the KXL System as summarized in Section 4.2 below. During irradiation, continue topical instillation of 1 drops of Photrexa Viscous onto the eye every 2 minutes for the 30 minute irradiation period.

4.2 KXL System operation approximate sequence:

- Device power is turned on by the user. The system then checks for startup errors and if the system is starting up correctly, a system calibration is performed. The system checks whether a partial treatment has been detected. If not, the system prepares for a new treatment.

- To begin preparing for treatment, the user enters the induction period for the instillation of the Photrexa or Photrexa Viscous in minutes and seconds.

- The user sets the UVA treatment time in minutes and seconds and the UVA power.

- The user is instructed to scan an RFID treatment activation card using the RFID reader.

- The user is prompted to sync the alignment remote with the KXL System and does so by pressing the sync button on the alignment remote.

- The physician prepares the eye for treatment by removing the epithelium. The KXL System then instructs the physician to apply the Photrexa Viscous or Photrexa.

- The KXL System tracks the induction time and notifies the user that the induction is complete.

- The UVA treatment is then performed.

- The KXL System tracks the treatment time, turns off the UVA and notifies the user when the treatment has been completed.

- Once the treatment has been completed, the system may be powered off.

5 Photrexa Viscous/Photrexa Pharmacodynamics and Pharmacokinetics

The systemic exposure to riboflavin (Vitamin B2) was not determined following topical ocular treatment with 0.1-0.12% riboflavin ophthalmic solutions.

Systemic riboflavin concentrations were not measured following topical administration of the riboflavin ophthalmic solutions at the proposed dosing regimen; it is not possible to explore the influence of intrinsic factors on riboflavin pharmacokinetics.

Assuming 100% bioavailability of riboflavin following topical ocular instillation of the proposed 0.12% riboflavin eyedrops, the average systemic exposure to riboflavin during one-time CCXL treatment of one eye in the 12-month UVX trials would not exceed 10 mg, which is below the Joint FAO/WHO Expert Committee on Food Additives upper limit of acceptable oral daily intake of riboflavin (35 mg for a 70 kg person).

6 Phase 3 Studies

In support for the two indications for this combination product: progressive keratoconus and corneal ectasia following refractive surgery, the applicant submitted three Phase 3 studies.

The clinical development program of Photrexa Viscous / Photrexa (riboflavin ophthalmic solution)/UVA irradiation in the treatment of progressive keratoconus involved two studies, UVX-001 and UVX-002. The clinical development program in the treatment of corneal ectasia following refractive surgery involved two studies, UVX-001 and UVX-003.

The studies were nearly identical in design and conduct. However, UVX-001 included both subjects with corneal ectasia and progressive keratoconus, whereas only corneal ectasia subjects were enrolled in UVX-003. Further, UVX-001 was a single-center study, both UVX-002 and UVX-003 were multi-center studies. All sites were located in the US.

As specified in the final SAP, Avedro has provided clinical study reports for UVX-001, UVX-002 and UVX-003 to describe each individual trial without pooling and pooled progressive keratoconus results (UVX-001 progressive keratoconus data and UVX-002 data) and pooled corneal ectasia results (UVX-001 cornea ectasia data and UVX-003 data).

Table of Clinical Studies

Study Identifier	Objective(s) of the Study	Study Design and Type of Control	Test Product(s); Dosage Regimen; Route of Administration	Number of Subjects Enrolled	Diagnosis of Patients	Duration of Treatment
UVX-001	Safety and Efficacy	Randomized sham-controlled	Photrexa/Photrexa Viscous 0.12% solution; clinical trial device - UVA light (365 nm; 3 mW/cm^2) Single Treatment	107; (53 drug; 54 sham)	Patients with progressive keratoconus and corneal ectasia following refractive surgery	Pre-treatment and during irradiation: Photrexa/Photrexa Viscous 0.12% solution 1 drop every two min for 30 min Clinical trial device: UVA light: 30 min
UVX-002	Safety and Efficacy	Randomized sham-controlled	Photrexa/Photrexa Viscous 0.12% solution; clinical trial device - UVA light (365 nm; 3 mW/cm^2) Single Treatment	147; (73 drug; 74 sham)	Patients with progressive keratoconus	Pre-treatment and during irradiation: Photrexa/Photrexa Viscous 0.12% solution 1 drop every two min for 30 min Clinical trial device: UVA light: 30 min
UVX-003	Safety and Efficacy	Randomized sham-controlled	Photrexa/Photrexa Viscous 0.12% solution; clinical trial device: UVA light (365 nm; 3 mW/cm^2) Single Treatment	130; (67 drug; 63 sham)	Patients with corneal ectasia following refractive surgery	Pre-treatment and during irradiation: Photrexa/Photrexa Viscous 0.12% solution 1 drop every two min for 30 min Clinical trial device: UVA light: 30 min

Source: 5.2 Tabular Listing of All Clinical Studies

The following subsections discuss the design of the individual clinical studies.

6.1. UVX-001: Safety and Effectiveness of Corneal Collagen Cross-Linking In Eyes with Corneal Ectasia or Progressive Keratoconus

Study UVX-001 was a single-center study conducted in the United States (US). The study was conducted under US Investigational New Drug (IND) application 78,933.

6.1.1 General Study Design

This was a Phase 3, single-center, randomized, sham-controlled, open-label clinical study to investigate the safety and effectiveness of corneal collagen cross-linking (CXL, performed using riboflavin/UVA irradiation) for slowing the progressive changes in corneal curvature in eyes with corneal ectasia following refractive surgery or progressive keratoconus. An unmasked sham control was used whereby subjects went through the same drug administration procedure but without epithelial debridement or UVA irradiation.

On Day 0, eligible subjects were randomized into one of two treatment groups: the CXL group and the control (sham) group. Subjects with bilateral corneal ectasia or keratoconus had only 1 eye designated for study treatment (i.e., the study eye). The planned sample size was 160 subjects with corneal ectasia (80 eyes per treatment group) and 160 subjects with progressive keratoconus (80 eyes per treatment group).

Subjects were evaluated at 8 study visits: screening/baseline, Day 0 (randomization/treatment day), and Day 1, Week 1, and Month 1, 3, 6, and 12 after treatment.

At Month 3 or later, subjects whose eye(s) had not developed any contraindications for performing the CXL treatment were given the option of having CXL performed on their untreated fellow eyes (from CXL group) and untreated sham eye and untreated fellow eye (from sham control group). After treatment, these eyes were followed for 12 months according to the same schedule and protocol as the study eye in the CXL group.

The assessments in this study included manual keratometry, Pentacam measurements, corneal topography, manifest refraction, BSCVA, uncorrected visual acuity (UCVA), intraocular pressure, adverse events (AEs) and complications, dilated fundus examination, slit lamp examination, endothelial cell counts, and questionnaires for quality of vision (Refractive Status Vision Profile [RSVP] questionnaire) and subjective visual complaints.

Subjects in the CXL group had topical anesthetic administered to the study eye, and the corneal epithelium was removed. Subjects then received riboflavin ophthalmic solution with dextran in the study eye for 30 minutes (1 drop instilled onto the cornea every 2

minutes, with additional drops as needed to achieve adequate riboflavin saturation of the corneal tissue; i.e., yellow flare in the anterior chamber on slit lamp examination. If corneal thickness was < 400 microns in eyes in the CXL group after treatment with riboflavin ophthalmic solution with dextran, a second solution was instilled into the study eye: riboflavin without dextran (2 drops instilled every 5 to 10 seconds until corneal thickness increased to at least 400 microns). After the riboflavin pretreatment regimen was completed, study eyes in the CXL group were exposed to UVA light (365 nm at an irradiance of 3 mW/cm^2) for 30 minutes, with riboflavin ophthalmic solution with dextran continuing to be administered every 2 minutes during this time.

Subjects in the sham control treatment group had topical anesthetic administered to the study eye but did not have the corneal epithelium removed. Study eyes were treated with riboflavin ophthalmic solution as described above (both pretreatment and during the irradiation procedure). Subjects underwent the same UV irradiation procedure as described for subjects in the CXL group except the UVA light source was not illuminated during the procedure.

For both treatment groups, the total dose of riboflavin solution over the 30-minute pretreatment and 30-minute irradiation periods was calculated to be approximately 32 drops, or 1.6 mL (1 drop = 50 µL, 1.6 mL = 1.6 mg riboflavin).

6.1.2. Investigational Products

Riboflavin Drug Product

Photrexa Viscous: The riboflavin ophthalmic solution with dextran was a phosphate buffered saline solution containing 0.1% riboflavin and 20% dextran (b) (4), adjusted to a pH of 7.0, and packaged in 3 mL sterile dropper bottles for topical ophthalmic use. Lot numbers: 09MD0903, 81220, 80709, 80118, 80417.

Photrexa: The riboflavin ophthalmic solution without dextran was a phosphate buffered saline solution containing 0.1% riboflavin in sterile water, adjusted to a pH of 7.0, and packaged in 0.5 mL sterile pre-filled syringes for topical ophthalmic use. Lot numbers: 12072007, 12112008.

UVA Irradiation

Per the study protocols, the UVA intensity was fixed at 3 mW/cm^2 and could not be changed by the user. The duration of the UV illumination was set at 30 minutes. After 30 minutes, the UVA light source automatically switched off. The operators were instructed to keep track of the irradiation time independently to confirm actual treatment time. The only device settings that the Investigators had the ability to change were the working distance and the illumination aperture. As part of site start-up and training for use of the clinical trial device, investigators were instructed to select the medium aperture setting (9.5 mm) prior to irradiation. Details of the treatment procedure were captured in the subjects' source documents and in the electronic case report forms (eCRFs). Procedure details included the actual number and dosing times of riboflavin as well as UV illumination aperture and time. Thus any variations in the treatment procedure, whether

based on investigator discretion or not, were collected in the eCRF. Variations in the study procedures that were not consistent with the protocol, such as not following the riboflavin dosing regimen or continuing with the procedure despite a corneal thickness of <400 µm, were categorized and collected as protocol deviations.

6.1.3 Inclusion/Exclusion Criteria

Inclusion

Subjects who have one or both eyes that meet all of the following criteria:

1. 14 years of age or older
2. Had a diagnosis of:

    a. corneal ectasia after refractive corneal surgery (e.g., laser-assisted in-situ keratomileusis [LASIK], photorefractive keratectomy [PRK], or epi-LASIK) or

    b. progressive keratoconus defined as 1 or more of the following changes over a period of 24 months or less before randomization:

    - An increase of = 1.00 diopter (D) in the steepest keratometry value (or simulated keratometry [simK])
    - An increase of = 1.00 D in regular astigmatism evaluated by subjective manifest refraction
    - A myopic shift (decrease in the spherical equivalent) of = 0.50 D on subjective manifest refraction
    - A decrease ≥ 0.1 mm in the back optical zone radius in rigid contact lens wearers where other information was not available.

    [NOTE: Subjects with a clear history of progression but without prior documentation could have been followed and re-examined at a later visit to confirm progression.]

3. Had central or inferior steepening on the Pentacam map.
4. Had axial topography consistent with keratoconus or corneal ectasia
5. For progressive keratoconus, presence of one or more findings associated with keratoconus, such as:
    a. Fleischer ring
    b. Vogt striae
    c. Corneal thinning
    d. Corneal scarring
    e. Scissoring of the retinoscopic reflex
6. Steepest keratometry (K_{max}) value = 47.00 D (progressive keratoconus only)
7. I-S ratio > 1.5 on the Pentacam map or Orbscan map (progressive keratoconus only)

8. Had a BSCVA worse than 20/20 (<53 letters on Early Treatment of Diabetic Retinopathy Study [ETDRS] chart)
9. Contact Lens Wearers Only:

Removal of contact lenses for the required period of time prior to the Screening refraction:

Contact Lens Type	Minimum Discontinuation Time
Soft	3 days
Soft Extended Wear	1 week
Soft Toric	2 weeks
Rigid gas permeable	2 weeks

Exclusion

Subjects who met any of the following criteria were excluded from this study:

1. Eyes classified as either normal, atypical normal (except corneal ectasia), or keratoconus suspect on the severity grading scheme.
2. For progressive keratoconus, a history of previous corneal surgery or the insertion of Intacs in the eye(s) to be treated.
3. Corneal pachymetry at the screening exam that was < 400 microns at the thinnest point measured by Pentacam in the eye(s) to be treated when the riboflavin with dextran solution alone was to be used or < 300 microns when the riboflavin without dextran was to be used.
4. Previous ocular condition (other than refractive error) in the eye(s) to be treated that could have predisposed the eye for future complications, for example:
    a. History of corneal disease (e.g., herpes simplex, herpes zoster keratitis, recurrent erosion syndrome, corneal melt, corneal dystrophy, etc.)
    b. Clinically significant corneal scarring in the CXL treatment zone that was not related to keratoconus or corneal ectasia or prior refractive surgery or, in the investigator's opinion, would interfere with the cross-linking procedure.
5. A history of chemical injury or delayed epithelial healing in the eye(s) to be treated.
6. Pregnancy (including plan to become pregnant) or lactation during the course of the study
7. A known sensitivity to study medications
8. Subjects with nystagmus or any other condition that would have prevented a steady gaze during the CXL treatment or other diagnostic tests.
9. Subjects with a current condition that, in the investigator's opinion, would have interfered with or prolonged epithelial healing.

6.1.4 Schedule of Visits and Procedures

Table 4: Schedule of Visits and Procedures

Procedure	Screen	Treatment Visit[a]	Post-Treatment Visits					
			1 Day	1 Week	1 Month	3 Months	6 Months	12 Month
Medical History	X	X	X	X	X	X	X	X
Ocular History[b]	X	X	X	X	X	X	X	X
Medication History	X	X	X	X	X	X	X	X
Demographics	X							
BSCVA[c]	X			X	X	X	X	X
UCVA[d]	X		X	X	X	X	X	X
Manifest Refraction	X	X		X	X	X	X	X
Confocal microscopy	X							X
Intraocular Pressure Measurement[e]	X			X	X	X	X	X
Slit Lamp Exam[f]	X		X	X	X	X	X	X
Endothelial cell count[g]	X					X		X
Dilated Fundus Examination	X							X
Pentacam Pachymetry, Keratometry	X				X	X	X	X
Corneal Topography	X				X	X	X	X
Manual keratometry	X				X	X	X	X
OPD scan	X				X	X	X	X
RSVP Questionnaire	X				X	X	X	X
Subjective Complaint Questionnaire	X				X	X	X	X
Sign Consent	X							
Complications		X	X	X	X	X	X	X

Source: 5.3.5.1 UVX-001 Section 9.5.1.1

6.1.5 Primary Efficacy Variable

The primary efficacy evaluation was based on corneal curvature, as measured by maximum keratometry (Kmax) evaluated over time. According to the applicant, “Study success is defined as a difference of at least 1 diopter in the mean change in Kmax from baseline to Months 3 and 12 between the CXL treatment group and the control group.” The baseline score was defined as the closest measurement prior to treatment for the eye in question.

Of note, the primary efficacy endpoint was originally planned as the change in Kmax from baseline at Month 3 for the primary study eye for each subject. However, the applicant extended the primary efficacy endpoint from Month 3 to Month 12. The change was documented in the final Statistical Analysis Plan (SAP). According to the applicant, this change occurred after study completion but prior to conducting formal analyses.

6.1.6 Analysis Populations

The intent-to-treat (ITT) population consisted of all treated subjects, analyzed according to the randomized treatment. All safety and efficacy analyses were performed using the ITT population. All subjects received the appropriate randomized treatment; therefore, the ITT and safety populations are the same.

The per protocol (PP) set was to consist of all ITT subjects in whom there were no major protocol deviations, as defined at end of study.

6.1.7 Statistical Methodology

The change in K_{max} from baseline was evaluated for all study eyes randomized to the treatment and control groups. Data were summarized using descriptive statistics, and the differences in mean changes between the CXL treatment group and the control group at each time point were evaluated using a two sample t-test. The applicant stated, "An alpha level of 0.001 was allocated to Month 3 when an unplanned data review was conducted, and an alpha level of 0.049 was allocated to the final analysis at Month 12."

Additional analyses were conducted to test robustness of the results of the primary efficacy analyses. These analyses include a nonparametric Wilcoxon test and an analysis of covariance (ANCOVA) with baseline K_{max} value as the covariate.

Missing data were imputed using the last observation carried forward (LOCF) approach. For the subjects in the control group, the efficacy data at Month 3 or Month 6 prior to receiving corneal cross-linking treatment was carried forward to Month 12.

All efficacy analyses were completed using the intent-to-treat (ITT) population according to the randomized treatment.

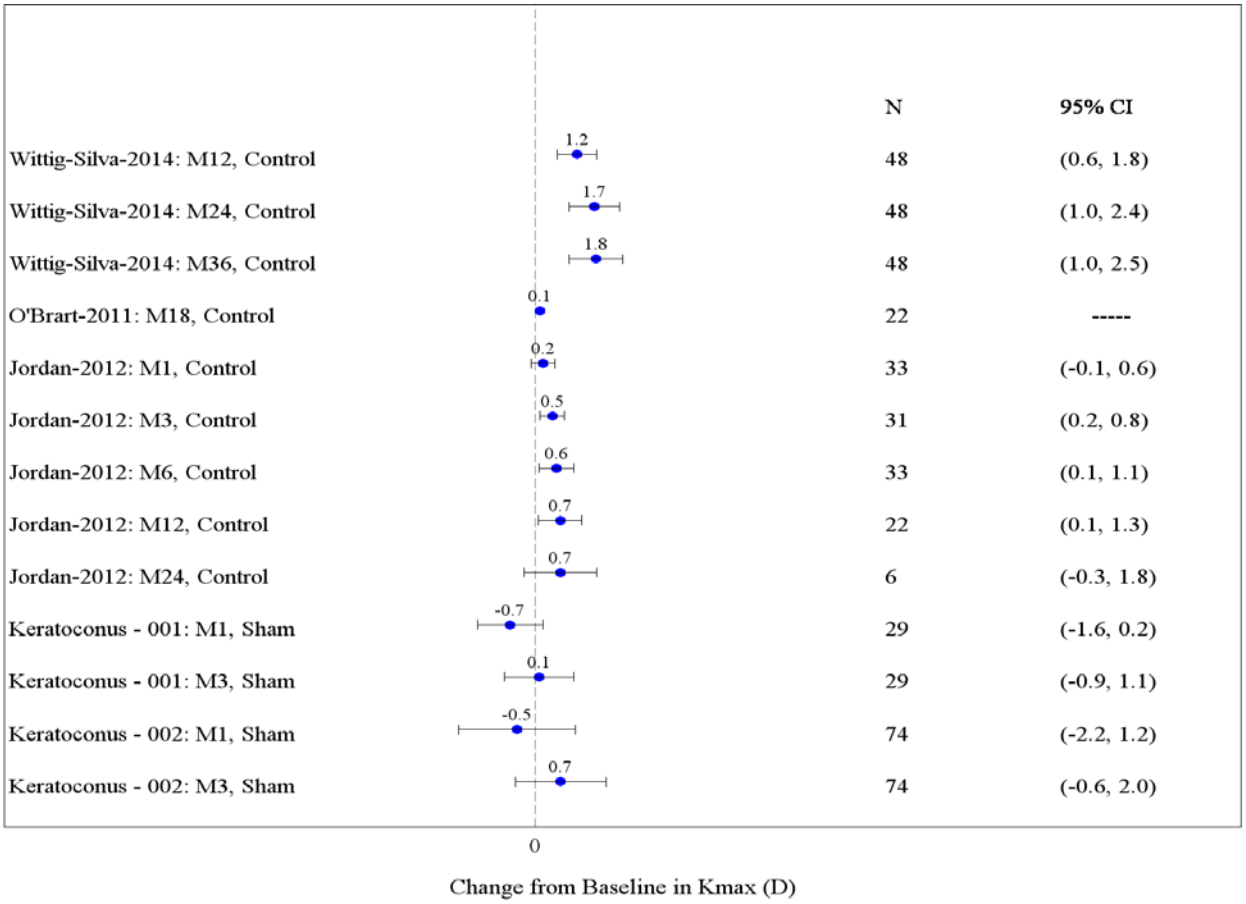
6.1.8 Rationale for the use of LOCF and the Month 12 endpoint

The applicant's primary efficacy analysis used the LOCF method to impute missing data for the control subjects who received subsequent CXL in the study eye after the Month 3 visit. The applicant considered LOCF a biologically plausible approach because of the progressive nature of keratoconus. Since there are no data to demonstrate that progressive keratoconus patients experience spontaneous remission, become free of disease or improve, the applicant claimed that the LOCF approach would not account for additional progression beyond Month 3 and would therefore provide a conservative measure of success of the cross-linking procedure.

The applicant provided numerous publications that were evaluated for further insight into the natural history of keratoconus and the response of keratoconus patients following CXL treatment. Figure 1 presents FDA findings from the literature review for the change from baseline in Kmax for control subjects. FDA included clinical trials that had long-term (≥12 months) data and/or a control group. There was a transient decrease in Kmax at Month 1, in subsequent visits, Kmax showed a gradual increase trend over time. These data suggest that keratoconus is a progressive disease and support the use of the sham

subjects' data at an earlier timepoint for the treatment comparison at a later timepoint (for example, Month 12).

Figure 1: Change from Baseline in Kmax for Sham/Control Subjects from Published Studies[5] and UVX studies



5 Wittig-Silva C, et al. A Randomized, Controlled Trial of Corneal Collagen Cross-Linking in Progressive Keratoconus, Three-Year Results. *Ophthalmology* 2014; 121 (4):812-821.

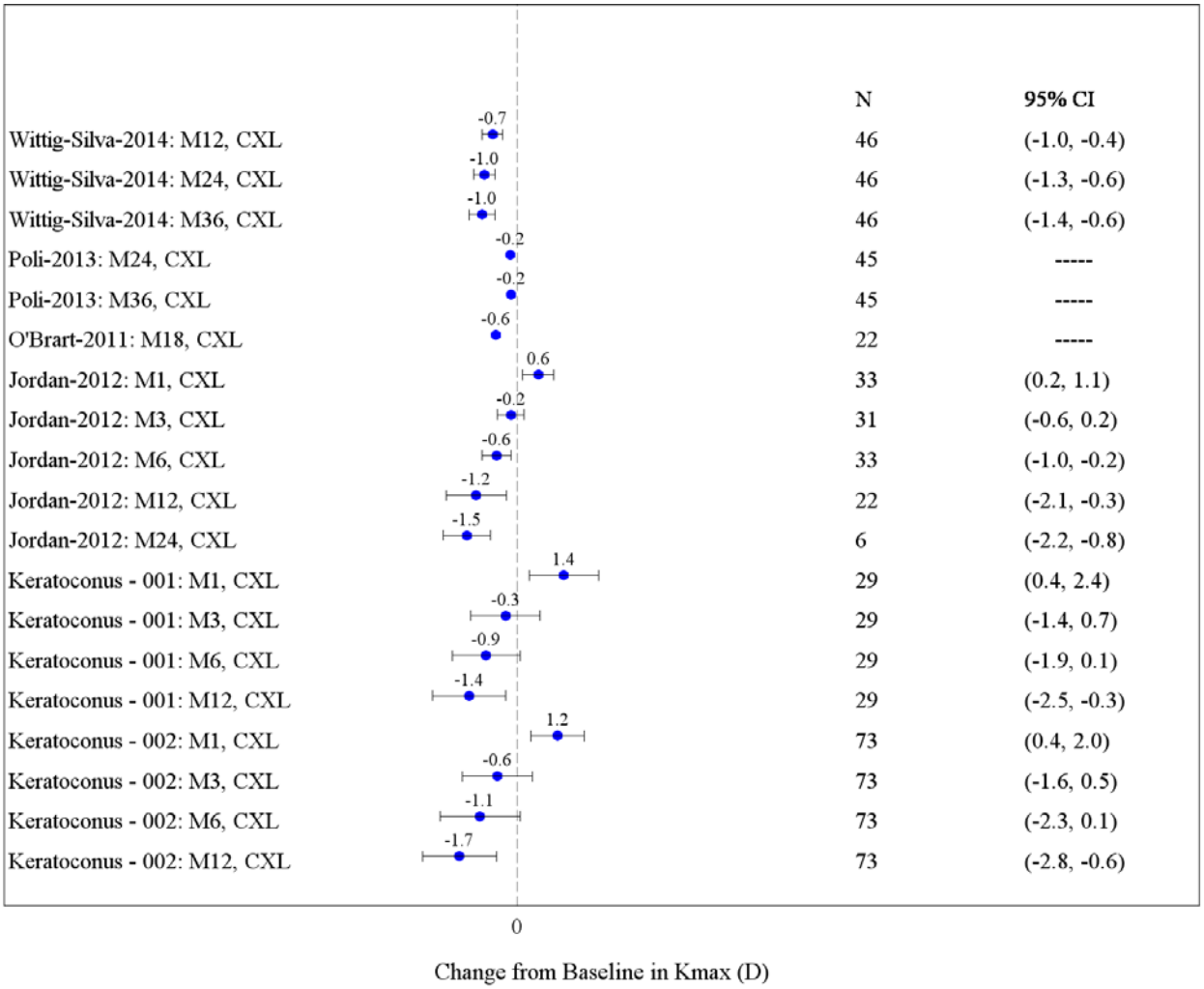
Poli M, et al. Prospective Study of Corneal Collagen Cross-linking Efficacy and Tolerance in the Treatment of Keratoconus and Corneal Ectasia: 3-Year Results. *Cornea* 2013; 23 (5): 583-590.

O'Brart D, et al. A randomised, prospective study to investigate the efficacy of riboflavin/ultraviolet A (370 nm) corneal collagen cross-linkage to halt the progression of keratoconus. *Br J Ophthalmol* 2011;95: 1519-1524.

Jordan CA. Identifying, Characterising and Modifying the Natural History and Progression of Keratoconus in New Zealand/ Aotearoa. A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Department of Ophthalmology, The University of Auckland, 2012.

As noted previously, the protocols defined the primary efficacy endpoint at Month 3. However, the primary efficacy endpoint was extended to Month 12. Figure 2 illustrates the change in Kmax from baseline for treated subjects. As seen in Figure 2, the change in Kmax from baseline at Month 3 was modest. A larger decrease occurred at visits after Month 3.

Figure 2: Change from Baseline in Kmax for Subjects from Published Studies and UVX Studies



6.2 UVX-002: Safety and Effectiveness of Corneal Collagen Cross-Linking in Eyes with Progressive Keratoconus

Study UVX-002 was a multicenter study conducted at 9 centers in the United States. The study was conducted under US Investigational New Drug (IND) application 77,882.

General Study Design
This was a prospective, randomized, parallel-group, open-label, sham-controlled, multicenter study to determine the safety and effectiveness of riboflavin ophthalmic solution/UVA irradiation for performing CXL in eyes with progressive keratoconus.

This trial is nearly identical in design, endpoints, and analyses to UVX-001 with the following exceptions:

- Only patients with progressive keratoconus were eligible to be enrolled
- Individuals who took Vitamin C supplements within one week before randomization were excluded.

Schedule of Visits
Identical to UVX-001 with the exception that Confocal Microscopy was optional in UVX-002.

6.3 UVX-003: Safety and Effectiveness of Corneal Collagen Cross-Linking in Eyes with Corneal Ectasia after Refractive Surgery

Study UVX-003 was a multicenter study conducted at 9 centers in the United States. The study was conducted under US Investigational New Drug (IND) application 77,882.

General Study Design
This was a prospective, randomized, parallel-group, open-label, sham-controlled, multicenter study to determine the safety and effectiveness of riboflavin ophthalmic solution/UVA irradiation for performing CXL in eyes with progressive keratoconus.

This trial is nearly identical in design, endpoints, and analyses to UVX-001 with the following exceptions:

- Only patients with corneal ectasia were eligible to be enrolled
- Individuals who took Vitamin C supplements within one week before randomization were excluded.

Schedule of Visits
Identical to UVX-001 with the exception that Confocal Microscopy was optional in UVX-003.

7 Demographics, Patient Disposition and Protocol Deviations

7.1 Demographics

7.1.1 Progressive Keratoconus Patients:

Table 4: Demographics: UVX-001 [Keratoconus Subjects], UVX-002 and Pooled Data (ITT Population)

		UVX-001		UVX-002		Pooled	
		CXL Group (N=29)	Control Group (N=29)	CXL Group (N=73)	Control Group (N=74)	CXL Group (N=102)	Control Group (N=103)
Age (yrs)	N	29	29	73	74	102	103
	Mean	33.3	36.9	30.2	34.2	31.1	35.0
	SD	7.59	12.53	10.08	11.52	9.51	11.82
	Median	33.9	37.5	29.0	31.9	29.7	33.8
	Min, Max	20, 50	16, 60	14, 57	15, 63	14, 57	15, 63
Gender	N	29	29	73	74	102	103
	Female - n (%)	8 (27.6%)	11 (37.9%)	19 (26.0%)	24 (32.4%)	27 (26.5%)	35 (34.0%)
	Male - n (%)	21 (72.4%)	18 (62.1%)	54 (74.0%)	50 (67.6%)	75 (73.5%)	68 (66.0%)
Ethnicity	N[a]	29	29	38	39	67	68
	Hispanic/Latino - n (%)	3 (10.3%)	3 (10.3%)	7 (18.4%)	3 (7.7%)	10 (14.9%)	6 (8.8%)
	Not Hispanic/Latino - n (%)	26 (89.7%)	26 (89.7%)	31 (81.6%)	36 (92.3%)	56 (85.1%)	63 (91.2%)
Race[b]	N[c]	29	29	71	74	100	103
	White - n (%)	19 (65.5%)	19 (65.5%)	54 (76.1%)	61 (82.4%)	73 (73.0%)	80 (77.7%)
	Black/African-American - n (%)	4 (13.8%)	4 (13.8%)	7 (9.9%)	7 (9.5%)	11 (11.0%)	11 (10.7%)
	Asian - n (%)	1 (3.4%)	2 (6.9%)	0	1 (1.4%)	1 (1.0%)	3 (2.9%)
	Other Race[d] - n (%)	5 (17.2%)	4 (13.8%)	10 (14.1%)	5 (6.8%)	15 (15.0%)	9 (8.7%)

[a] Percentages based on the number of subjects reporting ethnicity.
[b] As reported by the subject.
[c] Percentages are based on the number of subjects who reported race.
[d] In the pooled studies, race was reported as "other" for 10 Hispanics, 6 Indians, 2 Spanish, 1 Indian/South Asian, 1 Black/Asian, 1 Brazilian, 1 Latino , 1 Ethiopian, and 1 Moroccan.
Source: Table 14.1.5 (Section 14.1.1), UVX-001; Table 14.1.5, UVX-002; Table 14.1.5, Section 8.1

The planned sample size to evaluate progressive keratoconus was 160 subjects. However, enrollment into UVX-001 was terminated early when the investigator left the study site. At the time of the enrollment termination, the study had enrolled 58 progressive keratoconus subjects.

In the pooled studies, the CXL and sham control groups were generally comparable with regard to demographic characteristics. The mean age (range) was 31 years (range of 14 to 57 years) in the CXL group and 35 (15 to 63 years) in the sham control group. Most subjects in each treatment group were Caucasian (73%, CXL; 78%, control); the remaining subjects (overall frequencies) were black/African-American (11%), Asian (2%), or "other race" (12%). The majority of subjects in each treatment group were male (74%, CXL; 66%, control).

In the individual studies, the treatment groups were generally comparable with regards to demographic characteristics. The percentage of white subjects was higher in UVX-002

than in UVX-001. Otherwise, demographic characteristics for progressive keratoconus subjects in UVX-001 and subjects in UVX-002 were similar.

7.1.2 Corneal Ectasia Patients:

Table 5: Demographics: UVX-001 [Corneal Ectasia Subjects], UVX-003 and Pooled Data (ITT Population)

		UVX-001		UVX-003		Pooled	
		CXL Group (N=24)	Control Group (N=25)	CXL Group (N=67)	Control Group (N=63)	CXL Group (N=91)	Control Group (N=88)
Age (yrs)	N	24	25	67	63	91	88
	Mean	45.0	40.0	43.0	42.5	43.5	41.8
	SD	8.95	7.67	8.72	9.08	8.78	8.73
	Median	42.7	38.6	44.2	41.4	43.6	39.7
	Min, Max	28, 63	24, 57	22, 60	24, 62	22, 63	24, 62
Gender	N	24	25	67	63	91	88
	Female - n (%)	10 (41.7%)	8 (32.0%)	23 (34.3%)	16 (25.4%)	33 (36.3%)	24 (27.3%)
	Male - n (%)	14 (58.3%)	17 (68.0%)	44 (65.7%)	47 (74.6%)	58 (63.7%)	64 (72.7%)
Ethnicity	N[a]	24	24	27	27	51	51
	Hispanic/Latino - n (%)	2 (8.3%)	1 (4.2%)	9 (33.3%)	9 (33.3%)	11 (21.6%)	10 (19.6%)
	Not Hispanic/Latino - n (%)	22 (91.7%)	23 (95.8%)	18 (66.7%)	18 (66.7%)	40 (78.4%)	41 (80.4%)
Race[b]	N[c]	24	25	63	57	87	82
	White - n (%)	18 (75.0%)	21 (84.0%)	50 (79.4%)	45 (78.9%)	68 (78.2%)	66 (80.5%)
	Black/African-American - n (%)	3 (12.5%)	2 (8.0%)	7 (11.1%)	5 (8.8%)	10 (11.5%)	7 (8.5%)
	Asian - n (%)	0	0	3 (4.8%)	4 (7.0%)	3 (3.4%)	4 (4.9%)
	Other Race[d] - n (%)	3 (12.5%)	2 (8.0%)	3 (4.8%)	3 (5.3%)	6 (6.9%)	5 (6.1%)

[a] Percentages based on the number of subjects reporting ethnicity.
[b] As reported by the subject.
[c] Percentages are based on the number of subjects who reported race.
[d] In the pooled studies, race was reported as "other" for 6 Hispanics, 2 Middle Eastern, 1 Indian, 1 Latino, and 1 mixed.
Source: Table 14.1.5 (Section 14.1.2), UVX-001, Table 14.1.5, UVX-003, Table 14.1.5 (Section 8.2)

The planned sample size was 160 subjects to evaluate corneal ectasia in Study UVX-001. However as previously stated, enrollment into UVX-001 was terminated early when the investigator left the study site. At the time of the enrollment termination, the study had enrolled 49 corneal ectasia subjects.

In the pooled population, the CXL and sham control groups were generally comparable with regard to demographic and baseline characteristics. The mean age (range) was 44 years (22 to 63 years) in the CXL group and 42 years (24 to 62 years) in the sham control group. Most subjects in each treatment group were Caucasian (78%, CXL; 81%, control); the remaining subjects (overall frequencies) were black/African-American (10%), Asian (4%), or "other race" (7%). The majority of subjects in each treatment group were male (64%, CXL; 73%, control).

Demographic characteristics for corneal ectasia subjects in UVX-001 and subjects in UVX-003 were similar, although there were more Hispanic/Latino patients inUVX-003.

7.2 Subject Disposition

The section below provides subject disposition for their CXL study eye and sham control study eye. For information on control patients who received CXL treatment of the study eye, and information on fellow eyes, see Appendix D.

7.2.1 Progressive Keratoconus

Progressive Keratoconus Subjects, UVX-001, ITT Population

Received randomized therapy	CXL Group (N=29)	Sham Control (N=29)
Completed study (n, %)	20 (69%)	12 (41%)
Discontinued study* (n, %)	9 (31%)	17 (59%)

* The investigator left the study site and the study was terminated by the Sponsor.
(Source: Table 14.1.1 (Section 14.1.1))

The ITT population consisted of 58 progressive keratoconus subjects, with 29 subjects randomized to each of the 2 treatment groups. As shown in the table, half of the keratoconus subjects (55%) completed the study, with more subjects completing in the CXL group (69%) compared with the sham control group (41%). All subjects who discontinued prematurely did so because the investigator left the site and the study was terminated by the Sponsor. None of the subjects discontinued due to an AE.

Progressive Keratoconus Subjects, UVX-002, ITT Population

Received randomized therapy	CXL Group (N=73)	Sham Control (N=74)
Completed study (n, %)	65 (89%)	62 (84%)
Discontinued study (n, %)	8 (11%)	12 (16%)
Voluntary withdrawal	3 (4%)	8 (11%)
Lost to follow-up	5 (7%)	4 (5%)

(Source: Table 14.1.1 (Section 14.1))

A total of 147 subjects were randomized into the study (73, CXL group; 74, sham control group). Most subjects (86%) completed the study. The proportion of subjects who discontinued the study was 11% and 16% in the CXL and sham control groups, respectively. Reasons for discontinuation were voluntary withdrawal (unrelated to safety) and lost to follow-up.

Subject Disposition (ITT Population): UVX-001 (Progressive Keratoconus Subjects), UVX-002, and Pooled Studies

	UVX-001		UVX-002		Pooled Studies	
Category, n(%)	**CXL (N=29)**	**Sham (N=29)**	**CXL (N=73)**	**Sham (N=74)**	**CXL (N=102)**	**Sham (N=103)**
Randomized	29	29	73	74	102	103
Completed the study	20 (69.0%)	12 (41.4%)	65 (89.0%)	62 (83.8%)	85 (83.3%)	74 (71.8%)
Discontinued from study	9 (31.0%)	17 (58.6%)	8 (11.0%)	12 (16.2%)	17 (16.7%)	29 (28.2%)
Administrative	9 (31.0%)	17 (58.6%)	0	0	9 (8.8%)	17 (16.5%)
Voluntary withdrawal	0	0	3 (4.1%)	8 (10.8%)	3 (2.9%)	8 (7.8%)
Lost to follow-up	0	0	5 (6.8%)	4 (5.4%)	5 (4.9%)	4 (3.9%)

Source: UVX-001 CSR Table 7 and UVX-002 CSR Table 6.

The majority of subjects remained in the randomized treatment and had Kmax measurements until Month 3. The study design allowed the subjects in the sham group to receive the CXL treatment after Month 3. As a result, the number of the sham-treated subjects who remained on their assigned treatment dropped markedly after Month 3. As shown in the table below no subjects in the sham group in UVX-001 and only 2 subjects in UVX-002 remained on the assigned treatment and had efficacy data at Month 12.

Number of Progressive Keratoconus Subjects Remaining on Randomized Treatment and with Kmax Measurements by Visit: UVX-001 and UVX-002

	UVX-001		UVX-002	
Visit	**CXL (N=29)**	**Sham (N=29)**	**CXL (N=73)**	**Sham (N=74)**
Baseline	29	29	73	74
Month 1	29	28	70	73
Month 3	29	29	67	67
Month 6	28	18	67	21
Month 12	20	0	69	2

Source: Statistical Reviewer's analysis.

7.2.2 Corneal Ectasia

Corneal Ectasia Subjects, UVX-001, ITT Population

Received randomized therapy	CXL Group (N=24)	Sham Control (N=25)
Completed study (n, %)	20 (83%)	11 (44%)
Discontinued study (n, %)	4 (17%)	14 (56%)
Investigator left study*	3 (12%)	10 (40%)
Lost to follow-up	1 (4 %)	3 (12%)
Administrative	0	1 (4%)

* The investigator left the study site and the study was terminated by the Sponsor.
(Source: Table 14.1.1 (Section 14.1.2))

The ITT population consisted of 49 corneal ectasia subjects, with 24 subjects randomized the CXL group and 25 randomized to the sham control group. As shown in the table above, the majority of corneal ectasia subjects (63%) completed the study, with more subjects completing in the CXL group (83%) compared with the sham control group (44%). The proportion of subjects who discontinued the study was 17% and 56% in the CXL and sham control groups, respectively. The majority of subjects who discontinued prematurely did so because the investigator left the site and the study was terminated by the Sponsor.

Corneal Ectasia Subjects, UVX-003, ITT Population

Received randomized therapy	CXL Group (N=67)	Sham Control (N=63)
Completed study (n, %)	56 (84%)	48 (76%)
Discontinued study (n, %)	11 (16%)	15 (24%)
Voluntary withdrawal	0	5 (8%)
Lost to follow-up	6 (9%)	3 (5%)
Other	5 (7%)	7 (11%)

(Source: Table 14.1.1 (Section 14.1))

The ITT population consisted of 130 subjects, with 67 subjects randomized to the CXL group and 63 subjects randomized to the sham control group. As shown in the table above, most subjects (80%) completed the study. The proportion of subjects who discontinued the study was 16% and 24% in the CXL and sham control groups, respectively. Reasons for discontinuation were “other” (9%), lost to follow-up (7%), and voluntarily withdrawal (unrelated to safety) (4%).

Subject Disposition (ITT Population): UVX-001 (Corneal Ectasia Subjects), UVX-003, and Pooled Studies

	UVX-001		UVX-003		Pooled Studies	
Category, n(%)	**CXL (N=24)**	**Sham (N=25)**	**CXL (N=67)**	**Sham (N=63)**	**CXL (N=91)**	**Sham (N=88)**
Randomized	24	25	67	63	91	88
Completed the study	20 (83.3%)	11 (44.0%)	56 (83.6%)	48 (76.2%)	76 (83.5%)	59 (67.0%)
Discontinued from study	4 (16.7%)	14 (56.0%)	11 (16.4%)	15 (23.8%)	15 (16.5%)	29 (33.0%)
Administrative	0	1 (4.0%)	0	0	0	1 (1.1%)
Voluntary withdrawal	0	0	0	5 (7.9%)	0	5 (5.7%)
Lost to follow-up	1 (4.2%)	3 (12.0%)	6 (9.0%)	3 (4.8%)	7 (7.7%)	6 (6.8%)
Other	3 (12.5%)	10 (40.0%)	5 (7.5%)	7 (11.1%)	8 (8.8%)	17 (19.3%)

Source: UVX-001 CSR Table 8 and UVX-003 CSR Table 6.

The majority of corneal ectasia subjects remained on the randomized treatment and had Kmax measurements until Month 3. After Month 3, the number of the sham-treated subjects who remained on their assigned treatment dropped markedly. As seen in the table below no subjects in the sham group remained on the assigned treatment and had efficacy data at Month 12 in UVX-001. Only two sham subjects stayed on sham for the 12 month duration in UVX-003

Number of Corneal Ectasia Subjects Remaining on Randomized Treatment and with Kmax Measurements by Visit: UVX-001 and UVX-003

	UVX-001		UVX-003	
Visit	**CXL (N=24)**	**Sham (N=25)**	**CXL (N=67)**	**Sham (N=63)**
Baseline	24	25	63	63
Month 1	24	25	64	61
Month 3	23	24	65	61
Month 6	22	13	62	19
Month 12	20	0	52	2

Source: Statistical Reviewer's analysis.

7.2.3 Illumination Diameter in Clinical Studies

As part of site start-up and training for use of the clinical trial device, investigators were instructed to select the medium aperture setting (9.5 mm) prior to irradiation. The following table shows the number of subjects with different illumination diameters.

Number of Study Subjects by Illumination Diameter (CXL Group, ITT Population)

Illumination Diameter	UVX-001 Ectasia	UVX-001 Keratoconus	UVX-002 Keratoconus	UVX-003 Ectasia
Medium (9.5 mm)	24	29	61	56
Large (11.0 mm)	--	--	10	7

7.3 Protocol Deviations

Details of the treatment procedure were captured in the subjects' source documents and in the electronic case report forms (eCRFs). Procedure details included the actual number and dosing times of riboflavin ophthalmic solution as well as UVA illumination aperture and time. Thus any variations in the treatment procedure, whether based on investigator discretion or not, were collected in the eCRF. Variations in the study procedures that were not consistent with the protocol, such as not following the riboflavin dosing regimen or continuing with the procedure despite a corneal thickness of <400 µm, were categorized and collected as protocol deviations.

Tables below list Protocol Deviations by Indication. The tables below capture deviations that occurred in the CXL Study Eye, the Sham Control Study Eye, the Sham Study Eye following treatment with CXL (after Month 3), or the Fellow Eye (in both arms) following treatment with CXL (after Month 3). Additional details can be found in the tables listed in Appendix A (UVX-001), Appendix B (UVX-002) and Appendix C (UVX 003).

7.3.1 Progressive Keratoconus Patients

UVX-001 & UVX-002 Pooled (Keratoconus) – Counts of Protocol Deviations by Category

Violation/Deviation Reason	Subcategory	Number of Deviations	
		CXL Group (N=102)	Sham Control Group (N=103)
Did not meet inclusion/exclusion criteria	Exclusion #06: Pregnancy (including plan to become pregnant) or lactation during the course of the study.	0	1
Did not meet inclusion/exclusion criteria	Exclusion #10: Taking Vitamin C (ascorbic acid) within 1 week of treatment.	2	3
Did not meet inclusion/exclusion criteria	Inclusion #02: Having a diagnosis of progressive keratoconus defined as one or more of the following changes over a period of 24 months or less before randomization.	4	4

Violation/Deviation Reason	Subcategory	Number of Deviations	
		CXL Group (N=102)	Sham Control Group (N=103)
Did not meet inclusion/exclusion criteria	Inclusion #07: I-S ratio > 1.5 on the Pentacam map or topography map	0	3
Did not meet inclusion/exclusion criteria	Inclusion #08. BSCVA worse than 20/20 (<53 letters on ETDRS chart)	0	1
Did not meet inclusion/exclusion criteria	Inclusion #09: Contact Lens Wearers Only: Removal of contact lenses for the required period of time prior to the screening refraction.	0	2
Did not obtain proper consent prior to performing study procedure	--	12	15
Not treated per randomization assignment	--	1	1
BSCVA not done	--	11	12
UCVA not done	--	2	14
Manifest refraction not done	--	5	3
IOP measurement not done	--	113	169
Slit lamp exam not done	--	4	5
Endothelial cell count not done	--	33	26
Dilated fundus exam not done	--	5	1
Pentacam pachymetry, keratometry not done	--	3	12
Ultrasound pachymetry not done	--	0	1
Manual keratometry not done	--	14	33
RSVP questionnaire not done	--	11	8
Patients questionnaire not done	--	19	16
Other (Specify)	Artificial Tears/BSS/water used instead of protocol specified hypotonic saline.	23	24
	Contact Lens Wearer - Refraction not stable/stability check not done	5	2
	Crossover eye/ Fellow eye not treated within 6 months of study eye treatment	3	5
	Data point not available/reported	6	4
	Exam done on different date	0	1
	Exam not done	6	11
	Fellow eye did not qualify for treatment	1	0
	ICF documentation improper/incomplete	1	0
	Keratoconus progression time period too long	2	3
	Keratoconus severity incorrect.	3	1
Other (Specify) Cont'd.	RSVP done at treatment visit, rather than screening.	1	0

Violation/Deviation Reason	Subcategory	Number of Deviations	
		CXL Group (N=102)	Sham Control Group (N=103)
	Riboflavin dosing not per protocol	7	19
	Screening exams not repeated when treatment > 30 days after screening	3	2
	Treatment and screening on same day	0	1
	Treatment not within 30 days of screening	0	1
	Visit not done.	12	29
	Visit out of protocol specified window	56	73
	Wrong eye randomized	1	0

7.3.2 Corneal Ectasia Patients

UVX-001 & UVX-003 Pooled (Ectasia) - Counts of Protocol Deviations by Category

Violation/Deviation Reason	Subcategory	Number of Deviations	
		CXL Group (N = 91)	Sham Control Group (N = 88)
Did not meet inclusion/exclusion criteria	Exclusion #08. Taking Vitamin C (ascorbic acid) supplements within 1 week of the cross-linking treatment.	1	1
Did not meet inclusion/exclusion criteria	Inclusion #04: BSCVA worse than 20/20 (<55 letters on ETDRS chart).	2	1
Did not meet inclusion/exclusion criteria	Inclusion #05. Contact Lens Wearers Only: Removal of contact lenses for the required period of time prior to the screening refraction.	2	0
Did not obtain proper consent prior to performing study procedure	--	12	9
BSCVA not done	--	8	26
UCVA not done	--	8	15
Manifest refraction not done	--	3	7
IOP measurement not done	--	66	118
Slit lamp exam not done	--	3	9
Endothelial cell count not done	--	26	26
Pentacam pachymetry, keratometry not done	--	7	6
Ultrasound pachymetry not done	--	4	0
Corneal topography not done	--	1	1
Manual keratometry not done	--	42	29

RSVP questionnaire not done	--	24	14
Patients questionnaire not done	--	15	14
Other (Specify)	Artificial Tears/BSS/water used instead of protocol specified hypotonic saline.	23	24
	Contact Lens Wearer - Refraction not stable/stability check not done	6	5
	Crossover eye/ Fellow eye not treated within 6 months of study eye treatment	4	4
	Data point not available/reported	7	5
	Exam not done	4	8
	ICF documentation improper/incomplete	5	3
	Pachymetry under 400 microns	.	2
	RSVP done at treatment visit, rather than screening.	3	3
	Riboflavin dosing not per protocol	7	12
	Screening exams not repeated when treatment > 30 days after screening	.	1
	Treatment and screening on same day	1	.
	Treatment not within 30 days of screening	3	3
	UV Light illumination time < 30 mins	2	1
	Visit not done.	11	13
	Visit out of protocol specified window	39	45

8 Primary Analysis Results

For completeness, results are presented for evaluations at Months 1, 3, 6 and 12.

For histograms showing change in Kmax from baseline at the Month 3 visit, see Appendix E.

8.1 Progressive Keratoconus Patients

8.1.1 UVX-001

K_{max} and Change in K_{max} from Baseline in the Randomized Study Eye (Keratoconus Subjects, UVX-001, ITT Population; LOCF)

		CXL	Sham Control	Change from Baseline			
		Group	Group	CXL	Sham Control		
Visit	Statistic	(N=29)	(N=29)	(N=29)	(N=29)	Difference[1]	p-value [2]
Baseline	Mean (SD)	60.6 (7.3)	61.9 (8.3)				
	Median	59.2	62.0				
	Min, Max	49.5, 79.2	47.7, 81.3				
Month 1	Mean (SD)	62.0 (8.4)	61.2 (8.3)	1.4 (2.7)	-0.7 (2.5)	----	0.0007 *
	Median	60.1	60.2	0.9	-0.2	2.1 (0.7,3.5)	0.0029 **
	Min, Max	51.5, 89.4	47.5, 78.6	-1.4, 13.9	-7.9, 4.8	2.1 (0.7,3.5)	0.0031 ***
Month 3	Mean (SD)	60.3 (8.2)	62.0 (9.4)	-0.3 (2.7)	0.1 (2.6)	----	0.2048 *
	Median	58.3	60.8	-0.7	-0.1	-0.5 (-1.9,0.9)	0.5085 **
	Min, Max	48.0, 86.2	47.5, 87.4	-5.4, 10.7	-7.4, 6.6	-0.4 (-1.7,1.0)	0.5918 ***
Month 6	Mean (SD)	59.7 (8.1)	62.3 (9.5)	-0.9 (2.6)	0.5 (3.0)	----	0.0557 *
	Median	57.7	60.8	-1.1	0	-1.4 (-2.9,0.1)	0.0674 **
	Min, Max	48.0, 82.6	47.5, 84.1	-5.2, 7.1	-6.8, 7.6	-1.3 (-2.8,0.2)	0.0838 ***
Month 12	Mean (SD)	59.2 (7.8)	62.3 (9.5)	-1.4 (2.8)	0.5 (3.0)	----	0.0170 *
	Median	58.4	60.8	-1.0	0	-1.9 (-3.4,-0.3)	0.0175 **
	Min, Max	48.6, 82.6	47.5, 84.1	-7.8, 7.1	-6.8, 7.6	-1.8 (-3.4,-0.3)	0.0217 ***

[1] Difference in mean change from baseline in Kmax (CXL – Control).
[2] Three p-values are presented here, including
* P-value on difference in distribution between CXL and Control by Wilcoxon test.
** P-value on difference between CXL and Control by t-test.
*** P-value on difference between CXL and Control by ANCOVA with baseline as covariate.

Source: UVX-001 CSR Table 14.2.1.1.2 and Reviewer's analysis.

The difference between the CXL and control groups in mean change from baseline in Kmax progressively increased, in favor of CXL, from Month 3 through Month 12 for progressive keratoconus subjects. The difference between treatment groups was less than the clinical threshold of 1.0 D at Month 3 (–0.3 D vs. 0.1 D) and exceeded 1.0 D at Month 6 (–0.9 D vs. 0.5 D) and Month 12 (–1.4 D vs. 0.5 D). The difference of 0.5D at Month 3 was not statistically significant; however, the difference of 1.9 D at Month 12 was statistically significant. It is worth noting that the majority of the subjects in the sham control group received corneal crosslinking treatment (CXL) after Month 3 and their Kmax data after CXL treatment were imputed based on a LOCF strategy.

The applicant conducted sensitivity analysis using the observed data, which confirmed the finding at Month 3. The sensitivity analysis after Month 3 was less meaningful as the

number of observations in the randomized study eye markedly decreased after Month 3 in the control group when the sham study eye could receive CXL treatment.

8.1.2 UVX-002

Table 1: K_{max} and Change in K_{max} from Baseline in the Randomized Study Eye (Keratoconus Subjects, UVX-002, ITT Population; LOCF)

		CXL	Sham Control	Change from Baseline			
		Group	Group	CXL	Sham Control		
Visit	Statistic	(N=73)	(N=74)	(N=73)	(N=74)	Difference[1]	p-value [2]
Baseline	Mean (SD)	61.0 (9.8)	59.8 (9.2)				
	Median	58.0	57.5				
	Min, Max	47.8, 96.4	48.3, 90.3				
Month 1	Mean (SD)	62.2 (9.4)	59.3 (11.9)	1.2 (3.4)	-0.5 (7.2)	----	0.0009 *
	Median	59.4	57.3	1.0	-0.1	1.7 (-0.1,3.5)	0.0678 **
	Min, Max	49.3, 93.8	0, 91.3	-16.8, 8.1	-58.4, 8.0	1.7 (-0.1,3.6)	0.0622 ***
Month 3	Mean (SD)	60.4 (8.9)	60.5 (10.9)	-0.6 (4.4)	0.7 (5.6)	----	0.5076 *
	Median	58.4	57.8	0	-0.1	-1.3 (-3.0,0.3)	0.1142 **
	Min, Max	47.8, 89.5	48.8, 108.0	-32.7, 5.5	-8.5, 43.6	-1.2 (-2.8,0.4)	0.1426 ***
Month 6	Mean (SD)	59.9 (8.3)	61.0 (11.3)	-1.1 (5.1)	1.2 (5.7)	----	0.0059 *
	Median	57.9	58.0	-0.5	-0.1	-2.2 (-4.0,-0.5)	0.0129 **
	Min, Max	47.3, 87.5	49.4, 108.0	-36.2, 11.6	-8.5, 43.6	-2.1 (-3.8,-0.4)	0.0177 ***
Month 12	Mean (SD)	59.3 (8.5)	61.0 (11.3)	-1.7 (4.7)	1.2 (5.7)	----	<0.0001*
	Median	58.0	58.0	-1.0	-0.1	-2.9 (-4.6,-1.2)	0.0010 **
	Min, Max	46.6, 90.9	49.4, 108.0	-31.6, 7.3	-8.5, 43.6	-2.8 (-4.5,-1.1)	0.0015 ***

[1] Difference in mean change from baseline in Kmax (CXL – Control).

[2] Three p-values are presented here, including

* P-value on difference in distribution between CXL and Control by Wilcoxon test.

** P-value on difference between CXL and Control by t-test.

*** P-value on difference between CXL and Control by ANCOVA with baseline as covariate.

Source: UVX-002 CSR Table 14.2.1.1.3 and Reviewer's analysis.

The difference between the CXL and sham control groups in mean change from baseline Kmax progressively increased, in favor of CXL, from Month 3 through Month 12. The difference between treatment groups exceeded 1.0 D at Month 3 (–0.6 D vs. 0.7 D), Month 6 (–1.1 D vs. 1.2 D), and Month 12 (–1.7 D vs. 1.2 D). Although a difference of 1.3 D was observed in the mean change in Kmax from baseline to Month 3 between the CXL group and the sham control group, the difference was not statistically significant. The large mean difference (1.3 D) may have been driven by one large decrease in Kmax experienced by a subject in the CXL group and one large increase in Kmax experienced by a subject in the sham control group. These two groups were not differentiable in terms of the median (0 vs -0.1 D). The difference between treatment groups in mean change from baseline Kmax was statistically significant at Month 12. Similar to the

previous study, the majority of the subjects in the sham control group received corneal crosslinking treatment (CXL) after Month 3 and their Kmax data after CXL treatment were imputed based on LOCF strategy.

The applicant conducted sensitivity analysis using the observed data, which confirmed the finding at Month 3. The sensitivity analysis after Month 3 was less meaningful as the number of observations in the randomized study eye dropped markedly after Month 3 in the control group when the sham study eye could receive CXL treatment.

8.2 Corneal Ectasia Patients

8.2.1 UVX-001

Table 2: K_{max} and Change in K_{max} from Baseline in the Randomized Study Eye (Corneal Ectasia Subjects, UVX-001, ITT Population; LOCF)

		CXL Group	Sham Control Group	Change from Baseline			
				CXL	Sham Control	Difference	
Visit	Statistic	(N=24)	(N=25)	(N=24)	(N=25)	95% CI [1]	p-value [2]
Baseline	Mean (SD)	56.3 (6.3)	55.0 (5.5)				
	Median	56.2	55.2				
	Min, Max	47.4, 71.6	47.0, 68.2				
Month 1	Mean (SD)	57.4 (7.6)	55.8 (6.0)	1.1 (2.1)	0.8 (1.7)	----	0.1966 *
	Median	57.2	55.5	0.9	0.5	0.3 (-0.8,1.3)	0.6408 **
	Min, Max	42.9, 77.0	47.7, 67.1	-4.5, 6.0	-3.0, 6.5	0.1 (-0.9,1.1)	0.8622 ***
Month 3	Mean (SD)	56.4 (7.0)	56.0 (6.4)	0.1 (1.3)	1.0 (1.7)	----	0.0374 *
	Median	55.1	56.0	0.0	0.7	-0.9 (-1.8,-0.1)	0.0382 **
	Min, Max	47.6, 73.8	47.6, 70.4	-2.5, 3.3	-1.0, 7.3	-1.1 (-1.8,-0.3)	0.0068 ***
Month 6	Mean (SD)	55.7 (6.6)	56.0 (6.2)	-0.6 (1.6)	1.0 (1.7)	----	0.0010 *
	Median	53.2	56.6	-0.8	0.6	-1.7 (-2.6,-0.7)	0.0010 **
	Min, Max	47.7, 70.4	47.6, 70.0	-4.5, 3.3	-1.0, 6.9	-1.7 (-2.7,-0.8)	0.0006 ***
Month 12	Mean (SD)	55.3 (6.6)	56.0 (6.2)	-1.0 (1.7)	1.0 (1.7)	----	<0.0001 *
	Median	53.3	56.6	-0.9	0.6	-2.0 (-3.0,-1.1)	0.0001 **
	Min, Max	47.0, 71.4	47.6, 70.0	-4.6, 3.3	-1.0, 6.9	-2.1 (-3.1,-1.2)	<.0001 ***

[1] Difference in mean change from baseline in Kmax (CXL – Control).

[2] Three p-values are presented here, including

* P-value on difference in distribution between CXL and Control by Wilcoxon test.

** P-value on difference between CXL and Control by t-test.

*** P-value on difference between CXL and Control by ANCOVA with baseline as covariate.

Source: UVX-001 CSR Table 14.2.1.1.2 and Reviewer's analysis.

When the primary efficacy endpoint was tested at Month 3, a statistically significant difference (0.9 D) in the mean change in Kmax from baseline between the CXL group and the sham control group was observed. The difference between the CXL and sham

control groups in mean change from baseline Kmax progressively increased, in favor of CXL, from Month 3 through Month 12. The difference between treatment groups was slightly less than 1.0 D at Month 3 (0.1 D vs. 1.0 D) and exceeded 1.0 D at Month 6 (–0.6 D vs. 1.0 D) and Month 12 (–1.0 D vs. 1.0 D). The difference between treatment groups in mean change from baseline Kmax was statistically significant at Month 12. The majority of the subjects in the sham control group received corneal crosslinking treatment (CXL) after Month 3, and their Kmax data after CXL treatment were imputed.

The applicant conducted sensitivity analysis using the observed data, which confirmed the finding at Month 3. The sensitivity analysis after Month 3 was less meaningful as the number of observations in the randomized study eye markedly decreased after Month 3 in the control group when the sham study eye could receive CXL treatment.

8.2.2 UVX-003

Table 3: K_{max} and Change in K_{max} from Baseline in the Randomized Study Eye (Corneal Ectasia Subjects, UVX-003, ITT Population; LOCF)

		CXL	Sham Control	Change from Baseline			
		Group	Group	CXL	Sham Control		
Visit	Statistic	(N=67)	(N=63)	(N=67)	(N=63)	Difference[1]	p-value [2]
Baseline [3]	Mean (SD)	55.1 (7.1)	54.7 (6.8)				
	Median	53.9	52.9				
	Min, Max	44.9, 74.5	42.9, 76.3				
Month 1	Mean (SD)	56.0 (7.0)	54.7 (6.7)	1.0 (1.8)	0.0 (1.1)	----	0.0019 *
	Median	55.7	53.4	0.6	0.1	1.0 (0.4,1.5)	0.0005 **
	Min, Max	45.2, 75.8	43.4, 75.1	-3.1, 5.8	-2.2, 2.4	1.0 (0.4,1.5)	0.0004 ***
Month 3	Mean (SD)	54.9 (7.0)	55.3 (6.8)	-0.2 (2.4)	0.6 (1.9)	----	0.0418 *
	Median	53.4	53.8	0.1	0.5	-0.8 (-1.6,-0.0)	0.0386 **
	Min, Max	44.8, 77.3	43.4, 77.6	-8.6, 6.8	-2.7, 11.9	-0.8 (-1.5,-0.0)	0.0417 ***
Month 6	Mean (SD)	54.6 (6.6)	55.2 (7.0)	-0.5 (2.0)	0.5 (2.3)	----	0.0045 *
	Median	53.3	53.8	-0.2	0.5	-1.0 (-1.8,-0.3)	0.0084 **
	Min, Max	45.0, 71.4	43.3, 77.6	-8.4, 2.6	-8.6, 11.9	-1.0 -1.7,-0.3)	0.0086 ***
Month 12	Mean (SD)	54.5 (6.8)	55.2 (7.0)	-0.5 (2.2)	0.5 (2.3)	----	0.0017 *
	Median	53.5	54.1	-0.3	0.5	-1.1 (-1.9,-0.3)	0.0080 **
	Min, Max	44.9, 74.3	43.3, 77.6	-10.2, 3.8	-8.6, 11.9	-1.1 (-1.8,-0.3)	0.0087 ***

[1] Difference in mean change from baseline in Kmax (CXL – Control).
[2] Three p-values are presented here, including
* P-value on difference in distribution between CXL and Control by Wilcoxon test.
** P-value on difference between CXL and Control by t-test.
*** P-value on difference between CXL and Control by ANCOVA with baseline as covariate.
[3] Four subjects in CXL group did not have a K_{max} measurement at baseline.
Source: UVX-003 CSR Table 14.2.1.1.3 and Reviewer's analysis.

When the primary efficacy endpoint was tested at Month 3, a statistically significant difference (0.8 D) in the mean change in Kmax from baseline to Month 3 between the CXL group and the sham control group was observed. The difference between the CXL and control groups in mean change from baseline Kmax favored CXL from Month 3 through Month 12. The difference between treatment groups was less than 1.0 D at Month 3 (–0.2 D vs. 0.6 D) and reached 1.0 D at Month 6 (–0.5 D vs. 0.5 D) and Month 12 (–0.5 D vs. 0.5 D). The difference between treatment groups in mean change from baseline Kmax was statistically significant at Month 12. These observations were based on the analysis in which missing data was imputed using LOCF. The majority of the subjects in the sham control group received corneal crosslinking treatment (CXL) after Month 3 and their Kmax data after CXL treatment were imputed.

The applicant conducted a sensitivity analysis using the observed data, which confirmed the finding at Month 3. The sensitivity analysis after Month 3 was less meaningful as the number of observations in the randomized study eye dropped markedly after Month 3 in the control group when the sham study eye could receive CXL treatment.

8.3 Additional Analyses using Observed Values

For information on analyses of mean change from baseline Kmax in the randomized study eye using observed valued, see Appendix E.

9 Safety

Adverse events were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 14.1. nomenclature.

9.1 Deaths

There were no subject deaths in any treatment group in any trial.

9.2 Nonfatal Serious Adverse Events

UVX-001

In the CXL group, no keratoconus or corneal ectasia subjects experienced a serious adverse event during the study. Two subjects in the control group (1, keratoconus; 1, corneal ectasia) experienced a serious adverse event. Subject 00211 (keratoconus) had serious adverse events of two suicide attempts from baseline to Month 3. Subject 03203 (corneal ectasia) had a serious adverse event of head injury from baseline to Month 3.

Subject 00211 (keratoconus subject, sham control group) was a 20-year-old Caucasian, non-Hispanic female who received control treatment OD on (b) (6). On (b) (6) (b) (6) (Day 26) and again on (b) (6) (Day 72), the subject attempted suicide, resulting in hospitalization on each occasion. Treatment included 1 liter IV N-acetylcysteine, 50g PO charcoal, and PO Mucomyst (dose unknown) for the first suicide

attempt and 1 liter IV N-acetylcysteine and 50g PO charcoal for the second attempt. Outcome was reported as resolved (same day as onset). The subject remained in the study and received CXL treatment OD (crossover from sham) on 21 Oct 2008. She completed the study and attended all follow-up visits through Month 12 (except for Month 1, which was missed due to the attempted suicide).

Subject 03203 (corneal ectasia subject, sham control group) was a 50-year-old Caucasian, non-Hispanic male who received control treatment OS on (b) (6). On (b) (6) (Day 34), the subject experienced severe head injury and was hospitalized. The event was considered by the investigator to be unrelated to study drug, UVA light, and epithelial defect. Outcome was reported as resolved (date not reported). The subject received CXL treatment OS (crossover from sham) on 28 May 2008. The subject's last evaluation was at Month 3; thereafter, the subject was lost to follow-up and was discontinued from the study.

UVX-002

None of the subjects in the keratoconus CXL group and 3 subjects in the control group experienced a serious adverse event during the study. In the control group, serious adverse events were corneal ulcer following CXL in the sham eye (Subject 02206); appendicitis requiring appendectomy (Subject 08201); and an infectious cat bite requiring hospitalization (Subject 10211). Each of these events occurred after Month 3.

Subject 02206 (sham control group) was a 19-year-old Caucasian, non-Hispanic male who received sham treatment OS (14 July 2008) and subsequently received CXL treatment OU at the Month 6 follow-up visit (19 December 2008). He developed a corneal ulcer (OS) with onset 3 days after receiving CXL treatment. The corneal ulcer persisted. On 05 January 2009, the investigator considered this event to be of severe intensity and serious. The investigator applied a pressure patch and treated the condition with Zymar, fortified vancomycin, Pred Forte, bacitracin, doxycycline, and Refresh. The corneal ulcer resolved on 27 May 2009.

Subject 02206 in UVX-002, who developed a corneal ulcer OS, was originally a control patient OD and received CXL treatment OS at the six month OD follow-up.

Subject 08201 (sham control group) was a 35-year-old, Caucasian (ethnicity not reported) female who developed appendicitis approximately 5 months after baseline. She was hospitalized and had an appendectomy. Outcome was reported as resolved.

Subject 10211 (sham control group) was a 52-year-old, Caucasian, non-Hispanic female who was hospitalized for treatment of an infectious cat bite approximately 9 months after baseline. Outcome was reported as resolved.

UVX-003

One subject in the corneal ectasia CXL group and no subjects in the control group experienced a serious adverse vent during the study.

Subject 04308 (CXL group) was a 47-year-old Caucasian, non-Hispanic male who developed corneal epithelium defect (verbatim: epithelial growth OS) in the randomized eye on Day 35. The Lasik flap was lifted to remove the epithelial growth. The corneal epithelium defect resolved on Day 43.

9.3 Common Adverse Events

Number of subjects with adverse events, reported by ≥2% of subjects, through Month 3 in UVX-001, UVX-002, and UVX-003

	Progressive Keratoconus[1]		**Cornea Ectasia[2]**	
	CXL	Control	CXL	Control
	N=102	N=103	N=91	N=88
Any AE	87	44	82	38
Ocular AE	86	40	82	33
Corneal opacity	58	4	62	7
Punctate keratitis	25	8	18	3
Corneal striae	24	12	8	6
Corneal epithelium defect	23	1	24	3
Eye pain	17	3	24	-
Vision blurred	16	2	15	4
Photophobia	11	-	17	-
Conjunctival hyperaemia	10	1	4	3
Eye irritation	10	1	8	1
Visual acuity reduced	10	9	10	1
Ocular discomfort	-	-	8	-
Eye oedema	7	-	-	-
Dry eye	6	2	13	4
Eyelid oedema	5	-	5	1
Foreign body sensation	5	-	5	1
Lacrimation increased	5	-	9	1
Anterior chamber flare	4	-	5	2
Glare	4	1	2	-
Ocular hyperaemia	4	1	3	1
Corneal disorder	3	1	3	-
Corneal oedema	3	-	3	-
Visual impairment	3	2	4	1
Keratitis	-	-	3	-
Meibomian gland dysfunction	-	-	3	2
Anterior chamber cell	2	-	2	1
Diplopia	2	1	-	-

Eye discharge	2	1	-	-
Eye pruritus	2	-	-	-
Vitreous detachment	2	-	-	-
Corneal scar	7	5	3	1
Asthenopia	-	-	2	-
Eye complication assoc with device	2	-	-	-
Headache	4	-	7	3
Nasopharyngitis	2	1	-	-
Halo vision	-	-	2	-
Corneal abrasion	-	-	2	-
Dizziness	-	-	2	-

These are pooled common adverse event tables (i.e. UVX-001 and -002 for keratoconus and -001 and -003 for corneal ectasia). Note: subjects in the CXL group had topical anesthetic administered to the study eye, and the corneal epithelium was removed; subjects in the sham treatment group had topical anesthetic administered to the study eye but did not have the corneal epithelium removed.

The most common adverse events for either indication at ≥ 10% are corneal epithelium defect, corneal opacity, corneal striae, eye pain, and punctate keratitis. Most of these events appear to represent sequelae following corneal epithelial debridement.

Ocular Adverse Events ≥5% in any CXL Eye at any time

	Keratoconus	Corneal Ectasia	Keratoconus	Corneal Ectasia
	UVX-001	UVX-001	UVX-002	UVX-003
	(N=74)	(N=57)	(N=219)	(N=162)
Corneal opacity	64	54	114	94
Corneal epithelium defect	40	20	29	33
Corneal striae	32	15	38	12
Punctate keratitis	27	24	35	27
Visual acuity reduced	17	12	31	25
Vision blurred	16	12	26	24
Corneal scar	12		10	4
Eye pain	10	11	48	32
Eye irritation	7		11	13
Lacrimation increased	7	6	11	14
Foreign body sensation	6	5		10
Photophobia	6	17	22	25
Conjunctival hyperemia	5	3	14	13
Eye discharge	4			

	Keratoconus	Corneal Ectasia	Keratoconus	Corneal Ectasia
	UVX-001	UVX-001	UVX-002	UVX-003
	(N=74)	(N=57)	(N=219)	(N=162)
Cornea disorder		5		
Ocular discomfort		5	6	14
Dry eye		4	15	23
Anterior chamber flare		3	6	6
Cornea edema		3		
Meibomian gland dysfunction		3		9
Ocular hyperemia		3		5
Ulcerative keratitis		3		
Eyelid edema			10	10
Corneal thinning			7	
Eye edema			6	
Glare			6	
Eye pruritis			5	
Visual impairment			5	9
Blepharitis				6
Halo vision				5
Corneal abrasion				4
Keratitis				4

The proportion of CXL eyes with a treatment emergent adverse event (at any time) was generally comparable to the incidence of treatment emergent adverse events from baseline to Month 3.

9.4 IOP

IOP measurements were to be done at each treatment and follow-up visit; however, there were many protocol deviations. A total of 3013 IOP measurements were performed over the course of the three studies. One patient was reported to have an IOP elevation at one visit (i.e., IOP >30 mmHg) which returned to normal at the following visit.

9.5 Corneal Endothelial Cell Counts

Results are presented for baseline and Months 3 and 12 in UVX-001, UVX-002, and UVX-003; Months 1 and 6 were not planned visits for endothelial cell count determinations.

At Month 3 or later, subjects whose eye(s) had not developed any contraindications for performing the CXL treatment were given the option of having CXL performed on their untreated fellow eyes (from CXL group) and untreated sham eye and untreated fellow eye (from sham control group). After treatment, these eyes were followed for 12 months according to the same schedule and protocol as the study eye in the CXL group.

The p-values in the tables should not be used for a statistical inference as they were not adjusted for multiplicity.

Table 19: Endothelial Cell Count (/mm^2) in the Randomized Eye – Observed Values (Keratoconus Subjects, UVX-001, ITT Population)

				Change from Baseline	
Visit	Statistic	CXL Group (N=29)	Control Group (N=29)	CXL Group (N=29)	Control Group (N=29)
Baseline	n	26	28		
	Mean	2663	2454		
	SD	309.63	369.13		
	Median	2641	2493		
	Min, Max	2174, 3311	1600, 3304		
Month 3	n	26	29	23	28
	Mean	2576	2548	–97	109
	SD	335.29	403.79	291.33	243.3
	Median	2543	2530	–81	106
	Min, Max	1910, 3304	1615, 3387	–759, 354	–327, 643
Month 12	n	20	0	17	0
	Mean	2652	----	-50	----
	SD	381.78	----	307.30	----
	Median	2728	----	76.0	----
	Min, Max	1967, 3178	----	–666, 461	----

Source: SDN-032, Table 19, Module 1.6, Section 3.17.7.2.

Table 70: Endothelial Cell Count (/mm^2) in the Randomized Eye – Observed Values (Corneal Ectasia Subjects, UVX-001, ITT Population)

Visit	Statistic	CXL Group (N=24)	Control Group (N=25)	Change from Baseline: CXL Group (N=24)	Change from Baseline: Control Group (N=25)	p-value[a]
Baseline	n	22	23			
	Mean	2392	2550			
	SD	250.72	429.50			
	Median	2472	2500			
	Min, Max	1831, 2761	1808, 3406			
Month 3	n	20	22	19	20	
	Mean	2338	2516	–42	–75	0.6458
	SD	275.93	384.46	196.8	241.3	
	Median	2360	2584	–39	–87	
	Min, Max	1818, 2961	1681, 3333	–389, 290	–562, 631	
Month 12	n	20	0	18	0	
	Mean	2309	----	–65	----	----
	SD	247.41	----	162.4	----	
	Median	2296	----	–55	----	
	Min, Max	1755, 2746	----	–388, 174	----	

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: Table 14.3.4 (Section 14.3.5.2)

Table 20: Endothelial Cell Count (/mm^2) in the Randomized Eye – Observed Values (UVX-002, Safety Population)

Visit	Statistic	CXL Group (N=73)	Control Group (N=74)	Change from Baseline: CXL Group (N=73)	Change from Baseline: Control Group (N=74)
Baseline	n	68	66		
	Mean	2600	2627		
	SD	395.89	398.20		
	Median	2571	2692		
	Min, Max	1387, 3546	1186, 3407		
Month 3	n	60	62	58	58
	Mean	2486	2621	–88	–18
	SD	387.77	433.99	472.01	362.8
	Median	2467	2654	–67	–34
	Min, Max	1086, 3185	1052, 3472	–1820, 983	–872, 797
Month 12	n	60	1	58	1
	Mean	2615	2996	3.7	330
	SD	363.86		428.73	
	Median	2636	2996	67.5	330
	Min, Max	1529, 3322	2996, 2996	–1306, 969	330, 330

Source: SDN-032, Table 20, Module 1.6, Section 3.17.7.2.

Table 21: Endothelial Cell Count (/mm^2) in the Randomized Eye – Observed (UVX-003, ITT Population)

Visit	Statistic	CXL Group (N=67)	Control Group (N=63)	Change from Baseline: CXL Group (N=67)	Change from Baseline: Control Group (N=63)
Baseline	n	65	58		
	Mean	2518	2598		
	SD	578.76	417.76		
	Median	2525	2701		
	Min, Max	528, 5154	1629, 3592		
Month 3	n	57	55	57	51
	Mean	2447	2559	–45	–45
	SD	377.06	386.68	435.1	354.1
	Median	2467	2577	–51	–49
	Min, Max	1232, 3049	1706, 3412	–886, 1641	–857, 771
Month 12	n	49	2	49	2
	Mean	2380	2283	–124	–343
	SD	382.51	352.85	420.1	557.2
	Median	2392	2283	–129	–343
	Min, Max	1305, 3125	2033, 2532	–1220, 1085	–737, 51

Avedro believes that the variances observed in the ECC data sets for the UVX studies represent inherent errors of measurement of ECC in the keratoconus and corneal ectasia population. Values were reconfirmed against the source documentation by Avedro.

9.6 Corneal Thickness

The following tables summarize the observed results for corneal thickness at the apex and the thinnest location in the randomized eye at baseline and Month 1 to Month 12 in UVX-001, UVX-002, and UVX-003. The p-values should be interpreted with caution as they were not adjusted for multiplicity.

Table 65: Corneal Thickness (µm) at the Apex in the Randomized Eye – Observed Values (Keratoconus Subjects, UVX-001, ITT Population)

Visit	Statistic	CXL Group (N=29)	Control Group (N=29)	Change from Baseline: CXL Group (N=29)	Change from Baseline: Control Group (N=29)	p-value[a]
Baseline	n	29	29			
	Mean	461	450			
	SD	43.06	49.07			
	Median	462	454			
	Min, Max	358, 551	346, 535			
Month 1	n	29	28	29	28	
	Mean	436	449	–26	0.9	<0.0001
	SD	47.14	48.70	19.16	7.96	
	Median	442	455	–23	2.0	
	Min, Max	334, 523	340, 538	–76, 2	–17, 14	
Month 3	n	29	29	29	29	
	Mean	434	451	–27	1.1	<0.0001
	SD	47.63	48.41	17.21	10.05	
	Median	436	458	–33	4.0	
	Min, Max	325, 512	351, 539	–54, 5	–27, 22	
Month 6	n	28	18	28	18	
	Mean	455	444	–9.4	–1.9	0.1271
	SD	46.09	48.27	17.64	12.65	
	Median	445	442	–11	–1.5	
	Min, Max	350, 529	345, 533	–48, 25	–37, 14	
Month 12	n	20	0	20	0	
	Mean	466	----	–3.4	----	----
	SD	46.69	----	31.09	----	
	Median	457	----	–6.0	----	
	Min, Max	401, 567	----	–73, 84	----	

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-011, UVX-001 Clinical Study Report, Table 65.

Table 71: Corneal Thickness (µm) at the Apex in the Randomized Eye – Observed Values (Corneal Ectasia Subjects, UVX-001, ITT Population)

Visit	Statistic	CXL Group (N=24)	Control Group (N=25)	Change from Baseline		p-value[a]
				CXL Group (N=24)	Control Group (N=25)	
Baseline	n	24	25			
	Mean	446	433			
	SD	64.36	42.41			
	Median	432	436			
	Min, Max	350, 611	357, 497			
Month 1	n	24	25	24	25	
	Mean	426	429	–19	–3.8	0.0173
	SD	68.97	44.52	30.36	9.00	
	Median	413	436	–24	–3.0	
	Min, Max	326, 568	340, 503	–53, 99	–25, 13	
Month 3	n	23	24	23	24	
	Mean	416	425	–32	–5.0	<0.0001
	SD	68.25	42.09	14.26	11.03	
	Median	401	428	–32	–3.5	
	Min, Max	322, 568	342, 491	–73, 3	–46, 8	
Month 6	n	22	13	22	13	
	Mean	440	423	–9.6	–6.8	0.6275
	SD	69.31	38.90	17.55	12.92	
	Median	423	425	–9.0	–2.0	
	Min, Max	334, 574	346, 490	–41, 21	–35, 7	
Month 12	n	20	0	20	0	
	Mean	447	----	–2.3	----	----
	SD	64.96	----	18.95	----	
	Median	441	----	–1.5	----	
	Min, Max	351, 583	----	–28, 41	----	

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-011, UVX-001 Clinical Study Report, Table 71.

Table 38: Corneal Thickness (µm) at the Apex in the Randomized Eye – Observed Values (UVX-002, Safety Population)

Visit	Statistic	CXL Group (N=73)	Control Group (N=74)	Change from Baseline: CXL Group (N=73)	Change from Baseline: Control Group (N=74)	p-value[a]
Baseline	n	73	74			
	Mean	459	466			
	SD	44.36	43.04			
	Median	461	465			
	Min, Max	356, 586	353, 568			
Month 1	n	71	73	71	73	
	Mean	435	463	–24	–2.3	<0.0001
	SD	44.27	43.90	27.50	12.86	
	Median	436	464	–25	–2.0	
	Min, Max	319, 561	328, 555	–89, 120	–53, 25	
Month 3	n	68	66	68	66	
	Mean	430	467	–29	–0.0	<0.0001
	SD	43.68	43.07	19.24	11.05	
	Median	430	469	–28	0.0	
	Min, Max	340, 552	349, 561	–128, 19	–40, 26	
Month 6	n	68	20	68	20	
	Mean	442	469	–15	4.5	0.0064
	SD	41.65	54.96	24.97	33.54	
	Median	443	466	–17	–1.5	
	Min, Max	341, 554	376, 595	–120, 81	–32, 135	
Month 12	n	70	1	70	1	
	Mean	451	438	–7.1	–1.0	0.7432
	SD	43.14		18.37		
	Median	452	438	–5.5	–1.0	
	Min, Max	342, 559	438, 438	–98, 42	–1, –1	

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-011, UVX-002 Clinical Study Report, Table 38.

Table 38: Corneal Thickness (µm) at the Apex in the Randomized Eye – Observed Values (UVX-003, ITT Population)

Visit	Statistic	CXL Group (N=67)	Control Group (N=63)	Change from Baseline: CXL Group (N=67)	Change from Baseline: Control Group (N=63)	p-value[a]
Baseline	n	64	63			
	Mean	446	454			
	SD	54.98	58.96			
	Median	449	454			
	Min, Max	310, 586	282, 590			
Month 1	n	64	61	61	61	
	Mean	418	457	–29	3.4	<0.0001
	SD	56.13	57.34	18.45	18.23	
	Median	418	452	–28	0.0	
	Min, Max	293, 554	324, 579	–69, 18	–23, 111	
Month 3	n	65	61	63	61	
	Mean	414	457	–29	2.9	<0.0001
	SD	60.97	54.34	20.35	18.92	
	Median	417	453	–29	2.0	
	Min, Max	269, 552	337, 578	–111, 18	–22, 108	
Month 6	n	62	19	60	19	
	Mean	429	478	–11	0.9	0.0404
	SD	55.98	46.61	22.60	21.30	
	Median	430	456	–13	–2.0	
	Min, Max	286, 551	425, 566	–91, 84	–31, 63	
Month 12	n	56	2	55	2	
	Mean	446	524	–0.9	37.5	0.0145
	SD	57.32	16.97	20.64	40.31	
	Median	449	524	0.0	37.5	
	Min, Max	293, 559	512, 536	–55, 50	9, 66	

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)
Source: SDN-011, UVX-003 Clinical Study Report, Table 38.

9.7 Visual Acuity

BSCVA is summarized in the following tables. The p-values, as presented, were not adjusted for multiplicity. Thus, they should not be used for statistical inference.

UVX-001 Keratoconus

Table 44: Best Spectacle-Corrected Visual Acuity (ETDRS Letters Read) in the Randomized Eye – Observed (ITT Population: Keratoconus)

				Change from Baseline		
Visit	Statistic	CXL Group (N=29)	Control Group (N=29)	CXL Group (N=29)	Control Group (N=29)	p-value[a]
Baseline	n	29	29			
	Mean	32.4	31.7			
	SD	11.64	13.03			
	Median	35.0	33.0			
	Min, Max	5, 48	2, 50			
Month 1	n	29	28	29	28	
	Mean	31.4	35.5	-1.0	3.5	0.0994
	SD	12.40	12.43	9.87	10.24	
	Median	34.0	39.0	1.0	3.0	
	Min, Max	10, 50	5, 52	-30, 20	-15, 24	
Month 3	n	29	29	29	29	
	Mean	39.0	35.5	6.5	3.8	0.2985
	SD	10.01	14.26	10.56	9.43	
	Median	42.0	40.0	5.0	3.0	
	Min, Max	14, 52	1, 54	-27, 26	-14, 22	
Month 6	n	28	18	28	18	
	Mean	38.7	35.3	6.1	4.4	0.6189
	SD	9.78	11.05	10.84	10.61	
	Median	39.0	38.0	7.5	1.5	
	Min, Max	17, 53	2, 49	-14, 34	-13, 23	
Month 12	n	20	0	20	0	
	Mean	41.6		9.6		
	SD	10.82		8.80		
	Median	44.5		7.0		
	Min, Max	22, 55		-3, 28		

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-001, UVX-001 Clinical Study Report, Table 44.

UVX-001 Corneal Ectasia

Table 53: Best Spectacle-Corrected Visual Acuity (ETDRS Letters Read) in the Randomized Eye – Observed (ITT Population: Corneal Ectasia)

Visit	Statistic	CXL Group (N=24)	Control Group (N=25)	Change from Baseline		p-value[a]
				CXL Group (N=24)	Control Group (N=25)	
Baseline	n	24	25			
	Mean	37.7	34.5			
	SD	11.31	13.28			
	Median	39.5	37.0			
	Min, Max	0, 52	2, 50			
Month 1	n	24	25	24	25	
	Mean	37.2	34.6	-0.5	0.1	0.7913
	SD	10.86	14.12	9.44	6.74	
	Median	38.0	40.0	0.0	-1.0	
	Min, Max	6, 52	5, 53	-18, 19	-10, 20	
Month 3	n	23	24	23	24	
	Mean	43.6	34.9	5.3	0.2	0.0323
	SD	10.28	13.10	8.76	7.13	
	Median	45.0	37.5	7.0	1.0	
	Min, Max	18, 54	4, 52	-17, 19	-16, 20	
Month 6	n	22	13	22	13	
	Mean	43.8	29.3	6.7	-1.8	0.0124
	SD	12.42	13.17	10.25	6.93	
	Median	46.5	28.0	3.5	-2.0	
	Min, Max	2, 56	3, 50	-10, 24	-10, 16	
Month 12	n	20	0	20	0	
	Mean	42.2		5.6		
	SD	11.41		10.45		
	Median	44.5		5.0		
	Min, Max	2, 55		-17, 24		

[a] p-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-001, UVX-001 Clinical Study Report, Table 53.

Table 28: Best Spectacle-Corrected Visual Acuity (ETDRS Letters Read) in the Randomized Eye – Observed Values (UVX-002, ITT Population)

Visit	Statistic	CXL Group (N=73)	Control Group (N=74)	Change from Baseline		p-value[a]
				CXL Group (N=73)	Control Group (N=74)	
Baseline	n	73	73			
	Mean	33.5	33.2			
	SD	14.06	13.99			
	Median	37.0	38.0			
	Min, Max	0, 52	0, 55			
Month 1	n	72	71	72	70	
	Mean	33.5	35.0	0.3	1.6	0.3412
	SD	13.24	13.79	9.04	7.35	
	Median	37.5	37.0	0.0	2.0	
	Min, Max	3, 52	0, 57	–31, 21	–15, 21	
Month 3	n	69	69	69	68	
	Mean	37.7	34.6	4.1	1.2	0.0422
	SD	12.20	14.19	8.72	8.21	
	Median	40.0	36.0	3.0	2.0	
	Min, Max	3, 59	0, 59	–15, 25	–30, 20	
Month 6	n	68	20	68	20	
	Mean	38.5	33.6	5.7	–2.0	0.0064
	SD	12.60	14.59	10.70	10.89	
	Median	43.0	37.0	4.0	–1.0	
	Min, Max	5, 59	0, 49	–20, 45	–33, 15	
Month 12	n	66	2	66	2	
	Mean	38.6	39.0	4.8	0.0	0.5308
	SD	12.02	1.41	10.55	8.49	
	Median	40.5	39.0	3.0	0.0	
	Min, Max	4, 59	38, 40	–17, 35	–6, 6	

[a] P-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-011, UVX-002 Clinical Study Report, Table 28.

Table 28: Best Spectacle-Corrected Visual Acuity (ETDRS Letters Read) in the Randomized Eye – Observed Values (UVX-003, ITT Population)

Visit	Statistic	CXL Group (N=67)	Control Group (N=63)	Change from Baseline: CXL Group (N=67)	Change from Baseline: Control Group (N=63)	p-value[a]
Baseline	n	67	63			
	Mean	36.7	39.5			
	SD	13.66	11.90			
	Median	41.0	42.0			
	Min, Max	0, 60	0, 59			
Month 1	n	65	61	65	61	
	Mean	34.5	40.2	–2.0	0.8	0.1188
	SD	14.60	11.44	10.02	9.64	
	Median	38.0	43.0	–1.0	0.0	
	Min, Max	5, 55	3, 58	–28, 19	–35, 30	
Month 3	n	64	58	64	58	
	Mean	38.6	40.4	2.4	0.0	0.1427
	SD	13.45	12.14	8.60	9.18	
	Median	40.0	42.5	2.0	1.0	
	Min, Max	1, 60	4, 58	–17, 39	–22, 24	
Month 6	n	61	18	61	18	
	Mean	40.4	43.5	3.8	0.6	0.1854
	SD	14.59	9.66	9.16	8.20	
	Median	45.0	46.0	3.0	0.0	
	Min, Max	0, 65	16, 58	–15, 31	–19, 24	
Month 12	n	55	2	55	2	
	Mean	40.9	41.0	5.9	–1.5	0.2348
	SD	14.56	5.66	8.66	2.12	
	Median	44.0	41.0	5.0	–1.5	
	Min, Max	0, 64	37, 45	–16, 30	–3, 0	

[a] P-values are on difference between CXL and control by t-test (p-value is 2-sided, significance level 0.05)

Source: SDN-011, UVX-003 Clinical Study Report, Table 28.

9.8 ≥ 15-Letter Loss in Best Corrected Visual Acuity in CXL Study Eyes and Sham Control Study Eyes

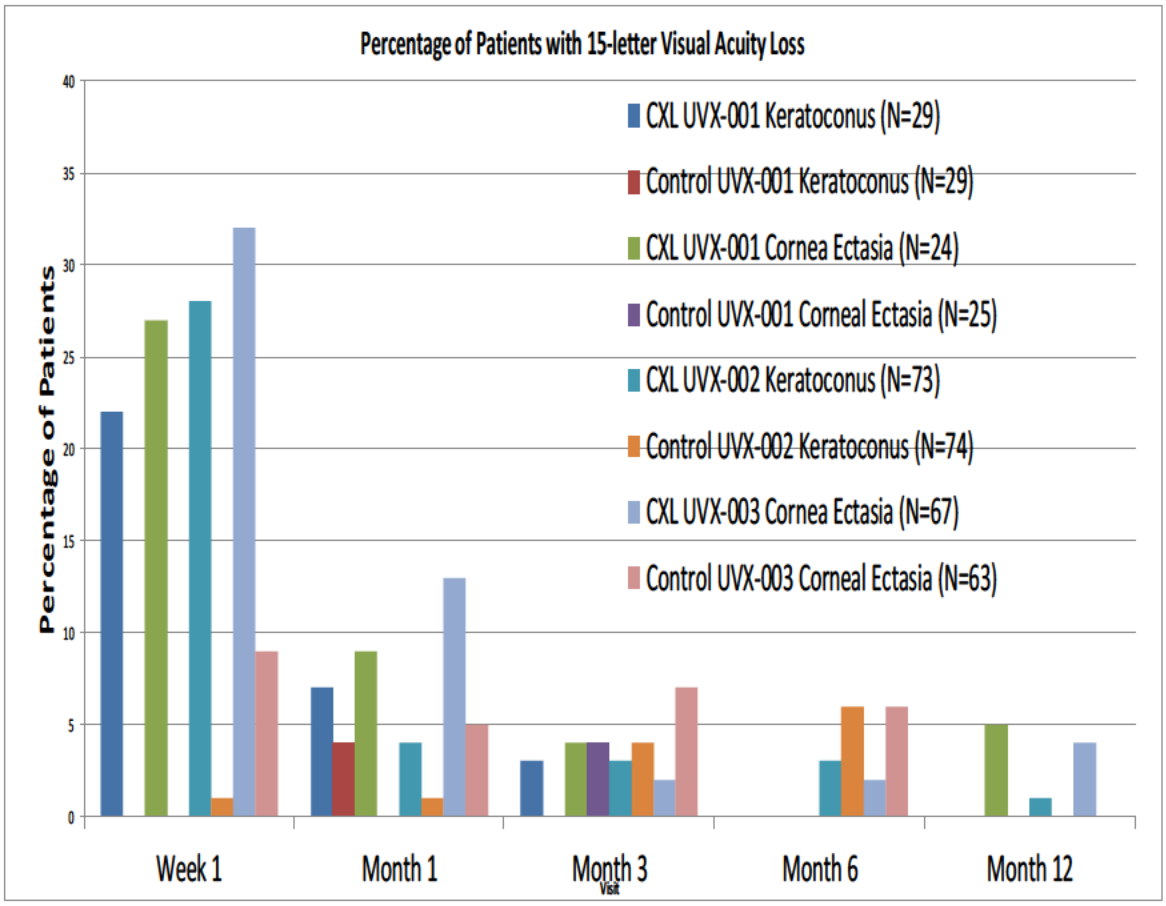


Table 67: Best Spectacle-Corrected Visual Acuity Loss of ≥15 Letters (Keratoconus Subjects, UVX-001, ITT Population)

Visit	Category		CXL Group (N=29)	Control Group (N=29)
Week 1	N		27	27
	No	n (%)	21 (77.8%)	27 (100.0%)
	Yes	n (%)	6 (22.2%)	0
Month 1	N		29	27
	No	n (%)	27 (93.1%)	26 (96.3%)
	Yes	n (%)	2 (6.9%)	1 (3.7%)
Month 3	N		29	27
	No	n (%)	28 (96.6%)	27 (100.0%)
	Yes	n (%)	1 (3.4%)	0
Month 6	N		28	17
	No	n (%)	28 (100.0%)	17 (100.0%)
	Yes	n (%)	0	0
Month 12	N		20	0
	No	n (%)	20 (100.0%)	0
	Yes	n (%)	0	0
Month 12 (LOCF)	N		29	28
	No	n (%)	29 (100.0%)	28 (100.0%)
	Yes	n (%)	0	0

Source: Table 14.3.9 (Section 14.3.5.1)

Table 73: Best Spectacle-Corrected Visual Acuity Loss of ≥15 Letters (Corneal Ectasia Subjects, UVX-001, ITT Population)

Visit	Category		CXL Group (N=24)	Control Group (N=25)
Week 1	N		22	24
	No	n (%)	16 (72.7%)	24 (100.0%)
	Yes	n (%)	6 (27.3%)	0
Month 1	N		23	24
	No	n (%)	21 (91.3%)	24 (100.0%)
	Yes	n (%)	2 (8.7%)	0
Month 3	N		22	23
	No	n (%)	21 (95.5%)	22 (95.7%)
	Yes	n (%)	1 (4.5%)	1 (4.3%)
Month 6	N		21	12
	No	n (%)	21 (100.0%)	12 (100.0%)
	Yes	n (%)	0	0
Month 12	N		19	0
	No	n (%)	18 (94.7%)	0
	Yes	n (%)	1 (5.3%)	0
Month 12 (LOCF)	N		23	24
	No	n (%)	22 (95.7%)	24 (100.0%)
	Yes	n (%)	1 (4.3%)	0

Source: Table 14.3.9 (Section 14.3.5.2)

Table 40: Best Spectacle-Corrected Visual Acuity Loss of ≥15 Letters (UVX-002, Safety Population)

Visit	Category		CXL Group (N=73)	Control Group (N=74)
Week 1	N		58	70
	No	n (%)	42 (72.4%)	69 (98.6%)
	Yes	n (%)	16 (27.6%)	1 (1.4%)
Month 1	N		67	68
	No	n (%)	64 (95.5%)	67 (98.5%)
	Yes	n (%)	3 (4.5%)	1 (1.5%)
Month 3	N		66	66
	No	n (%)	64 (97.0%)	63 (95.5%)
	Yes	n (%)	2 (3.0%)	3 (4.5%)
Month 6	N		64	17
	No	n (%)	62 (96.9%)	16 (94.1%)
	Yes	n (%)	2 (3.1%)	1 (5.9%)
Month 12	N		63	1
	No	n (%)	62 (98.4%)	1 (100.0%)
	Yes	n (%)	1 (1.6%)	0
Month 12 (LOCF)	N		69	71
	No	n (%)	68 (98.6%)	68 (95.8%)
	Yes	n (%)	1 (1.4%)	3 (4.2%)

Source: Table 14.3.9 (Section 14.3.5)

Table 40: Best Spectacle-Corrected Visual Acuity Loss of ≥15 Letters (UVX-003, ITT Population)

Visit	Category		CXL Group (N=67)	Control Group (N=63)
Week 1	N		60	58
	No	n (%)	41 (68.3%)	53 (91.4%)
	Yes	n (%)	19 (31.7%)	5 (8.6%)
Month 1	N		63	59
	No	n (%)	55 (87.3%)	56 (94.9%)
	Yes	n (%)	8 (12.7%)	3 (5.1%)
Month 3	N		61	58
	No	n (%)	60 (98.4%)	54 (93.1%)
	Yes	n (%)	1 (1.6%)	4 (6.9%)
Month 6	N		59	18
	No	n (%)	58 (98.3%)	17 (94.4%)
	Yes	n (%)	1 (1.7%)	1 (5.6%)
Month 12	N		53	2
	No	n (%)	51 (96.2%)	2 (100.0%)
	Yes	n (%)	2 (3.8%)	0
Month 12 (LOCF)	N		65	62
	No	n (%)	63 (96.9%)	57 (91.9%)
	Yes	n (%)	2 (3.1%)	5 (8.1%)

Source: Table 14.3.9 (Section 14.3.5)

In the UVX studies, a loss of visual acuity (as measured by BSCVA) of 15 letters or more was identified in the protocol as a safety parameter.

10 Demographic Interactions

Subgroup analyses were conducted for the primary efficacy endpoint based on age (< median or ≥ median); gender (male or female); race (white or non-white); and baseline disease severity (mild or moderate/severe). Disease severity was only reported for progressive keratoconus subjects. An analysis of adverse events by age category, gender, and race did not identify any safety concerns for any demographic subpopulation.

11 Pediatrics

A total of 33 pediatric subjects were enrolled in studies UVX-001 and UVX-002. No pediatric subjects were enrolled in UVX-003 and there were no pediatric ectasia subjects enrolled in UVX-001.

Pediatric Population

	UVX-001 (Keratoconus)		UVX-002	
	CXL Group	Sham Control Group	CXL Group	Sham Control Group
Age 14-18	0	1	7	3
Age 18-21	2	3	10	7

Progressive Keratoconus

In study UVX-001, one subject 14 – 18 years of age was randomized into the sham control group and remained in this group until the Month 6 visit, at which time the subject's sham eye was treated with CXL. The subject's fellow eye was also treated.

Five subjects 18 – 21 years of age were randomized to treatment: two in the CXL group and three in the sham control group. Of the two subjects randomized in the CXL group, one had their fellow eye treated. Of the three subjects randomized to the sham control group, two had their sham eye treated and one had their fellow eye treated.

In study UVX-002, ten (10) subjects 14 – 18 years of age were randomized to treatment: seven in the CXL group and three in the sham control group. Of the seven subjects randomized in the CXL group, five elected to have their fellow eye treated. Of the three subjects randomized to the sham control group, all had their sham eyes treated and two had their fellow eye treated.

Seventeen (17) subjects 18 – 21 years of age were randomized to treatment: ten in the CXL group and seven in the sham control group. Of the ten subjects randomized in the CXL group, five elected to have their fellow eye treated. Of the seven subjects randomized to the sham control group, all had their sham eyes treated and six had their fellow eye treated.

Mean Changes from Baseline Kmax in the Randomized Study Eye: Age 14-18 (UVX-001)					
				Change from Baseline	
		CXL Group	Sham Control Group	CXL Group	Sham Control Group
Visit	Statistic	(N=0)	(N=1)	(N=0)	(N=1)
Baseline	n	0	1		
	Mean		81.3		
	SD				
Month 3	n	0	1	0	1
Observed	Mean		87.4		6.1
	SD				
Month 6	n	0	1	0	1
Observed	Mean		84.1		2.8
	SD				
Month 12	n	0	1	0	1
LOCF	Mean		84.1		2.8
	SD				
Month 12	n	0	0	0	0
Observed	Mean				
	SD				

Mean Changes from Baseline Kmax in the Randomized Study Eye: Age 18-21 (UVX-001)					
		CXL	Sham Control	Change from Baseline	
		Group	Group	CXL Group	Sham Control Group
Visit	Statistic	(N=2)	(N=3)	(N=0)	(N=1)
Baseline	n	2	3		
	Mean	57.4	66.3		
	SD	6.86	10		
Month 3	n	2	3	2	3
Observed	Mean	57.8	67.1	0.4	0.8
	SD	7.6	9.5	0.7	3.4
Month 6	n	2	3	2	3
LOCF	Mean	57.7	67.1	0.3	0.8
	SD	8.3	9.5	1.5	3.4
Observed	n	2	0	2	0
	Mean	57.7		0.3	
	SD	8.3		1.5	
Month 12	n	2	3	2	3
LOCF	Mean	57.7	67.1	0.3	0.8
	SD	8.1	9.5	1.3	3.4
Month 12	n	2	0	2	0
Observed	Mean	57.7		0.3	
	SD	8.1		1.3	

Mean Changes from Baseline Kmax in the Randomized Study Eye: Age 18-21 (UVX-002)					
				Change from Baseline	
		CXL Group	Sham Control Group	CXL Group	Sham Control Group
Visit	Statistic	(N=10)	(N=7)	(N=10)	(N=7)
Baseline	n	10	7		
	Mean	65.8	66		
	SD	13.1	10.3		
Month 3	n	9	7	9	7
Observed	Mean	64.8	66.5	-1.2	0.5
	SD	13	11.1	1.7	4.1
Month 6					
LOCF	n	10	7	10	7
	Mean	65.1	68.8	-0.8	2.8
	SD	12.7	13.6	2.2	3.5
Observed	n	8	2	8	2
	Mean	66.3	78.4	-1.2	5.7
	SD	13.7	13.7	2.2	1.8
Month 12					
LOCF	n	10	7	10	7
	Mean	62.6	68.8	-3.2	2.8
	SD	11.7	13.6	5.4	3.5
Observed	n	10	0	10	0
	Mean	62.6		-3.2	
	SD	11.7		5.4	

Table 29: Endothelial Cell Count (/mm^2) in the Randomized: Age 14-18 (UVX-001 and UVX-002 Pooled, Safety Population)

Visit	Statistic	CXL Group (N=7)	Control Group (N=4)	Change from Baseline	
				CXL Group (N=7)	Control Group (N=4)
Baseline	n	7	3		
	Mean	2761	2803		
	SD	250.11	420.88		
	Median	2717	2648		
	Min, Max	2484, 3190	2481, 3279		
Month 3	n	6	4	6	3
Observed	Mean	2789	2723	99.5	-50
	SD	253.46	431.38	300.3	121.8
	Median	2755	2557	32.0	-60
	Min, Max	2427, 3185	2421, 3356	-306, 511	-166, 77
Month 3	n	7	4	7	3
LOCF	Mean	2846	2723	85.3	-50
	SD	276.6	431.4	276.7	121.8
	Median	2793	2557	0.0	-60
	Min, Max	2427, 3190	2421, 3356	-306, 511	-166, 77
Month 12	n	6	0	6	0
Observed	Mean	2747	--	57.7	--
	SD	363.73	--	327.3	--
	Median	2887	--	85.0	--
	Min, Max	2151, 3096	--	-523, 447	--
Month 12	n	7	4	7	3
LOCF	Mean	2810	2723	49.4	-50
	SD	371.9	431.4	299.6	121.8
	Median	2976	2557	68.0	-60
	Min, Max	2151, 3190	2421, 3356	-523, 447	-166, 77

Table 30: Endothelial Cell Count (/mm^2) in the Randomized: Age 18-21 (UVX-001 and UVX-002 Pooled, Safety Population)

Visit	Statistic	CXL Group (N=12)	Control Group (N=10)	Change from Baseline	
				CXL Group (N=12)	Control Group (N=10)
Baseline	n	11	10		
	Mean	2840	2923		
	SD	348.14	239.98		
	Median	2874	2883		
	Min, Max	2352, 3425	2688, 3407		
Month 3	n	9	10	9	10
Observed	Mean	2559	2843	-331	-80
	SD	591.15	262.63	604.6	284.0
	Median	2646	2782	-295	-15
	Min, Max	1111, 3003	2525, 3438	-1769, 364	-548, 424
Month 3	n	11	10	11	10
LOCF	Mean	2569	2843	-271	-80
	SD	541.9	262.6	557.1	284.0
	Median	2646	2782	-218	-15
	Min, Max	1111, 3003	2525, 3438	-1769, 364	-548, 424
Month 12	n	10	0	10	0
Observed	Mean	2626	--	-263	--
	SD	515.76	--	476.0	--
	Median	2793	--	-96	--
	Min, Max	1574, 3322	--	-1306, 210	--
Month 12	n	11	10	11	10
LOCF	Mean	2601	2849	-239	-74
	SD	496.2	264.9	458.5	286.1
	Median	2747	2782	-84	9.4
	Min, Max	1574, 3322	2525, 3438	-1306, 210	-548, 424

12 Potential Topics and Questions for the Committee

DRAFT TOPICS FOR DISCUSSION:

1. Study Design Topics
   a. Planned Enrollment and Size of Studies
   b. Study conduct /Data Quality
   c. Use of Last Observation Carried Forward
   d. Pre-specified Month 3 vs Month 12 endpoints
   e. Similarities and Differences between investigational and to be marketed device
   f. Size of Safety database
   g. Interpretation of Endothelial Cell Count Findings
   h. Use in pediatric patients- Applicability of extrapolation from adult data?
   i. Applicability of extrapolation to general keratoconus population
   j. Other potential safety issues

2. Do you have any suggestions regarding the draft labeling of the product?

3. Are additional studies needed? If so, please comment on type of study and timing.

4. Has adequate efficacy been demonstrated for the drug-device combination of Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and the KXL System for progressive keratoconus? Yes/No

5. Has adequate efficacy been demonstrated for the drug-device combination of Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and the KXL System for corneal ectasia following refractive surgery? Yes/No

6. Has adequate safety been demonstrated for the drug-device combination of Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and the KXL System for progressive keratoconus? Yes/No

7. Has adequate safety been demonstrated for the drug-device combination of Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and the KXL System for corneal ectasia following refractive surgery? Yes/No

8. Do you think the drug-device combination of Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and the KXL System should be approved for the treatment of progressive keratoconus? Yes/No

9. Do you think the drug-device combination of Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and the KXL System should be approved for the treatment of corneal ectasia following refractive surgery? Yes/No

13 PROPOSED LABELING

For the proposed package insert for Photrexa Viscous and Photrexa, See Appendix F.
For the proposed CXL Operator's Manual, See Appendix G.

14 POST APPROVAL STUDY

For a tabular synopsis of a proposed post-approval study, See Appendix H.

Appendix A- Protocol Deviations in Study UVX-001

Subject	Treatment	Violation/ Deviation Date	Associated Visit/Event	Violation/Deviation Reason	Violation/Deviation Reason/Details
00201	Primary Eye CXL	2007-12-27	Screening	Endothelial cell count not done	Protocol specified procedure not done for OD or OS
00201	Primary Eye CXL	2008-05-14	Month 3 Follow-Up	Other (Specify)	Visit out of range - 32 days late
00201	Primary Eye CXL	2009-03-04	Month 12 Follow-Up	Other (Specify)	Visit out of range - 4 days late
00202	Fellow Eye CXL	2008-10-03	Month 6 Follow-Up	Manual keratometry not Done	Manual keratometry, steep, not done during the month 6 visit for the study eye (right).
00202	Fellow Eye CXL	2008-10-03	Month 6 Follow-Up	Other (Specify)	Visit was approximately 10 weeks past the protocol specified study window for the study eye.
00202	Fellow Eye CXL	2008-12-31	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 follow up for fellow eye (left).
00202	Fellow Eye CXL	2009-03-05	Month 12 Follow-Up	IOP measurement not done	IOP not done for the study eye during the month 12 visit (right).
00202	Fellow Eye CXL	2009-03-05	Month 6 Follow-Up	IOP measurement not done	IOP not done during the month 6 visit for the fellow eye (left).
00203	Primary Eye CXL	2008-03-14	Week 1 Follow-Up	IOP measurement not done	OS, study eye
00203	Primary Eye CXL	2008-05-21	Month 3 Follow-Up	Endothelial cell count not done	Study eye (OS)
00203	Fellow Eye CXL	2008-08-22	Treatment	Other (Specify)	Subject had beverage (orange juice) containing vitamin C on the morning of study treatment.
00203	Fellow Eye CXL	2008-08-27	Week 1 Follow-Up	IOP measurement not done	OD, fellow eye
00203	Fellow Eye CXL	2008-11-18	Month 3 Follow-Up	IOP measurement not done	OD, fellow eye
00203	Fellow Eye CXL	2009-01-13	Month 6 Follow-Up	IOP measurement not done	OD, fellow eye
00203	Fellow Eye CXL	2009-01-13	Month 12 Follow-Up	IOP measurement not done	OS, treatment eye
00204	Primary Eye CXL	2008-03-12	Treatment	Other (Specify)	Keratoconus Severity Rating chosen "Severe" in error. Patient K flat was 54.5 - moderate.
00204	Primary Eye CXL	2008-03-12	Eligibility	Other (Specify)	Patient did not have Contact Lens Stability done
00205	Primary Eye CXL	2008-03-12	Screening	Other (Specify)	Subject did not meet requirement for contact lens stability OS CXL. The difference in MRSE between screening visit on 08Feb2008 and 12Mar2008 was 1.0 D.
00205	Primary Eye CXL	2008-03-12	Treatment	Other (Specify)	Randomization assignment incorrect for OS treatment. The keratoconus severity was incorrectly noted as severe (should have been mild); therefore the subject was incorrectly randomized
00205	Primary Eye CXL	2008-03-12	Treatment	Slit lamp exam not done	Protocol required procedure not done.
00205	Primary Eye CXL	2008-06-19	Month 3 Follow-Up	Other (Specify)	Visit out of range - 1 day late
00205	Primary Eye CXL	2008-10-09	Month 6 Follow-Up	Other (Specify)	Missed visit window - 15 days late
00205	Fellow Eye CXL	2008-11-14	Treatment	Other (Specify)	Refresh Plus Artificial Tears was used to increase OD Fellow CXL pachymetry instead of protocol specified Hypotonic Saline.
00205	Fellow Eye CXL	2008-11-15	Day 1 Follow-Up	Other (Specify)	Missed visit (Fellow eye OD)
00205	Fellow Eye CXL	2008-11-19	Week 1 Follow-Up	IOP measurement not done	Fellow eye OD
00205	Fellow Eye CXL	2009-02-06	Month 3 Follow-Up	IOP measurement not done	Fellow eye OD
00205	Fellow Eye CXL	2009-05-14	Month 6 Follow-Up	IOP measurement not done	OD, fellow eye.
00205	Fellow Eye CXL	2009-05-14	Month 12 Follow-Up	IOP measurement not done	OS CXL eye
00205	Fellow Eye CXL	2009-05-14	Month 12 Follow-Up	Other (Specify)	Visit out of range - 8 days late
00205	Fellow Eye CXL	2010-03-17	Month 12 Follow-Up	IOP measurement not done	OD Fellow
00205	Fellow Eye CXL	2010-03-17	Month 12 Follow-Up	Other (Specify)	Study visit was approximately 10 weeks past the protocol specified window.
00206	Primary Eye CXL	2008-02-19	Eligibility	Other (Specify)	I-S ratio for OD not done (site unable to calculate).
00206	Primary Eye CXL	2008-03-21	Treatment	Other (Specify)	Keratoconus Severity Scale checked "Severe" but it should have been "moderate" - 51.8
00206	Primary Eye CXL	2008-03-21	Treatment	Other (Specify)	Contact Lens Stability Check was not done on Tx Day. A stability check was later done and the topography avg Sim K Difference was >0.75 (2). Patient should not have been enrolled

00206	Primary Eye CXL	2008-03-21	Treatment	Did not meet inclusion/exclusion criteria	Subject did not meet inclusion criteria b/c the right eye progression was not shown only for left eye but right eye was the randomized eye.
00206	Primary Eye CXL	2008-03-27	Week 1 Follow-Up	IOP measurement not done	measurement not done
00206	Primary Eye CXL	2008-10-07	Month 6 Follow-Up	Other (Specify)	Visit was 4 days past protocol specified window.
00206	Fellow Eye CXL	2008-11-25	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS).
00207	Sham Eye CXL	2008-07-09	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry OD cross over eye instead of protocol specified hypotonic saline.
00207	Sham Eye CXL	2008-07-18	Week 1 Follow-Up	IOP measurement not done	OD Cross-over eye
00207	Sham Eye CXL	2008-07-31	Month 1 Follow-Up	IOP measurement not done	OD Cross-over
00207	Sham Eye CXL	2008-12-04	Month 6 Follow-Up	IOP measurement not done	OD Cross-over
00207	Fellow Eye CXL	2009-01-15	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry in the OS Fellow Eye instead of protocol specified Hypotonic Saline
00207	Fellow Eye CXL	2009-01-21	Week 1 Follow-Up	IOP measurement not done	OS Fellow CXL
00207	Fellow Eye CXL	2009-01-21	Week 1 Follow-Up	IOP measurement not done	Protocol specified procedure not done (fellow eye).
00207	Fellow Eye CXL	2009-07-29	Month 6 Follow-Up	IOP measurement not done	OS Fellow CXL
00208	Primary Eye CXL	2008-08-27	Month 3 Follow-Up	Endothelial cell count not done	Protocol required procedure not done.
00209	Primary Eye Sham	2008-05-28	Treatment	Other (Specify)	Keratoconus severity was chosen in error as study coordinator used K2 vs. K1 and subsequently chose "moderate". It should have been mild. The moderate card was choosen when mild should have been.
00209	Sham Eye CXL	2008-08-12	Week 1 Follow-Up	IOP measurement not done	Study eye (OD)
00209	Fellow Eye CXL	2009-02-13	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS).
00209	Fellow Eye CXL	2009-08-06	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OD).
00210	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	Visit not conducted within 30 days of screening.
00210	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	Site used Artificial Tears instead of protocol specified Hypotonic Saline to increase Pachymetry
00210	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	OS eligible, OD not at screening. OS was treatment eye. At treatment OS was stable w/better VA. OD checked for eligibility and found eligible. OD was treated instead of OS as first randomized.
00210	Primary Eye CXL	2008-09-26	Month 3 Follow-Up	Other (Specify)	Visit out of range - 1 day late
00210	Primary Eye CXL	2009-01-02	Month 6 Follow-Up	IOP measurement not done	Study eye (OD)
00210	Primary Eye CXL	2009-01-02	Month 6 Follow-Up	Other (Specify)	Visit conducted one day past protocol specified window.
00210	Fellow Eye CXL	2009-07-14	Treatment	Other (Specify)	Artificial Tears was used to increase pachymetry instead of protocol specified Hypotonic Saline.
00210	Fellow Eye CXL	2009-07-14	Treatment	Other (Specify)	OS Fellow eye not treated within protocol specified window of > or equal to 3 months and < or equal to 6 months (9/26/08-1/2/09) of first eye being treated
00210	Fellow Eye CXL	2009-08-13	Month 1 Follow-Up	IOP measurement not done	OS (Fellow eye)
00210	Fellow Eye CXL	2009-08-13	Month 12 Follow-Up	IOP measurement not done	OD (study eye)
00210	Fellow Eye CXL	2010-02-12	Month 6 Follow-Up	Other (Specify)	Study visit (for OS) conducted 16 days past window.
00210	Fellow Eye CXL	2010-02-12	Month 6 Follow-Up	IOP measurement not done	for fellow eye (OS)
00210	Fellow Eye CXL	2010-05-27	Month 12 Follow-Up	Endothelial cell count not done	fellow eye (OS)
00211	Primary Eye Sham	2008-06-05	Screening	Other (Specify)	Pt. did not qualify for study at Visit 2 (Avg. Sim K = .8). Orbscan from Visit 1 & 3 were used to qualify the patient.
00211	Primary Eye Sham	2008-08-07	Month 1 Follow-Up	Other (Specify)	Patient did not show up for this visit due to an SAE that occurred around the time of the visit.
00211	Sham Eye CXL	2008-10-21	Treatment	Pentacam pachymetry, keratometry not done	Pentacam thinnest point not done due to patient complications
00211	Sham Eye CXL	2008-10-28	Week 1 Follow-Up	IOP measurement not done	CRX-OVR OD
00211	Sham Eye CXL	2008-11-18	Month 1 Follow-Up	Other (Specify)	Visit not done. Patient was a no show.
00211	Sham Eye CXL	2009-02-10	Month 3 Follow-Up	IOP measurement not done	CRX-OVR OD
00211	Sham Eye CXL	2009-02-10	Month 3 Follow-Up	Other (Specify)	Visit out of window.

00211	Sham Eye CXL	2009-04-29	Month 6 Follow-Up	IOP measurement not done	CRX-OVR OD
00211	Sham Eye CXL	2010-02-03	Month 12 Follow-Up	Other (Specify)	Visit completed out of window.
00212	Primary Eye Sham	2008-07-18	Treatment	Ultrasound pachymetry not done	OD Sham, Pretreatment pachymetry not recorded.
00212	Sham Eye CXL	2008-09-26	Treatment	Other (Specify)	Refresh Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic Saline (OD X-over)
00212	Sham Eye CXL	2008-10-01	Week 1 Follow-Up	IOP measurement not done	Crossover, OD
00212	Sham Eye CXL	2008-12-09	Month 3 Follow-Up	IOP measurement not done	Crossover, OD
00212	Fellow Eye CXL	2009-01-23	Treatment	Other (Specify)	Refresh Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic Saline (OS Fellow CXL)
00212	Fellow Eye CXL	2009-01-27	Week 1 Follow-Up	IOP measurement not done	OS, fellow eye
00212	Fellow Eye CXL	2009-01-27	Week 1 Follow-Up	Other (Specify)	Visit out of range - 1 day early (OS Fellow CXL)
00212	Fellow Eye CXL	2009-02-27	Month 1 Follow-Up	IOP measurement not done	OS, fellow eye
00212	Fellow Eye CXL	2009-07-18	Treatment	Other (Specify)	Visit was conducted 35 days after screening, 5 days outside the visit window
00213	Primary Eye Sham	2008-07-01	Screening	Did not meet inclusion/exclusion criteria	Site was unable to obtain I-S ratio at screening for the study eye (left eye) and could therefore not confirm that it was greater than or equal to 1.5 on the Pentacam or Orbscan map
00213	Sham Eye CXL	2008-10-09	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye (OS).
00213	Sham Eye CXL	2008-10-15	Week 1 Follow-Up	IOP measurement not done	IOP was not done at the week 1 visit for the crossover eye (left eye)
00213	Fellow Eye CXL	2008-12-19	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the study/crossover eye (left eye).
00213	Fellow Eye CXL	2008-12-23	Week 1 Follow-Up	Other (Specify)	The week 1 visit for the fellow eye (right eye) was 1 day out of window (early).
00213	Fellow Eye CXL	2008-12-23	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-01-23	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-03-25	Month 6 Follow-Up	IOP measurement not done	IOP was not done at the Month 6 visit for the study/crossover eye (left eye)
00213	Fellow Eye CXL	2009-03-25	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-05-13	Month 12 Follow-Up	Other (Specify)	OS study visit (cross-over) conducted 19 weeks out of window (early).
00213	Fellow Eye CXL	2009-05-14	Month 12 Follow-Up	IOP measurement not done	IOP not done at the Month 12 visit for the crossover eye (left eye).
00213	Fellow Eye CXL	2009-05-14	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-12-15	Month 12 Follow-Up	Endothelial cell count not done	OD Fellow
00213	Fellow Eye CXL	2009-12-15	Month 12 Follow-Up	Endothelial cell count not done	Fellow eye (OD)
00214	Primary Eye CXL	2008-06-19	Screening	IOP measurement not done	OD CXL and OS Fellow
00214	Primary Eye CXL	2008-08-07	Treatment	Other (Specify)	Treatment for primary eye done greater than 30 days after screening visit.
00214	Primary Eye CXL	2008-08-12	Week 1 Follow-Up	IOP measurement not done	OD CXL
00214	Fellow Eye CXL	2008-11-12	Week 1 Follow-Up	IOP measurement not done	(OS) Fellow eye
00214	Fellow Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	(OS) Fellow eye
00214	Fellow Eye CXL	2009-01-08	Month 3 Follow-Up	Other (Specify)	Study visit out of range for fellow eye 6 days early
00214	Fellow Eye CXL	2009-01-08	Month 3 Follow-Up	IOP measurement not done	Fellow eye (OS)
00214	Fellow Eye CXL	2009-01-08	Month 3 Follow-Up	Endothelial cell count not done	Fellow eye (OS)
00214	Fellow Eye CXL	2009-01-08	Month 6 Follow-Up	IOP measurement not done	Study eye (OD)
00214	Fellow Eye CXL	2009-04-01	Month 6 Follow-Up	IOP measurement not done	Fellow eye (OS)
00215	Primary Eye Sham	2008-07-10	Screening	Other (Specify)	Subject discontinued RGP lens wear 12 days prior to the pre-treatment exam/first refraction (protocol requires 2 weeks).
00215	Primary Eye Sham	2008-07-10	Screening	Did not meet inclusion/exclusion criteria	Subject wore CL within 2 weeks of screening and CL stability not checked prior to Treatment
00215	Primary Eye Sham	2008-08-08	Screening	Other (Specify)	Subject was treated although contact lens stability recheck indicated that the eye was not stable. OD Sham
00215	Primary Eye Sham	2008-08-08	Treatment	Slit lamp exam not done	Slit Lamp exam was not done following the sham treatment for the study eye (right eye)
00215	Primary Eye Sham	2008-09-18	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry was not done at the Month 1 visit for the sham eye (right eye) due to distortion.

00215	Sham Eye CXL	2008-10-24	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline - OD X-over.
00215	Sham Eye CXL	2008-10-28	Week 1 Follow-Up	IOP measurement not done	IOP was not taken during the week 1 visit for the crossover eye (right eye)
00215	Sham Eye CXL	2008-10-28	Week 1 Follow-Up	Other (Specify)	The week 1 visit for the crossover eye (right eye) was 1 day out of window (early)
00215	Sham Eye CXL	2009-01-23	Month 3 Follow-Up	IOP measurement not done	IOP was not done during the Month 3 visit for the crossover eye (right eye).
00215	Sham Eye CXL	2009-04-30	Month 6 Follow-Up	IOP measurement not done	(Crossover)
00215	Sham Eye CXL	2010-01-15	Month 12 Follow-Up	Endothelial cell count not done	Protocol required procedure not done.
00215	Sham Eye CXL	2010-01-15	Month 12 Follow-Up	Other (Specify)	Visit out of range - 27 days late
00216	Primary Eye CXL	2008-08-28	Week 1 Follow-Up	IOP measurement not done	OD, study eye
00216	Primary Eye CXL	2008-09-17	Month 1 Follow-Up	IOP measurement not done	OD, study eye
00216	Fellow Eye CXL	2009-01-07	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye (OS).
00216	Fellow Eye CXL	2009-01-13	Week 1 Follow-Up	IOP measurement not done	Fellow eye, OS
00216	Fellow Eye CXL	2009-02-13	Month 1 Follow-Up	IOP measurement not done	OS, fellow eye
00216	Fellow Eye CXL	2009-02-13	Month 6 Follow-Up	IOP measurement not done	study eye, OD
00216	Fellow Eye CXL	2010-02-25	Month 12 Follow-Up	Endothelial cell count not done	OS, fellow eye
00217	Primary Eye Sham	2008-08-21	Treatment	Other (Specify)	Treatment did not occur within 30 days of screening
00217	Primary Eye Sham	2008-08-28	Week 1 Follow-Up	IOP measurement not done	OD, Sham
00217	Sham Eye CXL	2008-11-25	Week 1 Follow-Up	IOP measurement not done	OD, Crossover
00217	Sham Eye CXL	2009-02-03	Month 3 Follow-Up	IOP measurement not done	OD, crossover
00217	Sham Eye CXL	2009-05-26	Month 6 Follow-Up	IOP measurement not done	OD, crossover
00217	Fellow Eye CXL	2009-08-05	Treatment	Other (Specify)	OS Fellow eye treated more than 6 months after randomized eye by approximately 5 Months
00217	Fellow Eye CXL	2009-08-12	Week 1 Follow-Up	IOP measurement not done	OS, fellow eye
00217	Fellow Eye CXL	2010-02-10	Month 6 Follow-Up	IOP measurement not done	OS, fellow eye
00218	Primary Eye CXL	2008-09-04	Treatment	Other (Specify)	Subject ate tomato, potential vitamin C source morning of treatment.
00218	Primary Eye CXL	2008-09-04	Treatment	Other (Specify)	Treatment occurred more than 30 days after screening.
00218	Fellow Eye CXL	2008-11-20	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline.
00218	Fellow Eye CXL	2008-11-25	Week 1 Follow-Up	IOP measurement not done	Fellow eye, OS
00218	Fellow Eye CXL	2008-12-18	Month 1 Follow-Up	IOP measurement not done	OS, fellow eye
00218	Fellow Eye CXL	2009-02-11	Month 3 Follow-Up	IOP measurement not done	Fellow eye, OS
00218	Fellow Eye CXL	2009-02-11	Month 6 Follow-Up	IOP measurement not done	OD, study eye
00218	Fellow Eye CXL	2009-06-03	Month 6 Follow-Up	IOP measurement not done	OS, fellow eye
00218	Fellow Eye CXL	2009-06-03	Month 6 Follow-Up	IOP measurement not done	OS, fellow eye
00219	Primary Eye CXL	2008-09-04	Screening	Other (Specify)	Did not check topography during the contact lens stability check. Can't verify eye was stable. OD CXL
00219	Primary Eye CXL	2008-09-04	Screening	Dilated fundus exam not done	OD and OS
00219	Primary Eye CXL	2008-10-02	Treatment	Other (Specify)	Site used Refresh Plus to increase pachymetry instead of protocol specified Hypotonic Saline. OD CXL
00219	Primary Eye CXL	2008-10-10	Week 1 Follow-Up	IOP measurement not done	OD CXL
00219	Primary Eye CXL	2008-11-06	Month 1 Follow-Up	IOP measurement not done	OD CXL
00219	Primary Eye CXL	2009-01-08	Month 3 Follow-Up	Endothelial cell count not done	Technical problems with confocal microscope: deferred to 6 month visit; OD CXL
00219	Primary Eye CXL	2009-01-08	Month 3 Follow-Up	IOP measurement not done	OD CXL
00219	Primary Eye CXL	2009-04-16	Month 6 Follow-Up	IOP measurement not done	Study eye (OD)
00220	Primary Eye Sham	2008-10-29	Week 1 Follow-Up	IOP measurement not done	OD, Sham
00220	Primary Eye Sham	2008-11-19	Month 1 Follow-Up	IOP measurement not done	OD Sham

00220	Primary Eye Sham	2009-01-14	Month 3 Follow-Up	IOP measurement not done	OD Sham
00220	Sham Eye CXL	2009-05-05	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline, OD X-over
00220	Sham Eye CXL	2009-05-13	Week 1 Follow-Up	IOP measurement not done	OD, Crossover
00220	Sham Eye CXL	2009-06-04	Month 1 Follow-Up	IOP measurement not done	OD Crossover
00221	Primary Eye Sham	2008-10-28	Treatment	Other (Specify)	Treatment occurred greater than 30 days after screening visit.
00221	Primary Eye Sham	2008-11-05	Week 1 Follow-Up	IOP measurement not done	IOP not done during the week 1 visit for the sham eye (OS).
00221	Primary Eye Sham	2008-12-04	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 1 for the sham eye (OS - too distorted).
00221	Primary Eye Sham	2008-12-04	Month 1 Follow-Up	IOP measurement not done	IOP not done at Month 1 for the sham eye (OS).
00221	Primary Eye Sham	2009-01-20	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 3 for the sham eye (OS too distorted).
00221	Primary Eye Sham	2009-01-20	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the sham eye (OS)
00221	Sham Eye CXL	2009-04-17	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the sham eye (OS).
00221	Sham Eye CXL	2009-04-17	Month 6 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 6 for the sham eye (OS too distorted).
00221	Sham Eye CXL	2009-04-21	Week 1 Follow-Up	IOP measurement not done	IOP was not done at the Week 1 visit for the crossover eye (OS)
00221	Sham Eye CXL	2009-04-21	Week 1 Follow-Up	Other (Specify)	Week 1 visit for the crossover eye (OS) was 1 day out of window (early).
00221	Sham Eye CXL	2009-05-28	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 1 for the crossover eye (OS too distorted).
00221	Sham Eye CXL	2009-05-28	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the crossover eye (OS).
00221	Sham Eye CXL	2009-07-22	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 3 for the crossover eye (OS too distorted).
00221	Sham Eye CXL	2009-07-22	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the crossover eye (OS).
00221	Sham Eye CXL	2009-10-20	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the crossover eye (OS).
00221	Fellow Eye CXL	2009-12-17	Treatment	Other (Specify)	The fellow eye (OD) was not treated within 6 months following treatment of the study eye.
00221	Fellow Eye CXL	2009-12-17	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the fellow eye (OD).
00221	Fellow Eye CXL	2009-12-22	Week 1 Follow-Up	Manifest refraction not done	Manifest refraction not done at the week 1 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2009-12-22	Week 1 Follow-Up	IOP measurement not done	IOP not done at the week 1 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2009-12-22	Week 1 Follow-Up	BSCVA not done	BSCVA not done at the week 1 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2010-01-26	Month 1 Follow-Up	Other (Specify)	Month 1 follow-up visit for fellow eye OD CXL was not done. Subject did not show for visit scheduled for 26Jan2010.
00221	Fellow Eye CXL	2010-03-10	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2010-06-15	Month 12 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 12 for the crossover eye (OS too distorted).
00222	Primary Eye CXL	2008-11-04	Screening	Endothelial cell count not done	Cell count not done for primary study eye (OD).
00222	Primary Eye CXL	2008-11-05	Treatment	Other (Specify)	PI used artificial tears as opposed to the protocol required hypotonic 0.1% Riboflavin to increase pachymetry. OD Treatment Eye
00222	Primary Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	Protocol required procedure not done.
00222	Fellow Eye CXL	2009-02-13	Treatment	Other (Specify)	PI used artificial tears as opposed to the protocol required hypotonic 0.1% Riboflavin to increase pachymetry. OS Fellow Eye
00222	Fellow Eye CXL	2009-02-13	Treatment	Slit lamp exam not done	OS Fellow
00222	Fellow Eye CXL	2009-02-13	Month 3 Follow-Up	IOP measurement not done	Study eye
00222	Fellow Eye CXL	2009-03-12	Month 1 Follow-Up	IOP measurement not done	Fellow eye
00222	Fellow Eye CXL	2009-08-13	Month 6 Follow-Up	IOP measurement not done	Fellow eye
00223	Primary Eye Sham	2008-12-11	Week 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Primary Eye Sham	2009-01-08	Month 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Primary Eye Sham	2009-03-10	Month 3 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Sham Eye CXL	2009-05-12	Week 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.

00223	Sham Eye CXL	2009-06-04	Month 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Fellow Eye CXL	2009-08-06	Month 3 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Fellow Eye CXL	2009-08-13	Week 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Fellow Eye CXL	2009-09-02	Month 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00224	Primary Eye Sham	2008-12-10	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the sham eye (OS).
00224	Primary Eye Sham	2009-01-06	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the sham eye (OS).
00224	Sham Eye CXL	2009-03-05	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye (OS).
00224	Sham Eye CXL	2009-03-05	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the sham eye (OS).
00224	Sham Eye CXL	2009-03-10	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the crossover eye (OS).
00224	Sham Eye CXL	2009-04-15	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the crossover eye (OS).
00224	Sham Eye CXL	2009-07-29	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the crossover eye (OS).
00225	Primary Eye CXL	2008-12-18	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the study eye (OD).
00225	Primary Eye CXL	2008-12-23	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the study eye (OD).
00225	Primary Eye CXL	2009-01-21	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the study eye (OD).
00225	Primary Eye CXL	2009-03-25	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the study eye (OD).
00225	Fellow Eye CXL	2009-07-01	Week 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 for Fellow Eye (OS)
00225	Fellow Eye CXL	2009-07-30	Month 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 for Fellow Eye (OS)
00226	Primary Eye Sham	2009-01-14	Week 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00226	Primary Eye Sham	2009-02-11	Month 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00226	Primary Eye Sham	2009-04-14	Month 3 Follow-Up	IOP measurement not done	OD Sham - IOP measurement not done.
00226	Sham Eye CXL	2009-06-03	Treatment	IOP measurement not done	OD Treatment eye - IOP not done.
00226	Sham Eye CXL	2009-06-03	Treatment	Other (Specify)	OD Treatment eye - The site used Refresh Tears instead of Hypotonic Riboflavin to achieve a Pachymetry reading >/= 400 microns prior to treatment.
00226	Sham Eye CXL	2009-06-10	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2009-07-14	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2009-08-26	Month 3 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2009-12-16	Month 6 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2010-04-10	Month 12 Follow-Up	Endothelial cell count not done	OD Treatment eye - Endothelial cell count not done.
00227	Primary Eye CXL	2009-01-23	Treatment	Other (Specify)	Site used Refresh Artificial Tears instead of hypotonic riboflavin to achieve >/= 400 microns pachymetry reading.
00227	Primary Eye CXL	2009-01-28	Week 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00227	Primary Eye CXL	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00227	Primary Eye CXL	2009-04-17	Month 3 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00228	Primary Eye CXL	2008-12-02	Screening	IOP measurement not done	OD IOP measurement not done.
00228	Primary Eye CXL	2008-12-02	Screening	Endothelial cell count not done	OD Endothelial cell count not done (attempted).
00228	Primary Eye CXL	2008-12-02	Screening	IOP measurement not done	OS IOP measurement not done.

00228	Primary Eye CXL	2009-01-30	Treatment	Other (Specify)	Site used Refresh Artificial Tears instead of Hypotonic R boflavin to achieve >/= 400 micron Pachymetry prior to treatment.
00228	Primary Eye CXL	2009-02-04	Week 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00228	Primary Eye CXL	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00228	Primary Eye CXL	2009-04-17	Month 3 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-02-06	Treatment	Other (Specify)	The Site used Refresh Artificial Tears instead of Hypotonic Riboflavin to achieve >/= 400 micron Pachymetry reading prior to treatment. OD
00229	Primary Eye CXL	2009-02-07	Day 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-02-10	Week 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-02-10	Week 1 Follow-Up	Other (Specify)	Week 1 visit was out of window by 1 day early.
00229	Primary Eye CXL	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-04-21	Month 3 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00230	Primary Eye Sham	2009-03-04	Week 1 Follow-Up	Other (Specify)	Patient did not show up for Visit
00230	Primary Eye Sham	2009-04-02	Month 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Sham Eye CXL	2009-06-05	Month 3 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Sham Eye CXL	2009-06-05	Month 3 Follow-Up	Manual keratometry not done	Manual keratometry was done but cannot be measure greater than 52 diopters. Therefore reported Not Done.
00230	Sham Eye CXL	2009-06-05	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye per note to file.
00230	Sham Eye CXL	2009-06-09	Week 1 Follow-Up	Other (Specify)	Patient outside window (window = 6/10 to 6/19
00230	Sham Eye CXL	2009-06-09	Week 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements.
00230	Sham Eye CXL	2009-07-21	Week 1 Follow-Up	Other (Specify)	Patient outside window ... 6/26 to 7/17
00230	Sham Eye CXL	2009-07-21	Month 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements.
00230	Fellow Eye CXL	2009-08-28	Month 3 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Fellow Eye CXL	2009-09-01	Week 1 Follow-Up	Other (Specify)	Week 1 Visit Outside Window which was 9/2 to 9/11
00230	Fellow Eye CXL	2009-09-01	Week 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Fellow Eye CXL	2009-10-14	Month 1 Follow-Up	Other (Specify)	Patient outside visit window of 9/18 to 19/9
00230	Fellow Eye CXL	2009-10-14	Month 1 Follow-Up	IOP measurement not done	PI not aware of Protocol requirements
00230	Fellow Eye CXL	2010-02-05	Month 6 Follow-Up	IOP measurement not done	PI not aware of protocol requirements.
00231	Primary Eye Sham	2009-03-31	Week 1 Follow-Up	IOP measurement not done	OS Sham eye - IOP measurement not done.
00231	Primary Eye Sham	2009-06-23	Month 3 Follow-Up	IOP measurement not done	OS Sham eye - IOP measurement not done.
00231	Sham Eye CXL	2009-08-20	Treatment	Other (Specify)	The Site used Refresh Artificial Tears instead of Hypotonic R boflavin to achieve a Pachymetry reading >/= 400 microns prior to treatment.
00231	Sham Eye CXL	2009-08-26	Week 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00231	Sham Eye CXL	2009-09-24	Month 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00231	Sham Eye CXL	2009-11-18	Month 3 Follow-Up	Other (Specify)	Month 3 OS Treatment Eye was not done. Patient was a no show on 11/18/09. The site called and rescheduled on 11/24/09 and on 12/15/09. The subject was a no show both times.
00232	Primary Eye Sham	2009-04-01	Week 1 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.

00232	Primary Eye Sham	2009-04-28	Month 1 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00232	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	IOP measurement not done	Randomized sham control eye
00232	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	Other (Specify)	OS Sham - M3 out of window by 15 days.
00232	Sham Eye CXL	2009-09-24	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Artificial Tears instead of Hypotonic Riboflavin to try and achieve >/= 400 micron Pachymetry reading.
00232	Sham Eye CXL	2009-09-30	Week 1 Follow-Up	IOP measurement not done	Crossover eye
00232	Sham Eye CXL	2009-10-20	Month 1 Follow-Up	IOP measurement not done	Crossover eye
00233	Primary Eye Sham	2009-04-05	Treatment	Did not meet inclusion/exclusion criteria	OD Sham eye - subject drank Orange Juice on treatment day.
00233	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00233	Primary Eye Sham	2009-05-19	Month 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00233	Primary Eye Sham	2009-07-14	Month 3 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00233	Sham Eye CXL	2009-09-02	Month 6 Follow-Up	IOP measurement not done	IOP Sham eye - IOP measurement not done. OD
00233	Sham Eye CXL	2009-09-02	Treatment	Other (Specify)	OD Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading.
00233	Sham Eye CXL	2009-09-09	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00233	Sham Eye CXL	2009-10-07	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00234	Primary Eye Sham	2009-02-10	Screening	Did not meet inclusion/exclusion criteria	I-S Ratio = .346 on Screen visit
00234	Primary Eye Sham	2009-04-22	Week 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Primary Eye Sham	2009-05-21	Month 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Sham Eye CXL	2009-09-03	Month 6 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Sham Eye CXL	2009-09-03	Week 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Sham Eye CXL	2009-10-13	Month 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00235	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	IOP measurement not done	Change in CRC caused miscommunication of required procedures
00235	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	Other (Specify)	Visit out of range - 1 day early
00235	Primary Eye Sham	2009-05-19	Month 1 Follow-Up	IOP measurement not done	OS Sham - Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-09-03	Month 6 Follow-Up	Other (Specify)	Visit out of range - 1 day early (OS Sham)
00235	Sham Eye CXL	2009-09-03	Month 6 Follow-Up	IOP measurement not done	OS Sham - Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-09-08	Week 1 Follow-Up	IOP measurement not done	OS X-over - Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-10-13	Month 1 Follow-Up	IOP measurement not done	OS X-over- Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-12-18	Month 3 Follow-Up	IOP measurement not done	OS X-over- Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-12-18	Month 3 Follow-Up	Other (Specify)	3M visit out of range - 8 days late
00236	Primary Eye Sham	2009-01-12	Month 3 Follow-Up	IOP measurement not done	PI was not aware of the requirements of the protocol.
00236	Primary Eye Sham	2009-03-30	Month 6 Follow-Up	IOP measurement not done	PI was not aware of the requirements of the protocol.

00236	Sham Eye CXL	2009-10-29	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye (OD).
00236	Sham Eye CXL	2009-10-29	Month 6 Follow-Up	IOP measurement not done	PI was not aware of requirements of protocol
00236	Sham Eye CXL	2009-11-05	Week 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00236	Sham Eye CXL	2009-12-09	Month 1 Follow-Up	IOP measurement not done	PI was not aware of the requirements of the protocol
00237	Primary Eye CXL	2009-06-30	Treatment	Other (Specify)	OD Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading on treatment day.
00237	Primary Eye CXL	2009-07-08	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00237	Primary Eye CXL	2009-07-29	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00237	Primary Eye CXL	2009-12-17	Month 6 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00238	Primary Eye Sham	2009-07-16	Week 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Primary Eye Sham	2009-08-13	Month 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2009-12-17	Month 6 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2009-12-22	Week 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2010-01-12	Month 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2010-03-09	Month 3 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00239	Primary Eye Sham	2009-07-22	Week 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Primary Eye Sham	2009-08-26	Month 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Primary Eye Sham	2009-10-01	Month 3 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Sham Eye CXL	2009-12-09	Month 6 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Sham Eye CXL	2009-12-09	Treatment	Other (Specify)	OD Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading for treatment.
00239	Sham Eye CXL	2009-12-17	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00239	Sham Eye CXL	2010-01-20	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00239	Sham Eye CXL	2010-03-10	Month 3 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00239	Sham Eye CXL	2010-05-18	Month 6 Follow-Up	Other (Specify)	OD Treatment eye - Month 6 not done.
00240	Primary Eye Sham	2009-05-15	Screening	IOP measurement not done	OD - IOP measurement not done.
00240	Primary Eye Sham	2009-05-15	Screening	IOP measurement not done	OS - IOP measurement not done.
00240	Primary Eye Sham	2009-08-13	Week 1 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00240	Primary Eye Sham	2009-09-18	Month 1 Follow-Up	Other (Specify)	OS Sham - visit out of window, 1 day late.
00240	Primary Eye Sham	2009-11-19	Month 3 Follow-Up	Other (Specify)	OS Sham - visit out of window, 7 days late.
00240	Primary Eye Sham	2009-11-19	Month 3 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00240	Sham Eye CXL	2010-01-27	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading.
00240	Sham Eye CXL	2010-01-27	Month 6 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00240	Sham Eye CXL	2010-02-02	Week 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.

00240	Sham Eye CXL	2010-03-12	Month 1 Follow-Up	Other (Specify)	OS Treatment - visit out of window, 2 days late.
00240	Sham Eye CXL	2010-03-12	Month 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00240	Sham Eye CXL	2010-07-06	Month 6 Follow-Up	Other (Specify)	OS Treatment eye - M6 not done due to IRB closing study.
00240	Sham Eye CXL	2011-01-27	Month 12 Follow-Up	Other (Specify)	OS Treatment eye - M12 not done due to IRB closing study.
00241	Primary Eye Sham	2009-08-26	Week 1 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Primary Eye Sham	2009-09-30	Month 1 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Primary Eye Sham	2009-11-19	Month 3 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-01-26	Month 6 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-01-26	Treatment	Other (Specify)	OD X-over - Refresh Plus Artificial Tears used to increase pachymetry instead of protocol specified hypotonic saline.
00241	Sham Eye CXL	2010-02-02	Week 1 Follow-Up	IOP measurement not done	OD X-over - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-03-30	Month 1 Follow-Up	Other (Specify)	OD X-over - Visit out of window - 21 days late.
00241	Sham Eye CXL	2010-03-30	Month 1 Follow-Up	IOP measurement not done	OD X-over - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-05-04	Month 3 Follow-Up	Other (Specify)	OD X-over Eye - Subject didn't show for 3 month visit. Visit Range was 4/6/2010-5/4/2010.
00242	Primary Eye CXL	2009-08-20	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Tears to increase Pachymetry reading prior to treatment.
00242	Primary Eye CXL	2009-08-26	Week 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00243	Primary Eye CXL	2009-07-08	Screening	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OU
00243	Primary Eye CXL	2009-07-08	Screening	Dilated fundus exam not done	Dilated Fundus exam was not done at this visit for OU
00243	Primary Eye CXL	2009-08-25	Treatment	Other (Specify)	Artificial Tears were used to increase port debridement pachymetry measurement to 400. CXL OS
00243	Primary Eye CXL	2009-09-02	Week 1 Follow-Up	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OS
00243	Primary Eye CXL	2009-10-06	Month 1 Follow-Up	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OS
00243	Primary Eye CXL	2009-11-25	Month 3 Follow-Up	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OS
00244	Primary Eye Sham	2009-09-04	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Primary Eye Sham	2009-10-02	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Primary Eye Sham	2009-12-11	Month 3 Follow-Up	Other (Specify)	Month 3 Visit on 12/11/2009 outside window 11/5 to 12/3
00244	Primary Eye Sham	2009-12-11	Month 3 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Sham Eye CXL	2010-01-14	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS).
00244	Sham Eye CXL	2010-01-21	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Sham Eye CXL	2010-03-11	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00244	Sham Eye CXL	2010-03-11	Week 1 Follow-Up	Other (Specify)	Month 1 Visit on 3/11/2010 is outside the window 2/4/ to 2/25
00245	Primary Eye CXL	2009-08-11	Screening	Dilated fundus exam not done	Fundus exam for OD and OS was not performed per protocol; no explanation
00245	Primary Eye CXL	2009-09-02	Week 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Primary Eye CXL	2009-10-02	Month 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures

00245	Fellow Eye CXL	2009-11-19	Month 3 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2009-11-25	Week 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2009-12-22	Month 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures OD Fellow
00245	Fellow Eye CXL	2010-04-20	Month 6 Follow-Up	IOP measurement not done	OD Fellow - Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2010-04-20	Month 6 Follow-Up	Other (Specify)	OS Treatment - 6 month visit out of range - 40 days late
00246	Primary Eye CXL	2009-09-02	Screening	Did not obtain proper consent prior to performing study procedure	Subject didn't sign all required pages of ICF, specifically agreement to use and/or share their study related records. Subject did consent to participate in the study by signing his agreement.
00246	Primary Eye CXL	2009-09-03	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline - OS CXL
00246	Primary Eye CXL	2009-09-10	Week 1 Follow-Up	IOP measurement not done	OS CXL
00246	Primary Eye CXL	2009-10-08	Month 1 Follow-Up	IOP measurement not done	OS CXL
00246	Primary Eye CXL	2009-11-20	Month 3 Follow-Up	Manual keratometry not done	OS CXL
00246	Primary Eye CXL	2010-02-05	Month 6 Follow-Up	IOP measurement not done	OS CXL
00247	Primary Eye CXL	2009-09-01	Screening	Other (Specify)	Patient did not sign the RSVP
00247	Primary Eye CXL	2009-09-23	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00247	Primary Eye CXL	2010-10-14	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00248	Primary Eye CXL	2009-09-17	Screening	Dilated fundus exam not done	OU
00248	Primary Eye CXL	2009-09-23	Treatment	Other (Specify)	Hypotonic Riboflavin was not administered for Pachymetry <400, Artificial Tears were given instead
00248	Primary Eye CXL	2009-09-30	Week 1 Follow-Up	IOP measurement not done	OS
00248	Primary Eye CXL	2009-10-29	Month 1 Follow-Up	IOP measurement not done	OS
00248	Fellow Eye CXL	2009-12-15	Month 3 Follow-Up	RSVP questionnaire not done	OS
00248	Fellow Eye CXL	2009-12-15	Month 3 Follow-Up	IOP measurement not done	OS
00248	Fellow Eye CXL	2009-12-15	Treatment	Other (Specify)	Hypotonic riboflavin not administered for pachymetry <400l artificial tears given instead.
00248	Fellow Eye CXL	2009-12-15	Month 3 Follow-Up	Patients questionnaire not done	OS
00248	Fellow Eye CXL	2009-12-23	Week 1 Follow-Up	IOP measurement not done	OD
00248	Fellow Eye CXL	2010-01-14	Month 1 Follow-Up	IOP measurement not done	OD
00248	Fellow Eye CXL	2010-03-17	Month 3 Follow-Up	Endothelial cell count not done	OD
00249	Primary Eye Sham	2009-10-13	Week 1 Follow-Up	IOP measurement not done	Sham control
00249	Primary Eye Sham	2009-11-04	Month 1 Follow-Up	IOP measurement not done	Sham control
00249	Sham Eye CXL	2010-02-03	Treatment	Other (Specify)	PI used artificial tears instead of protocol required use of hypotonic saline to increase pachymetry for OD- crossover eye
00249	Sham Eye CXL	2010-02-03	Month 6 Follow-Up	Other (Specify)	Visit out of range - 21 days early for OD Sham
00249	Sham Eye CXL	2010-02-03	Month 6 Follow-Up	IOP measurement not done	sham control
00249	Sham Eye CXL	2010-02-11	Week 1 Follow-Up	IOP measurement not done	CXL Crossover eye
00249	Sham Eye CXL	2010-05-12	Month 3 Follow-Up	Other (Specify)	Pentacam Indices not captured for XCL crossover eye

00250	Primary Eye Sham	2009-10-01	Screening	Did not obtain proper consent prior to performing study procedure	Subject did not sign and date the PHI section of the consent form
00250	Primary Eye Sham	2009-10-15	Week 1 Follow-Up	IOP measurement not done	OD
00250	Primary Eye Sham	2009-11-18	Month 1 Follow-Up	IOP measurement not done	OD
00250	Primary Eye Sham	2009-12-22	Month 3 Follow-Up	UCVA not done	OD
00250	Primary Eye Sham	2010-03-30	Month 6 Follow-Up	IOP measurement not done	OD
00251	Primary Eye CXL	2009-11-11	Week 1 Follow-Up	IOP measurement not done	OS
00251	Primary Eye CXL	2010-01-28	Month 3 Follow-Up	IOP measurement not done	OS
00252	Primary Eye Sham	2009-11-12	Week 1 Follow-Up	IOP measurement not done	OD
00252	Primary Eye Sham	2009-12-17	Month 1 Follow-Up	IOP measurement not done	OD
00252	Primary Eye Sham	2010-01-21	Month 3 Follow-Up	IOP measurement not done	OD
00252	Primary Eye Sham	2010-04-20	Month 6 Follow-Up	IOP measurement not done	OD
00253	Primary Eye CXL	2009-11-17	Screening	Did not meet inclusion/exclusion criteria	Keratoconus progression in randomized eye (OD) qualified by increase in astigmatism of 1.0 D over a period of 33 months. (.24 months)
00253	Primary Eye CXL	2009-12-01	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements
00253	Primary Eye CXL	2010-01-05	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00253	Primary Eye CXL	2010-02-23	Month 3 Follow-Up	Other (Specify)	Patient did not sign RSVP
00253	Primary Eye CXL	2010-02-23	Month 3 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00253	Primary Eye CXL	2010-11-24	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the treatment eye
00254	Primary Eye CXL	2009-12-10	Week 1 Follow-Up	IOP measurement not done	OS XCL Eye
00254	Primary Eye CXL	2010-01-06	Month 1 Follow-Up	IOP measurement not done	OS XCL eye
00254	Primary Eye CXL	2010-02-24	Month 3 Follow-Up	IOP measurement not done	OS XCL eye
00255	Primary Eye Sham	2009-12-15	Week 1 Follow-Up	IOP measurement not done	OD Sham
00255	Primary Eye Sham	2010-01-07	Month 1 Follow-Up	IOP measurement not done	OD Sham
00255	Primary Eye Sham	2010-03-04	Month 3 Follow-Up	IOP measurement not done	OD Sham
00255	Primary Eye Sham	2010-06-22	Month 6 Follow-Up	Other (Specify)	6 month visit was missed
00256	Primary Eye Sham	2009-12-09	Screening	Other (Specify)	I-S Ratio not measured for fellow eye
00256	Primary Eye Sham	2009-12-17	Week 1 Follow-Up	IOP measurement not done	OS Sham Control
00256	Primary Eye Sham	2010-01-15	Month 1 Follow-Up	IOP measurement not done	OS Sham Control
00256	Primary Eye Sham	2010-03-04	Month 3 Follow-Up	IOP measurement not done	OS Sham Control
00256	Primary Eye	2010-06-24	Month 6	Other (Specify)	Subject was not seen for their 6 month visit.
	Sham		Follow-Up		
00257	Primary Eye CXL	2009-01-29	Month 1 Follow-Up	Other (Specify)	OS Treatment eye visit out of window 3 days late
00257	Primary Eye CXL	2009-12-15	Treatment	Other (Specify)	Site used artificial tears in addition to hypotonic riboflavin to increase pachymetry after debridement to greater than or equal to 400 microns before treatment
00257	Primary Eye CXL	2009-12-22	Week 1 Follow-Up	IOP measurement not done	OS - IOP measurement not done.
00257	Primary Eye CXL	2010-01-29	Month 1 Follow-Up	IOP measurement not done	OS - IOP measurement not done.
00257	Primary Eye CXL	2010-03-12	Month 3 Follow-Up	IOP measurement not done	OS - IOP measurement not done.
00257	Primary Eye CXL	2010-06-15	Month 6 Follow-Up	Other (Specify)	OS Treatment Eye - M6 not done, subject was a no show.
00257	Primary Eye CXL	2010-12-15	Month 12 Follow-Up	Other (Specify)	OS Treatment eye - M12 not done due to IRB closing study.
00258	Primary Eye CXL	2010-01-13	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading.

00258	Primary Eye CXL	2010-01-19	Week 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00258	Primary Eye CXL	2010-02-19	Month 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00258	Primary Eye CXL	2010-04-16	Month 3 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00258	Primary Eye CXL	2011-01-13	Month 12 Follow-Up	Other (Specify)	OS Treatment Eye - M12 not done due to IRB closing study.
03201	Primary Eye CXL	2008-01-03	Screening	Endothelial cell count not done	Endothelial cell count was done but could not be interpreted.
03201	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At treatment, PI used 5 drops of hypotonic riboflavin every 5 seconds for 3 doses, then brought dose back to 2 drops every 5 seconds, to increase corneal thickness.
03201	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At illumination time, PI alternated between hypotonic riboflavin and isotonic solution for the first half of treatment time to keep pachymetry above 400 microns.
03201	Primary Eye CXL	2008-04-18	Month 3 Follow-Up	Other (Specify)	Patient outside of window visit (3/15 to 4/12/2008)
03201	Primary Eye CXL	2008-07-10	Month 6 Follow-Up	IOP measurement not done	PI not aware of full protocol requirements
03201	Primary Eye CXL	2010-01-03	Screening	Other (Specify)	Contact Lens Stability not done prior to treatment
03202	Primary Eye CXL	2007-12-14	Screening	Endothelial cell count not done	Endothelial cell count was done but could not be computed. OD
03202	Primary Eye CXL	2007-12-14	Screening	Other (Specify)	Contact lens discontinue only 6 days prior to screening vs. 14 days for RGPs - discontinued 12/8/2007
03202	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At eight minutes into the illumination time, the PI switch from one drop of isotonic riboflavin to two drops of riboflavin and maintained this through the remainder of the illumination. OD
03202	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At 8 minutes into the illumination time, PI added hypotonic r boflavin at each interval for the remainder of the time in order to maintain corneal thickness. OD
03202	Primary Eye CXL	2008-04-03	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done at month 3. OD
03202	Fellow Eye CXL	2008-07-30	Treatment	Other (Specify)	PI used artificial tears after administration of as opposed to hypotonic riboflavin to increase pachymetry reading from 361 to 420.
03202	Fellow Eye CXL	2008-10-15	Month 3 Follow-Up	IOP measurement not done	IOP not done on month 3 visit. OS
03202	Fellow Eye CXL	2008-12-17	Month 12 Follow-Up	IOP measurement not done	IOP not done on month 12 visit. OD
03202	Fellow Eye CXL	2009-09-22	Month 12 Follow-Up	Manual keratometry not done	Manual keratometry was not done at Month 12 Visit. OS
03203	Primary Eye Sham	2008-04-17	Month 1 Follow-Up	Other (Specify)	Visit out of range - 7 days late: OS Sham
03203	Sham Eye CXL	2008-05-28	Treatment	Other (Specify)	OS Cross-over: Error in administration or recording of time of illumination
03203	Sham Eye CXL	2008-08-07	Month 3 Follow-Up	Other (Specify)	OS Cross-over: Kmax value and TKC indices not measured due to use of different pentacam than normally used on study.
03204	Primary Eye Sham	2008-01-24	Screening	Manual keratometry not done	OS Fellow
03204	Primary Eye Sham	2008-01-24	Screening	Endothelial cell count not done	OD Sham
03204	Primary Eye Sham	2008-03-07	Screening	Other (Specify)	Subject treated although contact lens stability check demonstrated that based on topography the refraction was not stable. OD Sham
03204	Primary Eye Sham	2008-03-07	Treatment	Other (Specify)	Treatment occurred greater than 30 days from screening - OD Sham
03204	Sham Eye CXL	2008-05-27	Treatment	Other (Specify)	Artificial tears in addition to hypotonic riboflavin used to increase pachymetry prior to illumination - OD Cross-over
03204	Fellow Eye CXL	2009-07-22	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry instead of protocol specified hypotonic riboflavin - OS Fellow
03204	Fellow Eye CXL	2009-07-22	Treatment	Other (Specify)	Treatment occurred more than 6 months after initial eye was treated - OS Fellow
03204	Fellow Eye CXL	2010-05-27	Month 12 Follow-Up	Endothelial cell count not done	OS Fellow
03205	Fellow Eye CXL	2008-09-05	Month 1 Follow-Up	Other (Specify)	1 Month follow up visit out of window. Subject was seen 3 weeks out of window.
03205	Fellow Eye CXL	2008-11-06	Treatment	Other (Specify)	Protocol deviation: use of artificial tears instead of Hypotonic 0.1% Riboflavin drops to increase Pachymetry.
03206	Primary Eye CXL	2008-03-18	Screening	Other (Specify)	Obtained consent on consent version 7, dated 10.24.2007, and updated consent version 8, dated 11.16.2007 should have been used.
03207	Primary Eye CXL	2008-04-16	Treatment	Other (Specify)	Artificial tears and distilled water drops were used to obtain Pachymetry measurement over 400.
03208	Primary Eye Sham	2008-04-23	Treatment	Other (Specify)	Subject didn't present with a stable refraction based on MRSE, but treatment occurred
03208	Primary Eye Sham	2008-06-04	Month 1 Follow-Up	Manual keratometry not done	OD Sham
03208	Sham Eye CXL	2008-07-30	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified hypotonic riboflavin. OD Cross-over.
03208	Sham Eye CXL	2008-07-30	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified hypotonic riboflavin. OS Fellow.

03208	Sham Eye CXL	2008-08-08	Week 1 Follow-Up	Slit lamp exam not done	OS Fellow
03209	Primary Eye CXL	2008-05-16	Elig bility	Other (Specify)	Site instilled sterile water in addition to riboflavin to assist in raising pachymetry values.
03209	Primary Eye CXL	2008-05-16	Screening	Other (Specify)	On the Consent, the subject indicated they wanted their PCP notified of study participation; however, the PCP's contact information was not completed.
03209	Primary Eye CXL	2008-12-12	Month 6 Follow-Up	Other (Specify)	Month 6 follow-up visit was conducted 14 days out of window. Visit should have occurred between 10/23/08 through 11/28/08.
03210	Primary Eye CXL	2008-06-12	Week 1 Follow-Up	IOP measurement not done	IOP not done at week 1 - Randomized Eye OS
03210	Fellow Eye CXL	2008-09-09	Treatment	Other (Specify)	PI used Artificial Tears rather than isotonic saline to increase corneal thickness. - Fellow OD
03210	Fellow Eye CXL	2008-09-18	Week 1 Follow-Up	IOP measurement not done	IOP not done at Week 1 - Fellow OD
03210	Fellow Eye CXL	2008-11-20	Month 6 Follow-Up	IOP measurement not done	IOP not done on Month 6 Visit - Randomized OS
03210	Fellow Eye CXL	2008-11-20	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 Visit - Fellow OD
03210	Fellow Eye CXL	2009-03-24	Month 6 Follow-Up	IOP measurement not done	IOP not done on Month 6 Visit - Fellow OD
03211	Primary Eye Sham	2008-05-29	Treatment	Other (Specify)	PI used artificial tears rather than hypotonic r boflavin in order to increase the corneal thickness (348 to 436).
03211	Primary Eye Sham	2008-06-03	Week 1 Follow-Up	IOP measurement not done	IOP not done at week 1 - Fellow OS
03211	Sham Eye CXL	2008-09-05	Treatment	Other (Specify)	PI used artificial tears rather than hypotonic r boflavin to increase corneal thickness (348 to 436). – OD
03211	Sham Eye CXL	2008-09-10	Week 1 Follow-Up	IOP measurement not done	IOP not done at Week 1 - Crossover OD
03211	Sham Eye CXL	2008-12-10	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 Visit - Crossover OD
03211	Sham Eye CXL	2008-12-10	Month 6 Follow-Up	IOP measurement not done	IOP not done at month 6 - Fellow - OS
03212	Primary Eye CXL	2008-06-24	Week 1 Follow-Up	IOP measurement not done	OS CXL
03212	Primary Eye CXL	2008-09-03	Month 3 Follow-Up	Corneal topography not done	OS CXL
03212	Primary Eye CXL	2008-11-20	Month 6 Follow-Up	IOP measurement not done	OS CXL
03212	Fellow Eye CXL	2009-07-29	Treatment	Other (Specify)	Fellow eye treated more than 6 months after first treated eye
03212	Fellow Eye CXL	2009-07-29	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified Hypotonic R boflavin - OD Fellow
03212	Fellow Eye CXL	2009-08-05	Week 1 Follow-Up	IOP measurement not done	OD Fellow
03212	Fellow Eye CXL	2009-10-14	Month 3 Follow-Up	RSVP questionnaire not done	OD Fellow
03212	Fellow Eye CXL	2009-10-14	Month 3 Follow-Up	Patients questionnaire not done	OD Fellow
03213	Primary Eye Sham	2008-09-04	Week 1 Follow-Up	IOP measurement not done	IOP not done at Week 1 Visit - Sham Eye - OD
03213	Primary Eye Sham	2008-09-17	Month 12 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 12 Visit as it was out of range - Crossover -OD
03213	Sham Eye CXL	2008-11-12	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness -OD
03213	Sham Eye CXL	2008-11-12	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness - OS
03213	Sham Eye CXL	2008-11-20	Week 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 Visit - Fellow - OS
03213	Sham Eye CXL	2008-11-20	Week 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 Visit - Crossover - OD
03213	Sham Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - Fellow - OS
03213	Sham Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - Crossover OD
03213	Sham Eye CXL	2008-12-04	Month 1 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 1 Visit as it was out of range - Crossover - OD
03213	Sham Eye CXL	2009-02-06	Month 3 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 3 Visit as it was out of range - Crossover - OD
03213	Sham Eye CXL	2009-05-21	Month 6 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 6 Visit as it was out of range - Crossover - OD
03214	Primary Eye Sham	2008-09-04	Week 1 Follow-Up	IOP measurement not done	OD
03214	Sham Eye CXL	2008-10-29	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic riboflavin (Crossover OD)
03214	Sham Eye CXL	2008-10-29	Month 3 Follow-Up	Other (Specify)	Visit out of range - 1 day early; OD Sham
03214	Sham Eye CXL	2008-10-29	Treatment	Other (Specify)	Illumination procedure was performed although pachymetry was not greater than or equal to 400.

03214	Sham Eye CXL	2008-11-20	Month 1 Follow-Up	IOP measurement not done	Crossover OD
03214	Sham Eye CXL	2009-01-28	Month 3 Follow-Up	IOP measurement not done	Crossover OD
03214	Fellow Eye CXL	2009-05-06	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic R boflavin
03214	Fellow Eye CXL	2009-05-06	Month 6 Follow-Up	IOP measurement not done	Crossover OD
03214	Fellow Eye CXL	2009-05-12	Week 1 Follow-Up	IOP measurement not done	fellow eye OS
03214	Fellow Eye CXL	2009-06-18	Month 1 Follow-Up	Other (Specify)	Visit out of range - 1 day late; OS Fellow
03214	Fellow Eye CXL	2009-06-18	Month 1 Follow-Up	IOP measurement not done	OS Fellow
03215	Primary Eye CXL	2008-08-19	Screening	Did not obtain proper consent prior to performing study procedure	Person obtaining consent did not sign and date the ICF.
03215	Primary Eye CXL	2008-08-26	Treatment	Other (Specify)	Eye was treated although eye did not meet stability criteria for MRSE. Difference was1.62 and needed to be less than or equal to 0.75D - OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Other (Specify)	Failed to measure and/or record debridement diameter - OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Slit lamp exam not done	OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Ultrasound pachymetry not done	Failed to measure and/or record pachymetry before debridement OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified Hypotonic R boflavin- OS CXL
03215	Primary Eye CXL	2008-09-30	Month 1 Follow-Up	IOP measurement not done	OS CXL
03215	Primary Eye CXL	2008-11-17	Month 3 Follow-Up	IOP measurement not done	OS CXL
03215	Fellow Eye CXL	2008-12-18	Month 1 Follow-Up	IOP measurement not done	OD Fellow
03215	Fellow Eye CXL	2009-02-24	Month 6 Follow-Up	IOP measurement not done	OS CXL
03215	Fellow Eye CXL	2009-02-24	Month 3 Follow-Up	IOP measurement not done	OD Fellow
03216	Primary Eye Sham	2008-08-13	Screening	Endothelial cell count not done	Not performed on OD
03216	Primary Eye Sham	2008-08-13	Screening	Endothelial cell count not done	Not performed on OS
03216	Primary Eye Sham	2008-09-10	Week 1 Follow-Up	IOP measurement not done	Not performed on OS Sham Eye
03216	Primary Eye Sham	2008-09-30	Month 1 Follow-Up	IOP measurement not done	Not performed on OS Sham Eye
03216	Sham Eye CXL	2008-11-25	Month 3 Follow-Up	IOP measurement not done	Not performed on Sham OS
03216	Sham Eye CXL	2010-01-20	Month 12 Follow-Up	Other (Specify)	Visit was conducted 1 day out of window. Visit should have occurred between 9/1/09 through 1/19/10
03217	Primary Eye CXL	2008-01-29	Other	Other (Specify)	Site personnel who obtained consent did not properly sign and date the consent where indicated.
03217	Primary Eye CXL	2008-09-17	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic R boflavin - OS CXL
03217	Primary Eye CXL	2008-09-17	Treatment	Other (Specify)	Subject was treated without verifying that refraction was stable. OS CXL
03217	Primary Eye CXL	2008-09-24	Week 1 Follow-Up	IOP measurement not done	Not performed on CXL Tx OS
03217	Primary Eye CXL	2008-12-12	Month 3 Follow-Up	IOP measurement not done	Not performed on CXL Tx OS
03218	Primary Eye CXL	2008-09-24	Treatment	Other (Specify)	Protocol deviation: use of artificial tears instead of Hypotonic 0.1% Riboflavin drops to increase Pachymetry
03218	Primary Eye CXL	2008-12-23	Month 3 Follow-Up	Other (Specify)	Protocol Violation: Month 3 Follow up visit did not occur.
03218	Primary Eye CXL	2010-01-21	Month 12 Follow-Up	Other (Specify)	Month 12 visit was two months out of window. Visit windows were 07/01/2009 through 11/18/2009.
03219	Primary Eye CXL	2008-12-18	Month 3 Follow-Up	IOP measurement not done	Deviation
03219	Fellow Eye CXL	2009-01-29	Treatment	Other (Specify)	Deviation: Use of artificial tears to increase Pachymetry.
03219	Fellow Eye CXL	2009-03-06	Month 1 Follow-Up	Manual keratometry not done	Deviation
03219	Fellow Eye CXL	2009-04-22	Month 3 Follow-Up	Other (Specify)	Deviation: Pentacam Indices not obtained.
03219	Fellow Eye CXL	2009-09-26	Treatment	Other (Specify)	Deviation: Use of artificial tears to increase Pachymetry.
03220	Primary Eye Sham	2008-10-13	Week 1 Follow-Up	IOP measurement not done	OS Sham
03220	Sham Eye CXL	2008-12-19	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic R boflavin - OS Cross-over
03220	Sham Eye CXL	2008-12-19	Month 3 Follow-Up	IOP measurement not done	OS Sham

03220	Sham Eye CXL	2008-12-23	Week 1 Follow-Up	Other (Specify)	Visit out of range - 1 day early - OS Cross-over
03220	Sham Eye CXL	2008-12-23	Week 1 Follow-Up	IOP measurement not done	OS Cross-over
03220	Sham Eye CXL	2009-01-23	Month 1 Follow-Up	IOP measurement not done	OS Cross-over
03220	Sham Eye CXL	2009-03-11	Month 3 Follow-Up	IOP measurement not done	OS Cross-over
03220	Sham Eye CXL	2009-06-18	Month 6 Follow-Up	IOP measurement not done	OS Cross-over
03221	Primary Eye Sham	2008-10-15	Week 1 Follow-Up	IOP measurement not done	Sham Eye – OD
03221	Primary Eye Sham	2009-01-08	Month 3 Follow-Up	IOP measurement not done	Sham Eye – OD
03221	Sham Eye CXL	2009-04-16	Treatment	Other (Specify)	PI used artificial tears versus hypotonic r boflavin to increase corneal thickness.
03221	Sham Eye CXL	2009-04-21	Week 1 Follow-Up	IOP measurement not done	Crossover – OD
03221	Sham Eye CXL	2009-05-21	Month 1 Follow-Up	IOP measurement not done	Crossover – OD
03221	Sham Eye CXL	2009-07-14	Month 3 Follow-Up	IOP measurement not done	Crossover – OD
03221	Sham Eye CXL	2009-10-28	Month 6 Follow-Up	IOP measurement not done	Crossover – OD
03222	Primary Eye Sham	2008-10-08	Screening	Endothelial cell count not done	OS
03222	Primary Eye Sham	2008-10-22	Week 1 Follow-Up	IOP measurement not done	OD Sham
03222	Primary Eye Sham	2008-11-19	Month 1 Follow-Up	IOP measurement not done	OD Sham
03222	Sham Eye CXL	2009-04-24	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic R boflavin - OD Cross-over
03222	Sham Eye CXL	2009-04-24	Treatment	Other (Specify)	Non-randomized OD was treated outside of the acceptable window of greater than 3 months and less than 6 months by 10 days: OD Cross-over
03222	Sham Eye CXL	2009-04-29	Week 1 Follow-Up	IOP measurement not done	OD Cross-over
03222	Sham Eye CXL	2009-06-03	Month 1 Follow-Up	IOP measurement not done	OD Cross-over
03223	Primary Eye Sham	2008-11-25	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - Sham OD
03223	Sham Eye CXL	2009-02-27	Treatment	Other (Specify)	PI used artificial tears as opposed to hypotonic riboflavin to increase corneal thickness. Crossover OD
03223	Sham Eye CXL	2009-02-27	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - Sham OD
03223	Sham Eye CXL	2009-03-04	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - Crossover OD
03223	Sham Eye CXL	2009-03-25	Month 1 Follow-Up	IOP measurement not done	IOP was not done on Month 1 Visit - Crossover OD
03223	Sham Eye CXL	2009-05-14	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - Crossover OD
03224	Primary Eye CXL	2008-12-03	Treatment	Other (Specify)	Deviation: Use of artificial tears to increase Pachymetry.
03224	Primary Eye CXL	2008-12-03	Treatment	Other (Specify)	Deviation: Last three drops of Medio-Cross R boflavin 0.1% (Isotonic) drops administered 1 minute apart instead of 2 minutes per protocol.
03224	Primary Eye CXL	2008-12-10	Week 1 Follow-Up	IOP measurement not done	Deviation
03224	Primary Eye CXL	2009-03-04	Month 3 Follow-Up	IOP measurement not done	Deviation
03225	Primary Eye Sham	2008-12-23	Week 1 Follow-Up	IOP measurement not done	Sham OS
03225	Primary Eye Sham	2009-01-27	Month 1 Follow-Up	IOP measurement not done	Sham OS
03225	Primary Eye Sham	2009-04-21	Month 3 Follow-Up	IOP measurement not done	Sham OS
03225	Sham Eye CXL	2009-07-07	Treatment	Other (Specify)	PI used Artificial Tears as opposed to hypotonic r boflavin to increase corneal thickness.
03225	Sham Eye CXL	2009-07-07	Month 6 Follow-Up	IOP measurement not done	Sham OS
03225	Sham Eye CXL	2009-07-16	Week 1 Follow-Up	IOP measurement not done	Crossover OS
03225	Sham Eye CXL	2009-08-18	Month 1 Follow-Up	IOP measurement not done	Crossover OS
03225	Sham Eye CXL	2009-10-13	Month 3 Follow-Up	Other (Specify)	After multiple calls the patient was a "no show" for Month 3 Visit.
03225	Sham Eye CXL	2010-01-08	Month 6 Follow-Up	IOP measurement not done	Crossover OS
03225	Sham Eye CXL	2010-05-22	Month 12 Follow-Up	Other (Specify)	After numerous call, the patient would not come in for 12 Month Visit, consequently, he was terminated on 8/1/8/2010 (mo. 6), as the IRB closed the study at the PI's request.
03226	Primary Eye Sham	2009-01-15	Treatment	IOP measurement not done	Deviation

03226	Primary Eye Sham	2009-01-20	Week 1 Follow-Up	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-04-16	Treatment	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-04-16	Treatment	Other (Specify)	Site used artificial tears instead of protocol specified hypotonic riboflavin to increase Pachymetry after debridement and before treatment -OS Cross-over
03226	Sham Eye CXL	2009-04-17	Week 1 Follow-Up	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-07-21	Month 3 Follow-Up	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-10-20	Month 6 Follow-Up	IOP measurement not done	Deviation
03227	Primary Eye Sham	2009-01-28	Week 1 Follow-Up	IOP measurement not done	Deviation
03227	Primary Eye Sham	2009-02-24	Month 1 Follow-Up	IOP measurement not done	Deviation
03227	Primary Eye Sham	2009-04-28	Month 3 Follow-Up	IOP measurement not done	Deviation
03227	Sham Eye CXL	2009-06-17	Month 6 Follow-Up	IOP measurement not done	Deviation
03227	Sham Eye CXL	2009-06-17	Treatment	Other (Specify)	Use of artificial tears to increase Pachymetry
03227	Sham Eye CXL	2009-06-24	Week 1 Follow-Up	IOP measurement not done	Deviation
03227	Sham Eye CXL	2009-09-09	Month 3 Follow-Up	IOP measurement not done	Deviation
03228	Primary Eye CXL	2009-01-22	Treatment	Other (Specify)	Patient used Artificial Tear in the place of Hypotonic Riboflavin to increase corneal thickness. CXL OD
03228	Primary Eye CXL	2009-03-05	Month 1 Follow-Up	IOP measurement not done	IOP not done at Month 1 Visit. CXL OD
03229	Primary Eye CXL	2009-02-03	Week 1 Follow-Up	IOP measurement not done	OS 1 Wk. Deviation IOP not obtained
03229	Primary Eye CXL	2009-02-24	Month 1 Follow-Up	IOP measurement not done	OS 1 Mo. Deviation IOP not obtained
03229	Primary Eye CXL	2009-08-04	Month 3 Follow-Up	IOP measurement not done	OS 6 Mo. Deviation IOP not obtained
03230	Primary Eye Sham	2009-01-08	Screening	Did not obtain proper consent prior to performing study procedure	Subject signed ICF in only one of two required places and didn't answer question regarding 'inform PCP
03230	Primary Eye Sham	2009-01-08	Screening	Endothelial cell count not done	Machine was down. ECC collected on 1/29/09 treatment visit - OS Sham
03230	Primary Eye Sham	2009-02-03	Week 1 Follow-Up	IOP measurement not done	OS Sham
03230	Primary Eye Sham	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OS Sham
03230	Primary Eye Sham	2009-04-24	Month 3 Follow-Up	IOP measurement not done	OS Sham
03230	Primary Eye Sham	2009-04-24	Month 3 Follow-Up	Endothelial cell count not done	OS Sham
03230	Sham Eye CXL	2009-07-01	Month 6 Follow-Up	IOP measurement not done	OS Sham
03230	Sham Eye CXL	2009-07-01	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic R boflavin - OS Cross-over
03230	Sham Eye CXL	2009-07-08	Week 1 Follow-Up	IOP measurement not done	OS Cross-over
03230	Sham Eye CXL	2009-08-04	Month 1 Follow-Up	IOP measurement not done	OS Cross-over
03230	Fellow Eye CXL	2009-11-18	Treatment	Other (Specify)	Fellow eye treated later than the 6 month visit for the randomized eye by approximately 4 months: OD Fellow
03230	Fellow Eye CXL	2009-11-18	Month 6 Follow-Up	IOP measurement not done	OS Cross-over
03230	Fellow Eye CXL	2010-02-19	Month 3 Follow-Up	IOP measurement not done	OD Fellow
03231	Primary Eye CXL	2009-01-30	Treatment	Other (Specify)	PI used artificial tears rather than hypotonic r boflavin to increase corneal thickness.
03231	Primary Eye CXL	2009-02-03	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - CXL - OS
03231	Primary Eye CXL	2009-03-11	Month 1 Follow-Up	IOP measurement not done	IOP was not done on Month 1 Visit - CXL - OS
03231	Primary Eye CXL	2009-04-24	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - CXL - OS
03232	Primary Eye CXL	2008-12-09	Screening	Endothelial cell count not done	Endothelial cell count was not done at screen - Fellow OD
03232	Primary Eye CXL	2009-03-03	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness. Tx - CXL - OS.
03232	Primary Eye CXL	2009-03-03	Treatment	Other (Specify)	Treatment Visit is outside 30 day window. Ocular measurements were done on this visit.
03232	Primary Eye CXL	2009-03-10	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - CXL- OS
03232	Primary Eye CXL	2009-04-14	Month 1 Follow-Up	IOP measurement not done	IOP was not done on Month 1 Visit - CXL- OS

03232	Primary Eye CXL	2009-06-04	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - CXL- OS
03233	Primary Eye Sham	2009-03-31	Week 1 Follow-Up	IOP measurement not done	OS Sham
03233	Primary Eye Sham	2009-05-08	Month 1 Follow-Up	IOP measurement not done	OS Sham
03233	Primary Eye Sham	2009-05-08	Month 1 Follow-Up	Other (Specify)	Visit out of range - 2 days late: OS Sham
03233	Primary Eye Sham	2009-06-17	Month 3 Follow-Up	IOP measurement not done	OS Sham
03234	Primary Eye Sham	2009-03-10	Screening	cell count not done	OS Fellow
03234	Primary Eye Sham	2009-03-10	Screening	Other (Specify)	Subject failed to sign PHI release as part of the ICF
03234	Primary Eye Sham	2009-04-14	Treatment	Other (Specify)	Treatment occurred more than 30 days after screening: OD Sham
03234	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	IOP measurement not done	OD Sham
03234	Primary Eye Sham	2009-05-21	Month 1 Follow-Up	IOP measurement not done	OD Sham
03234	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	IOP measurement not done	OD Sham
03234	Sham Eye CXL	2009-09-01	Month 6 Follow-Up	IOP measurement not done	OD Sham
03234	Sham Eye CXL	2009-09-01	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified Hypotonic R boflavin: OD Cross-over
03234	Sham Eye CXL	2009-09-09	Week 1 Follow-Up	IOP measurement not done	OD Cross-over
03234	Sham Eye CXL	2009-10-07	Month 1 Follow-Up	IOP measurement not done	OD Cross-over
03234	Sham Eye CXL	2010-02-03	Month 6 Follow-Up	IOP measurement not done	OD Cross-over
03235	Primary Eye CXL	2009-04-29	Treatment	Other (Specify)	PI used Artificial Tears as opposed to isotonic R boflavin to increase corneal thickness.
03235	Primary Eye CXL	2009-05-06	Week 1 Follow-Up	IOP measurement not done	IOP was not done at Week 1 Visit. CXL - OD
03235	Primary Eye CXL	2009-05-27	Month 1 Follow-Up	IOP measurement not done	IOP was not done at Month 1 Visit. CXL - OD
03235	Primary Eye CXL	2009-07-30	Month 3 Follow-Up	IOP measurement not done	IOP was not done at Month 3 Visit. CXL - OD
03235	Primary Eye CXL	2009-11-11	Month 6 Follow-Up	Manual keratometry not done	Manual Keratometry was not done on Month 6 Visit. CXL - OD
03236	Primary Eye Sham	2009-05-12	Week 1 Follow-Up	IOP measurement not done	OS SHAM 1 Wk. - Deviation IOP was not obtained.
03236	Primary Eye Sham	2009-06-17	Month 1 Follow-Up	IOP measurement not done	OS SHAM 1 Mo. Deviation IOP not obtained.
03236	Primary Eye Sham	2009-08-06	Month 3 Follow-Up	IOP measurement not done	OS 3 Mo Deviation-IOP not obtained
03236	Sham Eye CXL	2009-09-29	Week 1 Follow-Up	IOP measurement not done	OS Crossover 1 Wk. Deviation IOP not obtained.
03236	Sham Eye CXL	2009-10-30	Month 1 Follow-Up	IOP measurement not done	OS Crossover 1 Mo. Deviation IOP not obtained
03236	Sham Eye CXL	2009-12-31	Month 3 Follow-Up	IOP measurement not done	OS Crossover 3 Mo IOP not obtained
03237	Primary Eye CXL	2009-05-14	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic R boflavin: OD CXL
03237	Primary Eye CXL	2009-05-19	Week 1 Follow-Up	IOP measurement not done	OD CXL
03237	Primary Eye CXL	2009-06-23	Month 1 Follow-Up	IOP measurement not done	OD CXL
03237	Primary Eye CXL	2009-08-12	Month 3 Follow-Up	IOP measurement not done	OD CXL
03238	Primary Eye CXL	2009-03-26	Screening	Endothelial cell count not done	OS Fellow
03238	Primary Eye CXL	2009-05-14	Treatment	Other (Specify)	Artificial tears was used to increase pachymetry instead of protocol specified Hypotonic R boflavin: OS CXL
03238	Primary Eye CXL	2009-05-14	Treatment	Other (Specify)	Treatment was done more than 30 days after screening: OS CXL
03238	Primary Eye CXL	2009-05-20	Week 1 Follow-Up	IOP measurement not done	OS CXL
03238	Primary Eye CXL	2009-06-23	Month 1 Follow-Up	IOP measurement not done	OS CXL
03238	Primary Eye CXL	2009-08-18	Month 3 Follow-Up	IOP measurement not done	OS CXL
03239	Primary Eye Sham	2009-07-08	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done on Month 1 Visit - Sham - OS
03239	Primary Eye Sham	2009-09-08	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done on Month 3 Visit - Sham - OS
03239	Sham Eye CXL	2009-10-30	Month 6 Follow-Up	IOP measurement not done	IOP measurement not done on Month 6 Visit - Sham - OS
03239	Sham Eye CXL	2009-10-30	Treatment	Other (Specify)	PI used artificial tears as opposed to hypotonic riboflavin to increase corneal thickness. CRS-OVR – OS

03239	Sham Eye CXL	2009-11-03	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done on Week 1 Visit - CRS-OVR - OS
03239	Sham Eye CXL	2009-11-24	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done on Month 1 Visit - CRS-OVR - OS
03239	Sham Eye CXL	2010-01-19	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done on Month 3 Visit - CRS-OVR - OS
03240	Primary Eye CXL	2009-06-04	Treatment	Other (Specify)	OD Treatment Use of artificial tears to increase pachymetry
03240	Primary Eye CXL	2009-06-10	Week 1 Follow-Up	IOP measurement not done	OD 1 Wk. Deviation IOP Not obtained
03240	Primary Eye CXL	2009-07-17	Month 1 Follow-Up	Other (Specify)	OD 1 Mo. Deviation Visit took place 1 day out of window.
03240	Primary Eye CXL	2009-07-17	Month 1 Follow-Up	IOP measurement not done	OD 1Mo. Deviation IOP not obtained
03240	Primary Eye CXL	2009-12-01	Month 6 Follow-Up	IOP measurement not done	OD 6 Mo Deviation IOP not obtained
03241	Primary Eye Sham	2009-07-21	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done at Week 1 Visit - Sham - OD
03241	Primary Eye Sham	2009-08-25	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - Sham - OD
03241	Primary Eye Sham	2009-10-15	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done Month 3 - Sham OD
03241	Primary Eye Sham	2009-10-15	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done at Month 3 Visit - Sham - OD
03241	Sham Eye CXL	2010-01-15	Month 6 Follow-Up	IOP measurement not done	IOP measurement not done at Month 6 Visit - Sham - OD
03241	Sham Eye CXL	2010-01-15	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness.
03241	Sham Eye CXL	2010-01-21	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done at Week 1 Visit - CRS-ORV
03241	Sham Eye CXL	2010-02-18	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - CRS-ORV
03241	Sham Eye CXL	2010-03-31	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done at Month 3 Visit - CRS-ORV
03241	Sham Eye CXL	2010-07-27	Month 6 Follow-Up	IOP measurement not done	IOP measurement not done at Month 6 Visit - CRS-ORV
03242	Primary Eye Sham	2009-01-19	Week 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Week 1 Visit - CRS-OVR - OD
03242	Primary Eye Sham	2009-09-04	Week 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Week 1 Visit - Sham OD
03242	Primary Eye Sham	2009-10-07	Month 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 1 Visit - Sham OD
03242	Sham Eye CXL	2010-01-13	Treatment	Other (Specify)	PI used Artificial Tears as opposed to hypotonic R boflavin in order to increase corneal thickness.
03242	Sham Eye CXL	2010-01-13	Month 6 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 6 Visit - Sham OD
03242	Sham Eye CXL	2010-02-17	Month 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 1 Visit - CRS-OVR - OD
03242	Sham Eye CXL	2010-03-29	Month 3 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 6 Visit - CRS-OVR - OD
03243	Primary Eye CXL	2009-09-02	Treatment	Other (Specify)	PI used artificial tears as opposed to hypotonic riboflavin to increase corneal thickness. CXL – OS
03243	Primary Eye CXL	2009-09-09	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done on Week 1 - CXL - OS
03243	Primary Eye CXL	2009-10-16	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done on Month 1 - CXL - OS
03243	Primary Eye CXL	2009-11-20	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done on Month 3 - CXL - OS
03243	Primary Eye CXL	2009-11-20	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry not done on Month 3 - CXL - OS
03244	Primary Eye CXL	2009-10-20	Treatment	Other (Specify)	Deviation- OS Artificial tears used to increase pachymetry.
03244	Primary Eye CXL	2009-10-28	Week 1 Follow-Up	IOP measurement not done	Deviation OS 1 Wk. IOP not obtained.
03244	Primary Eye CXL	2009-12-11	Month 1 Follow-Up	IOP measurement not done	Deviation OS 1 Mo. IOP not obtained
03244	Primary Eye CXL	2009-12-11	Month 1 Follow-Up	Other (Specify)	Deviation 1 Mo. OS follow up visit done 10 days out of window.
03244	Primary Eye CXL	2010-01-19	Month 3 Follow-Up	IOP measurement not done	Deviation 3 Mo OS IOP not obtained
03245	Primary Eye Sham	2009-11-17	Day 1 Follow-Up	IOP measurement not done	Deviation 1 week OS SHAM IOP not obtained.
03245	Primary Eye Sham	2009-12-16	Month 1 Follow-Up	IOP measurement not done	Deviation 1 Mo OS SHAM IOP not obtained
03245	Primary Eye Sham	2010-01-15	Month 3 Follow-Up	IOP measurement not done	Deviation Mo 3 OS SHAM IOP not obtained
03245	Primary Eye Sham	2010-01-15	Month 3 Follow-Up	Other (Specify)	Deviation Visit out of range - 4 days early
03245	Primary Eye Sham	2010-04-14	Month 6 Follow-Up	IOP measurement not done	Deviation Mo 6 OS SHAM IOP not obtained.
03246	Primary Eye CXL	2009-11-19	Week 1 Follow-Up	IOP measurement not done	OS CXL

03246	Primary Eye CXL	2009-11-19	Screening	Other (Specify)	Subject did not sign HIPAA release section of ICF
03246	Primary Eye CXL	2009-12-22	Month 1 Follow-Up	IOP measurement not done	OS CXL
03247	Primary Eye CXL	2009-11-24	Treatment	Other (Specify)	Treatment Deviation OS Artificial tears used to increase Pachymetry
03247	Primary Eye CXL	2009-12-01	Week 1 Follow-Up	IOP measurement not done	1 Wk OS Deviation IOP not obtained
03247	Primary Eye CXL	2009-12-30	Month 1 Follow-Up	IOP measurement not done	1 Mo OS Deviation IOP not obtained
03247	Primary Eye CXL	2010-03-02	Month 3 Follow-Up	IOP measurement not done	3 Mo OS Deviation IOP not obtained
03248	Primary Eye Sham	2009-11-05	Screening	Endothelial cell count not done	IOP not performed on OS
03248	Primary Eye Sham	2009-12-10	Treatment	Other (Specify)	Treatment Day was > 30 days after Screening day. Screening occurred on 11/05/09. TX Visit occurred on 12/10/09.
03248	Primary Eye Sham	2010-01-14	Month 1 Follow-Up	IOP measurement not done	IOP not performed on the Sham OD
03249	Primary Eye Sham	2009-12-09	Screening	IOP measurement not done	Screen OD Deviation IOP not obtained
03249	Primary Eye Sham	2009-12-31	Week 1 Follow-Up	IOP measurement not done	1 Wk OD Deviation IOP not obtained
03249	Primary Eye Sham	2009-12-31	Week 1 Follow-Up	Other (Specify)	1 Wk. OD scheduled visit out of window by one day.
03249	Primary Eye Sham	2010-01-27	Month 1 Follow-Up	IOP measurement not done	1 Mo OD Deviation IOP not obtained
03249	Primary Eye Sham	2010-03-16	Month 3 Follow-Up	Other (Specify)	3 Mo OD Deviation visit was not done.

Appendix B – Protocol Deviations in Study UVX-002

Subject	Treatment	Violation /Deviation Date	Associated Visit/Event	Violation/Deviation Reason	Violation/Deviation Reason/Details
00201	Primary Eye CXL	2007-12-27	Screening	Endothelial cell count not Done	Protocol specified procedure not done for OD or OS
00201	Primary Eye CXL	2008-05-14	Month 3 Follow-Up	Other (Specify)	Visit out of range - 32 days late
00201	Primary Eye CXL	2009-03-04	Month 12 Follow-Up	Other (Specify)	Visit out of range - 4 days late
00202	Fellow Eye CXL	2008-10-03	Month 6 Follow-Up	Manual keratometry not Done	Manual keratometry, steep, not done during the month 6 visit for the study eye (right).
00202	Fellow Eye CXL	2008-10-03	Month 6 Follow-Up	Other (Specify)	Visit was approximately 10 weeks past the protocol specified study window for the study eye.
00202	Fellow Eye CXL	2008-12-31	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 follow up for fellow eye (left).
00202	Fellow Eye CXL	2009-03-05	Month 12 Follow-Up	IOP measurement not done	IOP not done for the study eye during the month 12 visit (right).
00202	Fellow Eye CXL	2009-03-05	Month 6 Follow-Up	IOP measurement not done	IOP not done during the month 6 visit for the fellow eye (left).
00203	Primary Eye CXL	2008-03-14	Week 1 Follow-Up	IOP measurement not done	OS, study eye
00203	Primary Eye CXL	2008-05-21	Month 3 Follow-Up	Endothelial cell count not Done	Study eye (OS)
00203	Fellow Eye CXL	2008-08-22	Treatment	Other (Specify)	Subject had beverage (orange juice) containing vitamin C on the morning of study treatment.
00203	Fellow Eye CXL	2008-08-27	Week 1 Follow-Up	IOP measurement not done	OD, fellow eye
00203	Fellow Eye CXL	2008-11-18	Month 3 Follow-Up	IOP measurement not done	OD, fellow eye
00203	Fellow Eye CXL	2009-01-13	Month 6 Follow-Up	IOP measurement not done	OD, fellow eye
00203	Fellow Eye CXL	2009-01-13	Month 12 Follow-Up	IOP measurement not done	OS, treatment eye
00204	Primary Eye CXL	2008-03-12	Treatment	Other (Specify)	Keratoconus Severity Rating chosen "Severe" in error. Patient K flat was 54.5 - moderate.
00204	Primary Eye CXL	2008-03-12	Eligibility	Other (Specify)	Patient did not have Contact Lens Stability done
00205	Primary Eye CXL	2008-03-12	Screening	Other (Specify)	Subject did not meet requirement for contact lens stability OS CXL. The difference in MRSE between screening visit on 08Feb2008 and 12Mar2008 was 1.0 D.
00205	Primary Eye CXL	2008-03-12	Treatment	Other (Specify)	Randomization assignment incorrect for OS treatment. The keratoconus severity was incorrectly noted as severe (should have been mild); therefore the subject was incorrectly randomized.
00205	Primary Eye CXL	2008-03-12	Treatment	Slit lamp exam not done	Protocol required procedure not done.
00205	Primary Eye CXL	2008-06-19	Month 3 Follow-Up	Other (Specify)	Visit out of range - 1 day late
00205	Primary Eye CXL	2008-10-09	Month 6 Follow-Up	Other (Specify)	Missed visit window - 15 days late
00205	Fellow Eye CXL	2008-11-14	Treatment	Other (Specify)	Refresh Plus Artificial Tears was used to increase OD Fellow CXL pachymetry instead of protocol specified Hypotonic Saline.
00205	Fellow Eye CXL	2008-11-15	Day 1 Follow-Up	Other (Specify)	Missed visit (Fellow eye OD)
00205	Fellow Eye CXL	2008-11-19	Week 1 Follow-Up	IOP measurement not done	Fellow eye OD
00205	Fellow Eye CXL	2009-02-06	Month 3 Follow-Up	IOP measurement not done	Fellow eye OD
00205	Fellow Eye CXL	2009-05-14	Month 6 Follow-Up	IOP measurement not done	OD, fellow eye.
00205	Fellow Eye CXL	2009-05-14	Month 12 Follow-Up	IOP measurement not done	OS CXL eye
00205	Fellow Eye CXL	2009-05-14	Month 12 Follow-Up	Other (Specify)	Visit out of range - 8 days late
00205	Fellow Eye CXL	2010-03-17	Month 12 Follow-Up	IOP measurement not done	OD Fellow
00205	Fellow Eye CXL	2010-03-17	Month 12 Follow-Up	Other (Specify)	Study visit was approximately 10 weeks past the protocol specified window.
00206	Primary Eye CXL	2008-02-19	Eligibility	Other (Specify)	I-S ratio for OD not done (site unable to calculate).
00206	Primary Eye CXL	2008-03-21	Treatment	Other (Specify)	Keratoconus Severity Scale checked "Severe" but it should have been "moderate" - 51.8

00206	Primary Eye CXL	2008-03-21	Treatment	Other (Specify)	Contact Lens Stability Check was not done on Tx Day. A stability check was later done and the topography avg Sim K Difference was >0.75 (2). Patient should not have been enrolled.
00206	Primary Eye CXL	2008-03-21	Treatment	Did not meet inclusion/exclusion criteria	Subject did not meet inclusion criteria b/c the right eye progression was not shown only for left eye but right eye was the randomized eye.
00206	Primary Eye CXL	2008-03-27	Week 1 Follow-Up	IOP measurement not done	measurement not done
00206	Primary Eye CXL	2008-10-07	Month 6 Follow-Up	Other (Specify)	Visit was 4 days past protocol specified window.
00206	Fellow Eye CXL	2008-11-25	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS).
00207	Sham Eye CXL	2008-07-09	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry OD cross over eye instead of protocol specified hypotonic saline.
00207	Sham Eye CXL	2008-07-18	Week 1 Follow-Up	IOP measurement not done	OD Cross-over eye
00207	Sham Eye CXL	2008-07-31	Month 1 Follow-Up	IOP measurement not done	OD Cross-over
00207	Sham Eye CXL	2008-12-04	Month 6 Follow-Up	IOP measurement not done	OD Cross-over
00207	Fellow Eye CXL	2009-01-15	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry in the OS Fellow Eye instead of protocol specified Hypotonic Saline
00207	Fellow Eye CXL	2009-01-21	Week 1 Follow-Up	IOP measurement not done	OS Fellow CXL
00207	Fellow Eye CXL	2009-01-21	Week 1 Follow-Up	IOP measurement not done	Protocol specified procedure not done (fellow eye).
00207	Fellow Eye CXL	2009-07-29	Month 6 Follow-Up	IOP measurement not done	OS Fellow CXL
00208	Primary Eye CXL	2008-08-27	Month 3 Follow-Up	Endothelial cell count not done	Protocol required procedure not done.
00209	Primary Eye Sham	2008-05-28	Treatment	Other (Specify)	Keratoconus severity was chosen in error as study coordinator used K2 vs. K1 and subsequently chose "moderate". It should have been mild. The moderate card was chosen when mild should have been.
00209	Sham Eye CXL	2008-08-12	Week 1 Follow-Up	IOP measurement not done	Study eye (OD)
00209	Fellow Eye CXL	2009-02-13	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS)
00209	Fellow Eye CXL	2009-08-06	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OD)
00210	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	Visit not conducted within 30 days of screening.
00210	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	Site used Artificial Tears instead of protocol specified Hypotonic Saline to increase Pachymetry
00210	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	OS elig ble, OD not at screening. OS was treatment eye. At treatment OS was stable w/better VA. OD checked for eligibility and found elig ble. OD was treated instead of OS as first randomized.
00210	Primary Eye CXL	2008-09-26	Month 3 Follow-Up	Other (Specify)	Visit out of range - 1 day late
00210	Primary Eye CXL	2009-01-02	Month 6 Follow-Up	IOP measurement not done	Study eye (OD)
00210	Primary Eye CXL	2009-01-02	Month 6 Follow-Up	Other (Specify)	Visit conducted one day past protocol specified window.
00210	Fellow Eye CXL	2009-07-14	Treatment	Other (Specify)	Artificial Tears was used to increase pachymetry instead of protocol specified Hypotonic Saline.
00210	Fellow Eye CXL	2009-07-14	Treatment	Other (Specify)	OS Fellow eye not treated within protocol specified window of > or equal to 3 months and < or equal to 6 months (9/26/08-1/2/09) of first eye being treated
00210	Fellow Eye CXL	2009-08-13	Month 1 Follow-Up	IOP measurement not done	OS (Fellow eye)
00210	Fellow Eye CXL	2009-08-13	Month 12 Follow-Up	IOP measurement not done	OD (study eye)
00210	Fellow Eye CXL	2010-02-12	Month 6 Follow-Up	Other (Specify)	Study visit (for OS) conducted 16 days past window.
00210	Fellow Eye CXL	2010-02-12	Month 6 Follow-Up	IOP measurement not done	for fellow eye (OS)
00210	Fellow Eye CXL	2010-05-27	Month 12 Follow-Up	Endothelial cell count not done	fellow eye (OS)

00211	Primary Eye Sham	2008-06-05	Screening	Other (Specify)	Pt. did not qualify for study at Visit 2 (Avg. Sim K = .8). Orbscan from Visit 1 & 3 were used to qualify the patient.
00211	Primary Eye Sham	2008-08-07	Month 1 Follow-Up	Other (Specify)	Patient did not show up for this visit due to an SAE that occurred around the time of the visit.
00211	Sham Eye CXL	2008-10-21	Treatment	Pentacam pachymetry, keratometry not done	Pentacam thinnest point not done due to patient complications
00211	Sham Eye CXL	2008-10-28	Week 1 Follow-Up	IOP measurement not done	CRX-OVR OD
00211	Sham Eye CXL	2008-11-18	Month 1 Follow-Up	Other (Specify)	Visit not done. Patient was a no show.
00211	Sham Eye CXL	2009-02-10	Month 3 Follow-Up	IOP measurement not done	CRX-OVR OD
00211	Sham Eye CXL	2009-02-10	Month 3 Follow-Up	Other (Specify)	Visit out of window.
00211	Sham Eye CXL	2009-04-29	Month 6 Follow-Up	IOP measurement not done	CRX-OVR OD
00211	Sham Eye CXL	2010-02-03	Month 12 Follow-Up	Other (Specify)	Visit completed out of window.
00212	Primary Eye Sham	2008-07-18	Treatment	Ultrasound pachymetry not done	OD Sham, Pretreatment pachymetry not recorded.
00212	Sham Eye CXL	2008-09-26	Treatment	Other (Specify)	Refresh Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic Saline (OD X-over)
00212	Sham Eye CXL	2008-10-01	Week 1 Follow-Up	IOP measurement not done	Crossover, OD
00212	Sham Eye CXL	2008-12-09	Month 3 Follow-Up	IOP measurement not done	Crossover, OD
00212	Fellow Eye CXL	2009-01-23	Treatment	Other (Specify)	Refresh Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic Saline (OS Fellow CXL)
00212	Fellow Eye CXL	2009-01-27	Week 1 Follow-Up	IOP measurement not done	OS, fellow eye
00212	Fellow Eye CXL	2009-01-27	Week 1 Follow-Up	Other (Specify)	Visit out of range - I day early (OS Fellow CXL)
00212	Fellow Eye CXL	2009-02-27	Month 1 Follow-Up	IOP measurement not done	OS, fellow eye
00212	Fellow Eye CXL	2009-07-18	Treatment	Other (Specify)	Visit was conducted 35 days after screening, 5 days outside the visit window
00213	Primary Eye Sham	2008-07-01	Screening	Did not meet inclusion/exclusion criteria	Site was unable to obtain I-S ratio at screening for the study eye (left eye) and could therefore not confirm that it was greater than or equal to 1.5 on the Pentacam or Orbscan map.
00213	Sham Eye CXL	2008-10-09	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS).
00213	Sham Eye CXL	2008-10-15	Week 1 Follow-Up	IOP measurement not done	IOP was not done at the week 1 visit for the crossover eye (left eye)
00213	Fellow Eye CXL	2008-12-19	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the study/crossover eye (left eye).
00213	Fellow Eye CXL	2008-12-23	Week 1 Follow-Up	Other (Specify)	The week 1 visit for the fellow eye (right eye) was 1 day out of window (early).
00213	Fellow Eye CXL	2008-12-23	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-01-23	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-03-25	Month 6 Follow-Up	IOP measurement not done	IOP was not done at the Month 6 visit for the study/crossover eye (left eye)
00213	Fellow Eye CXL	2009-03-25	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-05-13	Month 12 Follow-Up	Other (Specify)	OS study visit (cross-over) conducted 19 weeks out of window (early).
00213	Fellow Eye CXL	2009-05-14	Month 12 Follow-Up	IOP measurement not done	IOP not done at the Month 12 visit for the crossover eye (left eye).
00213	Fellow Eye CXL	2009-05-14	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the fellow eye (right eye).
00213	Fellow Eye CXL	2009-12-15	Month 12 Follow-Up	Endothelial cell count not done	OD Fellow
00213	Fellow Eye CXL	2009-12-15	Month 12 Follow-Up	Endothelial cell count not done	Fellow eye (OD)
00214	Primary Eye CXL	2008-06-19	Screening	IOP measurement not done	OD CXL and OS Fellow
00214	Primary Eye CXL	2008-08-07	Treatment	Other (Specify)	Treatment for primary eye done greater than 30 days after screening visit.
00214	Primary Eye CXL	2008-08-12	Week 1 Follow-Up	IOP measurement not done	OD CXL
00214	Fellow Eye CXL	2008-11-12	Week 1 Follow-Up	IOP measurement not done	(OS) Fellow eye

00214	Fellow Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	(OS) Fellow eye
00214	Fellow Eye CXL	2009-01-08	Month 3 Follow-Up	Other (Specify)	Study visit out of range for fellow eye 6 days early
00214	Fellow Eye CXL	2009-01-08	Month 3 Follow-Up	IOP measurement not done	Fellow eye (OS)
00214	Fellow Eye CXL	2009-01-08	Month 3 Follow-Up	Endothelial cell count not done	Fellow eye (OS)
00214	Fellow Eye CXL	2009-01-08	Month 6 Follow-Up	IOP measurement not done	Study eye (OD)
00214	Fellow Eye CXL	2009-04-01	Month 6 Follow-Up	IOP measurement not done	Fellow eye (OS)
00215	Primary Eye Sham	2008-07-10	Screening	Other (Specify)	Subject discontinued RGP lens wear 12 days prior to the pre-treatment exam/first refraction (protocol requires 2 weeks).
00215	Primary Eye Sham	2008-07-10	Screening	Did not meet inclusion/exclusion criteria	Subject wore CL within 2 weeks of screening and CL stability not checked prior to Treatment
00215	Primary Eye Sham	2008-08-08	Screening	Other (Specify)	Subject was treated although contact lens stability recheck indicated that the eye was not stable. OD Sham
00215	Primary Eye Sham	2008-08-08	Treatment	Slit lamp exam not done	Slit Lamp exam was not done following the sham treatment for the study eye (right eye)
00215	Primary Eye Sham	2008-09-18	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry was not done at the Month 1 visit for the sham eye (right eye) due to distortion.
00215	Sham Eye CXL	2008-10-24	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline - OD X-over.
00215	Sham Eye CXL	2008-10-28	Week 1 Follow-Up	IOP measurement not done	IOP was not taken during the week 1 visit for the crossover eye (right eye)
00215	Sham Eye CXL	2008-10-28	Week 1 Follow-Up	Other (Specify)	The week 1 visit for the crossover eye (right eye) was 1 day out of window (early)
00215	Sham Eye CXL	2009-01-23	Month 3 Follow-Up	IOP measurement not done	IOP was not done during the Month 3 visit for the crossover eye (right eye).
00215	Sham Eye CXL	2009-04-30	Month 6 Follow-Up	IOP measurement not done	(Crossover)
00215	Sham Eye CXL	2010-01-15	Month 12 Follow-Up	Endothelial cell count not done	Protocol required procedure not done.
00215	Sham Eye CXL	2010-01-15	Month 12 Follow-Up	Other (Specify)	Visit out of range - 27 days late
00216	Primary Eye CXL	2008-08-28	Week 1 Follow-Up	IOP measurement not done	OD, study eye
00216	Primary Eye CXL	2008-09-17	Month 1 Follow-Up	IOP measurement not done	OD, study eye
00216	Fellow Eye CXL	2009-01-07	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS)
00216	Fellow Eye CXL	2009-01-13	Week 1 Follow-Up	IOP measurement not done	Fellow eye, OS
00216	Fellow Eye CXL	2009-02-13	Month 1 Follow-Up	IOP measurement not done	OS, fellow eye
00216	Fellow Eye CXL	2009-02-13	Month 6 Follow-Up	IOP measurement not done	study eye, OD
00216	Fellow Eye CXL	2010-02-25	Month 12 Follow-Up	Endothelial cell count not done	OS, fellow eye
00217	Primary Eye Sham	2008-08-21	Treatment	Other (Specify)	Treatment did not occur within 30 days of screening
00217	Primary Eye Sham	2008-08-28	Week 1 Follow-Up	IOP measurement not done	OD, Sham
00217	Sham Eye CXL	2008-11-25	Week 1 Follow-Up	IOP measurement not done	OD, Crossover
00217	Sham Eye CXL	2009-02-03	Month 3 Follow-Up	IOP measurement not done	OD, crossover
00217	Sham Eye CXL	2009-05-26	Month 6 Follow-Up	IOP measurement not done	OD, crossover
00217	Fellow Eye CXL	2009-08-05	Treatment	Other (Specify)	OS Fellow eye treated more than 6 months after randomized eye by approximately 5 months
00217	Fellow Eye CXL	2009-08-12	Week 1 Follow-Up	IOP measurement not done	OS, fellow eye
00217	Fellow Eye CXL	2010-02-10	Month 6 Follow-Up	IOP measurement not done	OS, fellow eye
00218	Primary Eye CXL	2008-09-04	Treatment	Other (Specify)	Subject ate tomato, potential vitamin C source morning of treatment.
00218	Primary Eye CXL	2008-09-04	Treatment	Other (Specify)	Treatment occurred more than 30 days after screening.
00218	Fellow Eye CXL	2008-11-20	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline.
00218	Fellow Eye CXL	2008-11-25	Week 1 Follow-Up	IOP measurement not done	Fellow eye, OS

00218	Fellow Eye CXL	2008-12-18	Month 1 Follow-Up	IOP measurement not done	OS, fellow eye
00218	Fellow Eye CXL	2009-02-11	Month 3 Follow-Up	IOP measurement not done	Fellow eye, OS
00218	Fellow Eye CXL	2009-02-11	Month 6 Follow-Up	IOP measurement not done	OD, study eye
00218	Fellow Eye CXL	2009-06-03	Month 6 Follow-Up	IOP measurement not done	OS, fellow eye
00218	Fellow Eye CXL	2009-06-03	Month 6 Follow-Up	IOP measurement not done	OS, fellow eye
00219	Primary Eye CXL	2008-09-04	Screening	Other (Specify)	Did not check topography during the contact lens stability check. Can't verify eye was stable. OD CXL
00219	Primary Eye CXL	2008-09-04	Screening	Dilated fundus exam not done	OD and OS
00219	Primary Eye CXL	2008-10-02	Treatment	Other (Specify)	Site used Refresh Plus to increase pachymetry instead of protocol specified Hypotonic Saline. OD CXL
00219	Primary Eye CXL	2008-10-10	Week 1 Follow-Up	IOP measurement not done	OD CXL
00219	Primary Eye CXL	2008-11-06	Month 1 Follow-Up	IOP measurement not done	OD CXL
00219	Primary Eye CXL	2009-01-08	Month 3 Follow-Up	Endothelial cell count not done	Technical problems with confocal microscope: deferred to 6 month visit; OD CXL
00219	Primary Eye CXL	2009-01-08	Month 3 Follow-Up	IOP measurement not done	OD CXL
00219	Primary Eye CXL	2009-04-16	Month 6 Follow-Up	IOP measurement not done	Study eye (OD)
00220	Primary Eye Sham	2008-10-29	Week 1 Follow-Up	IOP measurement not done	OD, Sham
00220	Primary Eye Sham	2008-11-19	Month 1 Follow-Up	IOP measurement not done	OD Sham
00220	Primary Eye Sham	2009-01-14	Month 3 Follow-Up	IOP measurement not done	OD Sham
00220	Sham Eye CXL	2009-05-05	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline, OD X-over
00220	Sham Eye CXL	2009-05-13	Week 1 Follow-Up	IOP measurement not done	OD, Crossover
00220	Sham Eye CXL	2009-06-04	Month 1 Follow-Up	IOP measurement not done	OD Crossover
00221	Primary Eye Sham	2008-10-28	Treatment	Other (Specify)	Treatment occurred greater than 30 days after screening visit.
00221	Primary Eye Sham	2008-11-05	Week 1 Follow-Up	IOP measurement not done	IOP not done during the week 1 visit for the sham eye (OS).
00221	Primary Eye Sham	2008-12-04	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 1 for the sham eye (OS - too distorted).
00221	Primary Eye Sham	2008-12-04	Month 1 Follow-Up	IOP measurement not done	IOP not done at Month 1 for the sham eye (OS).
00221	Primary Eye Sham	2009-01-20	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 3 for the sham eye (OS too distorted).
00221	Primary Eye Sham	2009-01-20	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the sham eye (OS)
00221	Sham Eye CXL	2009-04-17	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the sham eye (OS).
00221	Sham Eye CXL	2009-04-17	Month 6 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 6 for the sham eye (OS too distorted).
00221	Sham Eye CXL	2009-04-21	Week 1 Follow-Up	IOP measurement not done	IOP was not done at the Week 1 visit for the crossover eye (OS)
00221	Sham Eye CXL	2009-04-21	Week 1 Follow-Up	Other (Specify)	Week 1 visit for the crossover eye (OS) was 1 day out of window (early).
00221	Sham Eye CXL	2009-05-28	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 1 for the crossover eye (OS too distorted).
00221	Sham Eye CXL	2009-05-28	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the crossover eye (OS).
00221	Sham Eye CXL	2009-07-22	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 3 for the crossover eye (OS too distorted).
00221	Sham Eye CXL	2009-07-22	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the crossover eye (OS).
00221	Sham Eye CXL	2009-10-20	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the crossover eye (OS).
00221	Fellow Eye CXL	2009-12-17	Treatment	Other (Specify)	The fellow eye (OD) was not treated within 6 months following treatment of the study eye.
00221	Fellow Eye CXL	2009-12-17	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic r boflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the fellow eye (OD).
00221	Fellow Eye CXL	2009-12-22	Week 1 Follow-Up	Manifest refraction not done	Manifest refraction not done at the week 1 visit for the fellow eye (OD).

00221	Fellow Eye CXL	2009-12-22	Week 1 Follow-Up	IOP measurement not done	IOP not done at the week 1 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2009-12-22	Week 1 Follow-Up	BSCVA not done	BSCVA not done at the week 1 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2010-01-26	Month 1 Follow-Up	Other (Specify)	Month 1 follow-up visit for fellow eye OD CXL was not done. Subject did not show for visit scheduled for 26Jan2010.
00221	Fellow Eye CXL	2010-03-10	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the fellow eye (OD).
00221	Fellow Eye CXL	2010-06-15	Month 12 Follow-Up	Manual keratometry not done	Manual Keratometry not done at Month 12 for the crossover eye (OS too distorted).
00222	Primary Eye CXL	2008-11-04	Screening	Endothelial cell count not done	Cell count not done for primary study eye (OD).
00222	Primary Eye CXL	2008-11-05	Treatment	Other (Specify)	PI used artificial tears as opposed to the protocol required hypotonic 0.1% R boflavin to increase pachymetry. OD Treatment Eye
00222	Primary Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	Protocol required procedure not done.
00222	Fellow Eye CXL	2009-02-13	Treatment	Other (Specify)	PI used artificial tears as opposed to the protocol required hypotonic 0.1% R boflavin to increase pachymetry. OS Fellow Eye
00222	Fellow Eye CXL	2009-02-13	Treatment	Slit lamp exam not done	OS Fellow
00222	Fellow Eye CXL	2009-02-13	Month 3 Follow-Up	IOP measurement not done	Study eye
00222	Fellow Eye CXL	2009-03-12	Month 1 Follow-Up	IOP measurement not done	Fellow eye
00222	Fellow Eye CXL	2009-08-13	Month 6 Follow-Up	IOP measurement not done	Fellow eye
00223	Primary Eye Sham	2008-12-11	Week 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover and at Month 12
00223	Primary Eye Sham	2009-01-08	Month 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at crossover and at Month 12
00223	Primary Eye Sham	2009-03-10	Month 3 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at crossover and at Month 12
00223	Sham Eye CXL	2009-05-12	Week 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at crossover and at Month 12
00223	Sham Eye CXL	2009-06-04	Month 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12
00223	Fellow Eye CXL	2009-08-06	Month 3 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Fellow Eye CXL	2009-08-13	Week 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00223	Fellow Eye CXL	2009-09-02	Month 1 Follow-Up	IOP measurement not done	PI was not aware that IOP's were a "requirement" at Screen, Week 1, Month 1, Month 3, Month 6, and Month 12. Consequently, they were generally done at Screen, at Crossover, and at Month 12.
00224	Primary Eye Sham	2008-12-10	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the sham eye (OS).
00224	Primary Eye Sham	2009-01-06	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the sham eye (OS).
00224	Sham Eye CXL	2009-03-05	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye (OS).
00224	Sham Eye CXL	2009-03-05	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the sham eye (OS).
00224	Sham Eye CXL	2009-03-10	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the crossover eye (OS).
00224	Sham Eye CXL	2009-04-15	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the crossover eye (OS).
00224	Sham Eye CXL	2009-05-26	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the crossover eye (OS).
00224	Sham Eye CXL	2009-07-29	Month 6 Follow-Up	IOP measurement not done	IOP not done at the Month 6 visit for the crossover eye (OS).
00225	Primary Eye CXL	2008-12-18	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic r boflavin artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the study eye (OD).

00225	Primary Eye CXL	2008-12-23	Week 1 Follow-Up	IOP measurement not done	IOP not done at the Week 1 visit for the study eye (OD).
00225	Primary Eye CXL	2009-01-21	Month 1 Follow-Up	IOP measurement not done	IOP not done at the Month 1 visit for the study eye (OD).
00225	Primary Eye CXL	2009-03-25	Month 3 Follow-Up	IOP measurement not done	IOP not done at the Month 3 visit for the study eye (OD).
00225	Fellow Eye CXL	2009-07-01	Week 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 for Fellow Eye (OS)
00225	Fellow Eye CXL	2009-07-30	Month 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 for Fellow Eye (OS)
00226	Primary Eye Sham	2009-01-14	Week 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00226	Primary Eye Sham	2009-02-11	Month 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00226	Primary Eye Sham	2009-04-14	Month 3 Follow-Up	IOP measurement not done	OD Sham - IOP measurement not done.
00226	Sham Eye CXL	2009-06-03	Treatment	IOP measurement not done	OD Treatment eye - IOP not done.
00226	Sham Eye CXL	2009-06-03	Treatment	Other (Specify)	OD Treatment eye - The site used Refresh Tears instead of Hypotonic R boflavin to achieve a Pachymetry reading >/= 400 microns prior to treatment.
00226	Sham Eye CXL	2009-06-10	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2009-07-14	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2009-08-26	Month 3 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2009-12-16	Month 6 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00226	Sham Eye CXL	2010-04-10	Month 12 Follow-Up	Endothelial cell count not done	OD Treatment eye - Endothelial cell count not done.
00227	Primary Eye CXL	2009-01-23	Treatment	Other (Specify)	Site used Refresh Artificial Tears instead of hypotonic riboflavin to achieve >/= 400 microns pachymetry reading.
00227	Primary Eye CXL	2009-01-28	Week 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00227	Primary Eye CXL	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00227	Primary Eye CXL	2009-04-17	Month 3 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00228	Primary Eye CXL	2008-12-02	Screening	IOP measurement not done	OD IOP measurement not done.
00228	Primary Eye CXL	2008-12-02	Screening	Endothelial cell count not done	OD Endothelial cell count not done (attempted).
00228	Primary Eye CXL	2008-12-02	Screening	IOP measurement not done	OS IOP measurement not done.
00228	Primary Eye CXL	2009-01-30	Treatment	Other (Specify)	Site used Refresh Artificial Tears instead of Hypotonic Riboflavin to achieve >/= 400 micron Pachymetry prior to treatment.
00228	Primary Eye CXL	2009-02-04	Week 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00228	Primary Eye CXL	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00228	Primary Eye CXL	2009-04-17	Month 3 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-02-06	Treatment	Other (Specify)	The Site used Refresh Artificial Tears instead of Hypotonic Riboflavin to achieve >/= 400 micron Pachymetry reading prior to treatment. OD
00229	Primary Eye CXL	2009-02-07	Day 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-02-10	Week 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-02-10	Week 1 Follow-Up	Other (Specify)	Week 1 visit was out of window by 1 day early.
00229	Primary Eye CXL	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00229	Primary Eye CXL	2009-04-21	Month 3 Follow-Up	IOP measurement not done	OD IOP measurement not done.
00230	Primary Eye Sham	2009-03-04	Week 1 Follow-Up	Other (Specify)	Patient did not show up for Visit
00230	Primary Eye Sham	2009-04-02	Month 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Sham Eye CXL	2009-06-05	Month 3 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Sham Eye CXL	2009-06-05	Month 3 Follow-Up	Manual keratometry not done	Manual keratometry was done but can not be measure greater than 52 diopters. Therefore reported Not Done.

00230	Sham Eye CXL	2009-06-05	Treatment	Other (Specify)	Following debridement and pretreatment with isotonic r boflavin artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye per note to file.
00230	Sham Eye CXL	2009-06-09	Week 1 Follow-Up	Other (Specify)	Patient outside window (window = 6/10 to 6/19
00230	Sham Eye CXL	2009-06-09	Week 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements.
00230	Sham Eye CXL	2009-07-21	Week 1 Follow-Up	Other (Specify)	Patient outside window ... 6/26 to 7/17
00230	Sham Eye CXL	2009-07-21	Month 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements.
00230	Fellow Eye CXL	2009-08-28	Month 3 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Fellow Eye CXL	2009-09-01	Week 1 Follow-Up	Other (Specify)	Week 1 Visit Outside Window which was 9/2 to 9/11
00230	Fellow Eye CXL	2009-09-01	Week 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00230	Fellow Eye CXL	2009-10-14	Month 1 Follow-Up	Other (Specify)	Patient outside visit window of 9/18 to 19/9
00230	Fellow Eye CXL	2009-10-14	Month 1 Follow-Up	IOP measurement not done	PI not aware of Protocol requirements
00230	Fellow Eye CXL	2010-02-05	Month 6 Follow-Up	IOP measurement not done	PI not aware of protocol requirements.
00231	Primary Eye Sham	2009-03-31	Week 1 Follow-Up	IOP measurement not done	OS Sham eye - IOP measurement not done.
00231	Primary Eye Sham	2009-06-23	Month 3 Follow-Up	IOP measurement not done	OS Sham eye - IOP measurement not done.
00231	Sham Eye CXL	2009-08-20	Treatment	Other (Specify)	The Site used Refresh Artificial Tears instead of Hypotonic Riboflavin to achieve a Pachymetry reading >/= 400 microns prior to treatment.
00231	Sham Eye CXL	2009-08-26	Week 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00231	Sham Eye CXL	2009-09-24	Month 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00231	Sham Eye CXL	2009-11-18	Month 3 Follow-Up	Other (Specify)	Month 3 OS Treatment Eye was not done. Patient was a no show on 11/18/09. The site called and rescheduled on 11/24/09 and on 12/15/09. The subject was a no show both times
00232	Primary Eye Sham	2009-04-01	Week 1 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00232	Primary Eye Sham	2009-04-28	Month 1 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00232	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	IOP measurement not done	Randomized sham control eye
00232	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	Other (Specify)	OS Sham - M3 out of window by 15 days.
00232	Sham Eye CXL	2009-09-24	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Artificial Tears instead of Hypotonic Riboflavin to try and achieve >/= 400 micron Pachymetry reading.
00232	Sham Eye CXL	2009-09-30	Week 1 Follow-Up	IOP measurement not done	Crossover eye
00232	Sham Eye CXL	2009-10-20	Month 1 Follow-Up	IOP measurement not done	Crossover eye
00233	Primary Eye Sham	2009-04-05	Treatment	Did not meet inclusion/exclusion criteria	OD Sham eye - subject drank Orange Juice on treatment day.
00233	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00233	Primary Eye Sham	2009-05-19	Month 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00233	Primary Eye Sham	2009-07-14	Month 3 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00233	Sham Eye CXL	2009-09-02	Month 6 Follow-Up	IOP measurement not done	IOP Sham eye - IOP measurement not done. OD
00233	Sham Eye CXL	2009-09-02	Treatment	Other (Specify)	OD Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading.
00233	Sham Eye CXL	2009-09-09	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00233	Sham Eye CXL	2009-10-07	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00234	Primary Eye Sham	2009-02-10	Screening	Did not meet inclusion/exclusion criteria	I-S Ratio = .346 on Screen visit
00234	Primary Eye Sham	2009-04-22	Week 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Primary Eye Sham	2009-05-21	Month 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements

00234	Sham Eye CXL	2009-09-03	Month 6 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Sham Eye CXL	2009-09-03	Week 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00234	Sham Eye CXL	2009-10-13	Month 1 Follow-Up	IOP measurement not done	Misunderstanding by PI of Protocol Requirements
00235	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	IOP measurement not done	Change in CRC caused miscommunication of required procedures
00235	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	Other (Specify)	Visit out of range - 1 day early
00235	Primary Eye Sham	2009-05-19	Month 1 Follow-Up	IOP measurement not done	OS Sham - Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-09-03	Month 6 Follow-Up	Other (Specify)	Visit out of range - 1 day early (OS Sham)
00235	Sham Eye CXL	2009-09-03	Month 6 Follow-Up	IOP measurement not done	OS Sham - Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-09-08	Week 1 Follow-Up	IOP measurement not done	OS X-over - Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-10-13	Month 1 Follow-Up	IOP measurement not done	OS X-over- Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-12-18	Month 3 Follow-Up	IOP measurement not done	OS X-over- Change in CRC resulted in miscommunication of required visit procedures
00235	Sham Eye CXL	2009-12-18	Month 3 Follow-Up	Other (Specify)	3M visit out of range - 8 days late
00236	Primary Eye Sham	2009-01-12	Month 3 Follow-Up	IOP measurement not done	PI was not aware of the requirements of the protocol.
00236	Primary Eye Sham	2009-03-30	Month 6 Follow-Up	IOP measurement not done	PI was not aware of the requirements of the protocol.
00236	Sham Eye CXL	2009-10-29	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the crossover eye (OD).
00236	Sham Eye CXL	2009-10-29	Month 6 Follow-Up	IOP measurement not done	PI was not aware of requirements of protocol
00236	Sham Eye CXL	2009-11-05	Week 1 Follow-Up	IOP measurement not done	PI was not aware of protocol requirements
00236	Sham Eye CXL	2009-12-09	Month 1 Follow-Up	IOP measurement not done	PI was not aware of the requirements of the protocol
00237	Primary Eye CXL	2009-06-30	Treatment	Other (Specify)	OD Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading on treatment day.
00237	Primary Eye CXL	2009-07-08	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00237	Primary Eye CXL	2009-07-29	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00237	Primary Eye CXL	2009-12-17	Month 6 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00238	Primary Eye Sham	2009-07-16	Week 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Primary Eye Sham	2009-08-13	Month 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2009-12-17	Month 6 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2009-12-22	Week 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2010-01-12	Month 1 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00238	Sham Eye CXL	2010-03-09	Month 3 Follow-Up	IOP measurement not done	Change in CRC resulted in miscommunication of required visit procedures
00239	Primary Eye Sham	2009-07-22	Week 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Primary Eye Sham	2009-08-26	Month 1 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Primary Eye Sham	2009-10-01	Month 3 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Sham Eye CXL	2009-12-09	Month 6 Follow-Up	IOP measurement not done	OD Sham eye - IOP measurement not done.
00239	Sham Eye CXL	2009-12-09	Treatment	Other (Specify)	OD Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading for treatment.
00239	Sham Eye CXL	2009-12-17	Week 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00239	Sham Eye CXL	2010-01-20	Month 1 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00239	Sham Eye CXL	2010-03-10	Month 3 Follow-Up	IOP measurement not done	OD Treatment eye - IOP measurement not done.
00239	Sham Eye CXL	2010-05-18	Month 6 Follow-Up	Other (Specify)	OD Treatment eye - Month 6 not done.

00240	Primary Eye Sham	2009-05-15	Screening	IOP measurement not done	OD - IOP measurement not done.
00240	Primary Eye Sham	2009-05-15	Screening	IOP measurement not done	OS - IOP measurement not done.
00240	Primary Eye Sham	2009-08-13	Week 1 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00240	Primary Eye Sham	2009-09-18	Month 1 Follow-Up	Other (Specify)	OS Sham - visit out of window, 1 day late.
00240	Primary Eye Sham	2009-11-19	Month 3 Follow-Up	Other (Specify)	OS Sham - visit out of window, 7 days late.
00240	Primary Eye Sham	2009-11-19	Month 3 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00240	Sham Eye CXL	2010-01-27	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading.
00240	Sham Eye CXL	2010-01-27	Month 6 Follow-Up	IOP measurement not done	OS Sham - IOP measurement not done.
00240	Sham Eye CXL	2010-02-02	Week 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00240	Sham Eye CXL	2010-03-12	Month 1 Follow-Up	Other (Specify)	OS Treatment - visit out of window, 2 days late.
00240	Sham Eye CXL	2010-03-12	Month 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00240	Sham Eye CXL	2010-07-06	Month 6 Follow-Up	Other (Specify)	OS Treatment eye - M6 not done due to IRB closing study.
00240	Sham Eye CXL	2011-01-27	Month 12 Follow-Up	Other (Specify)	OS Treatment eye - M12 not done due to IRB closing study.
00241	Primary Eye Sham	2009-08-26	Week 1 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Primary Eye Sham	2009-09-30	Month 1 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Primary Eye Sham	2009-11-19	Month 3 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-01-26	Month 6 Follow-Up	IOP measurement not done	OD Sham - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-01-26	Treatment	Other (Specify)	OD X-over - Refresh Plus Artificial Tears used to increase pachymetry instead of protocol specified hypotonic saline.
00241	Sham Eye CXL	2010-02-02	Week 1 Follow-Up	IOP measurement not done	OD X-over - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-03-30	Month 1 Follow-Up	Other (Specify)	OD X-over - Visit out of window - 21 days late.
00241	Sham Eye CXL	2010-03-30	Month 1 Follow-Up	IOP measurement not done	OD X-over - Change in CRC resulted in miscommunication of required visit procedures
00241	Sham Eye CXL	2010-05-04	Month 3 Follow-Up	Other (Specify)	OD X-over Eye - Subject didn't show for 3 month visit. Visit Range was 4/6/2010-5/4/2010.
00242	Primary Eye CXL	2009-08-20	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Tears to increase Pachymetry reading prior to treatment.
00242	Primary Eye CXL	2009-08-26	Week 1 Follow-Up	IOP measurement not done	OS Treatment eye - IOP measurement not done.
00243	Primary Eye CXL	2009-07-08	Screening	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OU
00243	Primary Eye CXL	2009-07-08	Screening	Dilated fundus exam not done	Dilated Fundus exam was not done at this visit for OU
00243	Primary Eye CXL	2009-08-25	Treatment	Other (Specify)	Artificial Tears were used to increase port debridement pachymetry measurement to 400. CXL OS
00243	Primary Eye CXL	2009-09-02	Week 1 Follow-Up	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OS
00243	Primary Eye CXL	2009-10-06	Month 1 Follow-Up	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OS
00243	Primary Eye CXL	2009-11-25	Month 3 Follow-Up	IOP measurement not done	Intra Ocular Pressure was not done at this visit for OS
00244	Primary Eye Sham	2009-09-04	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Primary Eye Sham	2009-10-02	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Primary Eye Sham	2009-12-11	Month 3 Follow-Up	Other (Specify)	Month 3 Visit on 12/11/2009 outside window 11/5 to 12/3
00244	Primary Eye Sham	2009-12-11	Month 3 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Sham Eye CXL	2010-01-14	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic r boflavin for the crossover eye (OS).
00244	Sham Eye CXL	2010-01-21	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all requirements of the protocol.
00244	Sham Eye CXL	2010-03-11	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.

00244	Sham Eye CXL	2010-03-11	Week 1 Follow-Up	Other (Specify)	Month 1 Visit on 3/11/2010 is outside the window 2/4/ to 2/25
00245	Primary Eye CXL	2009-08-11	Screening	Dilated fundus exam not done	Fundus exam for OD and OS was not performed per protocol; no explanation
00245	Primary Eye CXL	2009-09-02	Week 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Primary Eye CXL	2009-10-02	Month 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2009-11-19	Month 3 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2009-11-25	Week 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2009-12-22	Month 1 Follow-Up	IOP measurement not done	Change in CRC; miscommunication of required visit procedures OD Fellow
00245	Fellow Eye CXL	2010-04-20	Month 6 Follow-Up	IOP measurement not done	OD Fellow - Change in CRC; miscommunication of required visit procedures
00245	Fellow Eye CXL	2010-04-20	Month 6 Follow-Up	Other (Specify)	OS Treatment - 6 month visit out of range - 40 days late
00246	Primary Eye CXL	2009-09-02	Screening	Did not obtain proper consent prior to performing study procedure	Subject didn't sign all required pages of ICF, specifically agreement to use and/or share their study related records. Subject did consent to participate in the study by signing his agreement
00246	Primary Eye CXL	2009-09-03	Treatment	Other (Specify)	Site used Refresh Plus Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Saline - OS CXL
00246	Primary Eye CXL	2009-09-10	Week 1 Follow-Up	IOP measurement not done	OS CXL
00246	Primary Eye CXL	2009-10-08	Month 1 Follow-Up	IOP measurement not done	OS CXL
00246	Primary Eye CXL	2009-11-20	Month 3 Follow-Up	Manual keratometry not done	OS CXL
00246	Primary Eye CXL	2010-02-05	Month 6 Follow-Up	IOP measurement not done	OS CXL
00247	Primary Eye CXL	2009-09-01	Screening	Other (Specify)	Patient did not sign the RSVP
00247	Primary Eye CXL	2009-09-23	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00247	Primary Eye CXL	2010-10-14	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00248	Primary Eye CXL	2009-09-17	Screening	Dilated fundus exam not done	OU
00248	Primary Eye CXL	2009-09-23	Treatment	Other (Specify)	Hypotonic R boflavin was not administered for Pachymetry <400, Artificial Tears were given instead
00248	Primary Eye CXL	2009-09-30	Week 1 Follow-Up	IOP measurement not done	OS
00248	Primary Eye CXL	2009-10-29	Month 1 Follow-Up	IOP measurement not done	OS
00248	Fellow Eye CXL	2009-12-15	Month 3 Follow-Up	RSVP questionnaire not done	OS
00248	Fellow Eye CXL	2009-12-15	Month 3 Follow-Up	IOP measurement not done	OS
00248	Fellow Eye CXL	2009-12-15	Treatment	Other (Specify)	Hypotonic r boflavin not administered for pachymetry <400l artificial tears given instead.
00248	Fellow Eye CXL	2009-12-15	Month 3 Follow-Up	Patients questionnaire not done	OS
00248	Fellow Eye CXL	2009-12-23	Week 1 Follow-Up	IOP measurement not done	OD
00248	Fellow Eye CXL	2010-01-14	Month 1 Follow-Up	IOP measurement not done	OD
00248	Fellow Eye CXL	2010-03-17	Month 3 Follow-Up	Endothelial cell count not done	OD
00249	Primary Eye Sham	2009-10-13	Week 1 Follow-Up	IOP measurement not done	Sham control
00249	Primary Eye Sham	2009-11-04	Month 1 Follow-Up	IOP measurement not done	Sham control
00249	Sham Eye CXL	2010-02-03	Treatment	Other (Specify)	PI used artificial tears instead of protocol required use of hypotonic saline to increase pachymetry for OD-crossover eye
00249	Sham Eye CXL	2010-02-03	Month 6 Follow-Up	Other (Specify)	Visit out of range - 21 days early for OD Sham
00249	Sham Eye CXL	2010-02-03	Month 6 Follow-Up	IOP measurement not done	sham control
00249	Sham Eye CXL	2010-02-11	Week 1 Follow-Up	IOP measurement not done	CXL Crossover eye
00249	Sham Eye CXL	2010-05-12	Month 3 Follow-Up	Other (Specify)	Pentacam Indices not captured for XCL crossover eye

00250	Primary Eye Sham	2009-10-01	Screening	Did not obtain proper consent prior to performing study procedure	Subject did not sign and date the PHI section of the consent form
00250	Primary Eye Sham	2009-10-15	Week 1 Follow-Up	IOP measurement not done	OD
00250	Primary Eye Sham	2009-11-18	Month 1 Follow-Up	IOP measurement not done	OD
00250	Primary Eye Sham	2009-12-22	Month 3 Follow-Up	UCVA not done	OD
00250	Primary Eye Sham	2010-03-30	Month 6 Follow-Up	IOP measurement not done	OD
00251	Primary Eye CXL	2009-11-11	Week 1 Follow-Up	IOP measurement not done	OS
00251	Primary Eye CXL	2010-01-28	Month 3 Follow-Up	IOP measurement not done	OS
00252	Primary Eye Sham	2009-11-12	Week 1 Follow-Up	IOP measurement not done	OD
00252	Primary Eye Sham	2009-12-17	Month 1 Follow-Up	IOP measurement not done	OD
00252	Primary Eye Sham	2010-01-21	Month 3 Follow-Up	IOP measurement not done	OD
00252	Primary Eye Sham	2010-04-20	Month 6 Follow-Up	IOP measurement not done	OD
00253	Primary Eye CXL	2009-11-17	Screening	Did not meet inclusion/exclusion criteria	Keratoconus progression in randomized eye (OD) qualified by increase in astigmatism of 1.0 D over a period of 33 months. (.24 months)
00253	Primary Eye CXL	2009-12-01	Week 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements
00253	Primary Eye CXL	2010-01-05	Month 1 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00253	Primary Eye CXL	2010-02-23	Month 3 Follow-Up	Other (Specify)	Patient did not sign RSVP
00253	Primary Eye CXL	2010-02-23	Month 3 Follow-Up	IOP measurement not done	PI was not aware of all protocol requirements.
00253	Primary Eye CXL	2010-11-24	Treatment	Other (Specify)	Treatment - Following debridement and pretreatment with isotonic riboflavin, artificial tears were used to bring pachymetry above 400 instead of using hypotonic riboflavin for the treatment eye
00254	Primary Eye CXL	2009-12-10	Week 1 Follow-Up	IOP measurement not done	OS XCL Eye
00254	Primary Eye CXL	2010-01-06	Month 1 Follow-Up	IOP measurement not done	OS XCL eye
00254	Primary Eye CXL	2010-02-24	Month 3 Follow-Up	IOP measurement not done	OS XCL eye
00255	Primary Eye Sham	2009-12-15	Week 1 Follow-Up	IOP measurement not done	OD Sham
00255	Primary Eye Sham	2010-01-07	Month 1 Follow-Up	IOP measurement not done	OD Sham
00255	Primary Eye Sham	2010-03-04	Month 3 Follow-Up	IOP measurement not done	OD Sham
00255	Primary Eye Sham	2010-06-22	Month 6 Follow-Up	Other (Specify)	6 month visit was missed
00256	Primary Eye Sham	2009-12-09	Screening	Other (Specify)	I-S Ratio not measured for fellow eye
00256	Primary Eye Sham	2009-12-17	Week 1 Follow-Up	IOP measurement not done	OS Sham Control
00256	Primary Eye Sham	2010-01-15	Month 1 Follow-Up	IOP measurement not done	OS Sham Control
00256	Primary Eye Sham	2010-03-04	Month 3 Follow-Up	IOP measurement not done	OS Sham Control
00256	Primary Eye Sham	2010-06-24	Month 6 Follow-Up	Other (Specify)	Subject was not seen for their 6 month visit.
00257	Primary Eye CXL	2009-01-29	Month 1 Follow-Up	Other (Specify)	OS Treatment eye visit out of window 3 days late
00257	Primary Eye CXL	2009-12-15	Treatment	Other (Specify)	Site used artificial tears in addition to hypotonic riboflavin to increase pachymetry after debridement to greater than or equal to 400 microns before treatment
00257	Primary Eye CXL	2009-12-22	Week 1 Follow-Up	IOP measurement not done	OS - IOP measurement not done.
00257	Primary Eye CXL	2010-01-29	Month 1 Follow-Up	IOP measurement not done	OS - IOP measurement not done.
00257	Primary Eye CXL	2010-03-12	Month 3 Follow-Up	IOP measurement not done	OS - IOP measurement not done.
00257	Primary Eye CXL	2010-06-15	Month 6 Follow-Up	Other (Specify)	OS Treatment Eye - M6 not done, subject was a no show.
00257	Primary Eye CXL	2010-12-15	Month 12 Follow-Up	Other (Specify)	OS Treatment eye - M12 not done due to IRB closing study.

00258	Primary Eye CXL	2010-01-13	Treatment	Other (Specify)	OS Treatment eye - Site used Refresh Artificial Tears to increase Pachymetry reading.
00258	Primary Eye CXL	2010-01-19	Week 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00258	Primary Eye CXL	2010-02-19	Month 1 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00258	Primary Eye CXL	2010-04-16	Month 3 Follow-Up	IOP measurement not done	OS Treatment Eye - IOP measurement not done.
00258	Primary Eye CXL	2011-01-13	Month 12 Follow-Up	Other (Specify)	OS Treatment Eye - M12 not done due to IRB closing study.
01201	Primary Eye CXL	2008-04-28	Treatment	Not treated per randomization assignment	Subject with "severe" keratoconus. Randomization card = "moderate" with tx to be given = Sham-Control. Subject was tx with CXL (OS).
01201	Primary Eye CXL	2008-05-01	Week 1 Follow-up	BSCVA not done	OS/CXL - BSCVA not done
01201	Primary Eye CXL	2008-05-01	Week 1 Follow-up	Other (Specify)	S/CXL – out of window (2 days early)
01202	Primary Eye Sham	2008-04-28	Treatment	Not treated per randomization assignment	Subject documented with "moderate" keratoconus, randomization card "severe" & assigned tx as "CXL-Tx. Initial Tx received was Sham-Control (OS).
01202	Sham Eye CXL	2008-07-31	Week 1 Follow-up	Other (Specify)	OS/CRS-OVR – out of window (2 days early)
01202	Fellow Eye CXL	2008-11-25	Week 1 Follow-up	Other (Specify)	OD/Fellow – out of window (1 day early)
01202	Fellow Eye CXL	2009-03-02	Month 6 Follow-up	Other (Specify)	OS/CRS-OVR – out of window (21 days late)
01202	Fellow Eye CXL	2009-03-02	Month 3 Follow-up	Other (Specify)	OD/Fellow – out of window (3 days late)
01202	Fellow Eye CXL	2009-08-14	Month 6 Follow-up	Other (Specify)	OD/Fellow – out of window (70 days late)
01202	Fellow Eye CXL	2010-03-12	Month 12 Follow-up	Other (Specify)	OD/Fellow – out of window (58 days late)
01203	Primary Eye CXL	2008-05-23	Week 1 Follow-up	Other (Specify)	OS/CXL – out of window (1 day early)
01203	Primary Eye CXL	2008-08-01	Month 1 Follow-up	Other (Specify)	OS/CXL – out of window (32 days late)
01203	Fellow Eye CXL	2008-08-25	Week 1 Follow-up	Other (Specify)	OD/CXL – Fellow eye - out of window 1 day
01203	Fellow Eye CXL	2008-08-25	Month 3 Follow-up	Endothelial cell count not done	OD/CXL – Endothelial cell count not done
01203	Fellow Eye CXL	2009-04-27	Month 6 Follow-up	Other (Specify)	OD-CLX Fellow Eye – out of window 29 days
01203	Fellow Eye CXL	2009-08-04	Month 12 Follow-up	Other (Specify)	OS/CXL – out of window (22 days late)
01204	Primary Eye Sham	2008-07-22	Month 1 Follow-Up	Other (Specify)	OD/Sham - out of window (1 day late).
01204	Sham Eye CXL	2008-09-18	Month 3 Follow-Up	Other (Specify)	OD/Sham - out of window (3 days late).
01204	Sham Eye CXL	2008-09-22	Week 1 Follow-Up	Other (Specify)	OD/Crossover - out of window (1 day early).
01204	Sham Eye CXL	2009-01-05	Month 3 Follow-Up	Other (Specify)	OD/Crossover - out of window (11 days late).
01204	Sham Eye CXL	2009-04-10	Month 6 Follow-Up	Other (Specify)	OD/Crossover - out of window (8 days late).
01205	Fellow Eye CXL	2008-10-03	Week 1 Follow-Up	Other (Specify)	OD/CXL - W1 out of window (1 day early).; OS/Fellow - W1 out of window (1 day early).; OD/CXL - W1 out of window (1 day early).; OS/Fellow - W1 out of window (1 day early).
01206	Primary Eye Sham	2008-06-20	Screening	Other (Specify)	I-S Ratio not done.
01206	Sham Eye CXL	2008-11-21	Treatment	Slit lamp exam not done	OS/Crossover - Slit lamp not done.
01206	Sham Eye CXL	2008-11-21	Month 3 Follow-Up	Other (Specify)	OS/Sham - out of window (18 days late).
01206	Sham Eye CXL	2008-11-24	Week 1 Follow-Up	Other (Specify)	OS/Crossover - out of window (2 days early).
01206	Sham Eye CXL	2009-01-20	Month 1 Follow-Up	Other (Specify)	OS/Crossover - out of window (18 days late).
01206	Sham Eye CXL	2009-03-10	Month 3 Follow-Up	Other (Specify)	OS/Crossover - out of window (3 days late).
01206	Fellow Eye CXL	2009-05-06	Month 3 Follow-Up	Endothelial cell count not done	OD/Fellow - Endothelial cell count not done.

01206	Fellow Eye CXL	2009-05-26	Month 3 Follow-Up	Other (Specify)	OD/Fellow - out of window (5 days late).
01206	Fellow Eye CXL	2009-10-09	Month 6 Follow-Up	Other (Specify)	OD/Fellow - out of window (4 days late).
01206	Fellow Eye CXL	2010-05-21	Month 12 Follow-Up	Other (Specify)	OS/Crossover - out of window (4 months late).
01206	Fellow Eye CXL	2010-05-21	Month 12 Follow-Up	Other (Specify)	OD/Fellow - out of window (4 days late).
02202	Primary Eye Sham	2008-08-11	Treatment	Other (Specify)	Sham Treatment: 26 minute dose time was 3 minutes after 24 minute dose time pre UV-light dosing period (not 2 minutes after per protocol).
02205	Fellow Eye CXL	2009-04-09	Other	Other (Specify)	Fellow eye received treatment more than 6 mo after the initial eye. Approval from study management obtained 1/21/09 but eye not treated until 4/9/09
02206	Fellow Eye CXL	2009-09-01	Month 1 Follow-Up	Patients questionnaire not done	Patient questionnaire was not done at Month 1 visit, but was completed during the Unscheduled visit #5 on 1/14/09.
02206	Fellow Eye CXL	2009-09-01	Month 1 Follow-Up	RSVP questionnaire not done	RSVP was not done at Month 1 visit, but was completed during the Unscheduled visit #5 on 1/14/09.
02206	Fellow Eye CXL	2009-09-01	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam was not done at Month 1 visit, but was completed during the Unscheduled visit #5 on 1/14/09.
02206	Fellow Eye CXL	2009-12-17	Month 12 Follow-Up	Manual keratometry not done	Site was unable to obtain due to irregularity of eye OS
02207	Primary Eye CXL	2008-07-31	Eligibility	Other (Specify)	Keratoconus progression was measured over a 25-month period instead of over a 24-month period. A protocol waiver was granted by Barbara Fant, Pharm.D. on 7/28/08.
02207	Primary Eye CXL	2008-11-18	Month 3 Follow-Up	Other (Specify)	Pentacam was done on 11/18/08 but the printout did not include the "K-MAX" and "TKC" values. The values are not available.
02207	Primary Eye CXL	2009-01-06	Month 6 Follow-Up	Other (Specify)	Pentacam was done on 01/09/09 but the printout did not include the "K-MAX" and "TKC" values. The values are not available.
02207	Primary Eye CXL	2009-07-08	Month 12 Follow-Up	Other (Specify)	Pentacam was done on 7/10/09 but the printout did not include the "K-MAX" and "TKC" values. The values are not available
02208	Sham Eye CXL	2009-04-17	Month 3 Follow-Up	Endothelial cell count not done	Unable to perform, image was of poor quality
02209	Primary Eye Sham	2009-03-09	Week 1 Follow-Up	Other (Specify)	Sham (OS) Week 1 visit is two days out of window (early)
02209	Primary Eye Sham	2009-04-14	Month 1 Follow-Up	Other (Specify)	Sham (OS) Month 1 visit fourteen days out of window (early)
02209	Primary Eye Sham	2009-05-19	Month 3 Follow-Up	Other (Specify)	Sham (OS) Month 3 visit is twenty six days out of window (early)
02209	Fellow Eye CXL	2009-11-30	Treatment	Other (Specify)	Crossover eye (OS) treated 9.5 months after randomized sham eye treated. No approval was obtained from the Sponsor for this deviation.
02209	Fellow Eye CXL	2009-11-30	Treatment	Other (Specify)	Fellow Eye OD teated 9.5 months after Randomized Eye treated. No approval was obtained from the Sponsor for this deviation.
02209	Fellow Eye CXL	2009-11-30	Treatment	Other (Specify)	Crossover Eye (OD) 30 minute dose time 1 minute after 28 minute dose time pre UV-light dosing period (not 2 minutes after per protocol).
02209	Fellow Eye CXL	2010-02-18	Month 3 Follow-Up	Endothelial cell count not done	Unable to count cells OD, poor image quality
02209	Fellow Eye CXL	2010-02-18	Month 3 Follow-Up	Endothelial cell count not done	Unable to count cells OS, poor image quality
02209	Fellow Eye CXL	2010-04-22	Month 6 Follow-Up	IOP measurement not done	Missed measurement OD
02209	Fellow Eye CXL	2010-04-22	Month 6 Follow-Up	IOP measurement not done	missed measurement OS
02210	Fellow Eye CXL	2009-11-04	Treatment	Other (Specify)	Fellow eye received treatment more than 6 months after the initial eye. No approval was obtained from the Sponsor for this deviation.
02210	Fellow Eye CXL	2009-12-18	Month 1 Follow-Up	Other (Specify)	The Month 1 follow up visit for the fellow eye (OS) was conducted 2 days out of window (late).
02210	Fellow Eye CXL	2010-11-04	Month 12 Follow-Up	Other (Specify)	The Month 12 visit for the fellow eye (OS) was not conducted; the subject was Lost to Follow Up.
02211	Primary Eye Sham	2009-04-29	Treatment	Other (Specify)	Treatment day, Sham OS: 22 minute dose time was 4 minutes after the 20 minute timepoint, pre UVX light exposure.
02211	Primary Eye Sham	2009-04-29	Treatment	Other (Specify)	Treatment day, Sham OS: 2 minute dose time was 3 minutes after the 0 minute timepoint, pre UVX light exposure.
02211	Primary Eye Sham	2009-04-29	Treatment	Other (Specify)	Treatment day, Sham OS: 4 minute dose time was 3 minutes after the 2 minute timepoint,pre UVX light exposure.
02211	Sham Eye CXL	2009-11-18	Treatment	Other (Specify)	CXL eye received treatment more than 6 months after the randomized eye.
02211	Sham Eye CXL	2010-02-12	Month 3 Follow-Up	Other (Specify)	The Month 3 Pentacam was done on 2/12/10 but the printout did not include the Pentacam Indices. The values are not available.
03202	Primary Eye CXL	2008-02-26	Eligibility	Did not meet inclusion/exclusion criteria	Keratoconus progression tracked over 33 months. Sponsor granted a Protocol Waiver prior to the subject being enrolled.
03204	Primary Eye Sham	2008-02-19	Screening	Did not meet inclusion/exclusion criteria	Progressive Keratoconus (Cylinder) was measured over a 25 month period, instead of the 24 month period allowed by the protocol.

03206	Primary Eye Sham	2008-04-01	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed at the treatment visit on 4/18/08 instead of prior to screening procedures on 4/1/08.
03206	Sham Eye CXL	2008-07-22	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	K Max not collected at OS 1M on 7/22/08.
03206	Sham Eye CXL	2008-11-18	Screening	Pentacam pachymetry, keratometry not done	K Max not collected at OD re-screen on 11/18/08.
03206	Fellow Eye CXL	2009-02-25	Treatment	IOP measurement not done	IOP was not taken during the treatment visit for the fellow eye (right eye).
03207	Primary Eye Sham	2008-04-24	Eligibility	Did not meet inclusion/exclusion criteria	Progression was assessed over a 32 month period which exceeds the window for determining elig bility
03209	Primary Eye Sham	2008-04-15	Screening	Did not obtain proper consent prior to performing study procedure	Subject was screened on 15Apr08, but did not sign consent form until Day 0 on 21May08.
03209	Sham Eye CXL	2009-06-16	Month 12 Follow-Up	Endothelial cell count not done	Source document notes site was unable to perform procedure, specific reason not specified.
03210	Primary Eye CXL	2008-04-15	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (5/14/08) instead of on screening day (4/15/08).
03210	Primary Eye CXL	2008-04-15	Screening	Endothelial cell count not done	Reason not specified.
03210	Primary Eye CXL	2008-04-15	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (5/14/08) instead of on screening day (4/15/08).
03210	Primary Eye CXL	2008-04-15	Screening	Did not obtain proper consent prior to performing study procedure	Subject was screened on 15 Apr 08, but did not sign consent form until Day 0 (Treatment) on 14 May 08.
03210	Primary Eye CXL	2008-08-05	Month 3 Follow-Up	Endothelial cell count not done	Reason not specified
03210	Primary Eye CXL	2009-03-17	Month 12 Follow-Up	BSCVA not done	Reason not specified
03211	Primary Eye CXL	2008-05-12	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (5/12/08) instead of on screening day (4/21/08).
03211	Primary Eye CXL	2008-05-12	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (5/12/08) instead of on screening day (4/21/08).
03211	Fellow Eye CXL	2008-12-01	Treatment	Other (Specify)	Patient had history of Intacs in the treated fellow eye (OD).
03212	Fellow Eye CXL	2009-01-05	Treatment	IOP measurement not done	Reason not specified.
03216	Primary Eye CXL	2008-05-19	Screening	Other (Specify)	Screening visit completed 5/19/08, 63 days before 7/21/08 treatment date (33 days out of visit window).
03216	Primary Eye CXL	2008-07-21	Treatment	IOP measurement not done	IOP was not taken during the treatment visit for the study eye (right eye).
03217	Primary Eye Sham	2008-06-02	Screening	Did not meet inclusion/exclusion criteria	Progressive Keratoconus was measured over a 30 month period instead of the allowed 24 month period of time.
03217	Fellow Eye CXL	2009-06-02	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed two days after screening on 6/4/08 instead of at or before screening which occurred on 6/2/08.
03218	Primary Eye CXL	2008-07-02	Treatment	Did not meet inclusion/exclusion criteria	Subject did not meet inclusion criteria #2. Progression shown over 27 months prior to randomization.
03219	Primary Eye CXL	2008-03-03	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed at the Treatment visit (7/14/08) instead if the Screening visit (3/3/08).
03220	Primary Eye Sham	2008-05-16	Screening	Did not obtain proper consent prior to performing study procedure	Subject screened on May 16, 2008, but did not sign consent form until Day 0 on July 16, 2008.
03220	Primary Eye Sham	2008-07-16	Treatment	Other (Specify)	Day 0 occurred 62 days after Screening visit. Clinical Research Consultants (Barbara Fant) sent an e-mail dated July 15, 2008 to the site (Dr Kristen Fry) approving the subject for randomization
03220	Primary Eye Sham	2008-07-16	Screening	Other (Specify)	Endothelial cell count not done OD. No reason given.
03220	Sham Eye CXL	2008-10-13	Month 3 Follow-Up	Other (Specify)	Endothelial cell count not done OD.
03221		2008-**-**	Month 1 Follow-Up	Other (Specify)	The subject missed the 1M visit for the fellow eye, OS.
03221		2008-**-**	Month 3 Follow-Up	Other (Specify)	The 3M visit for the fellow eye, OS, was missed by the subject.
03221	Primary Eye Sham	2008-06-10	Eligibility	Other (Specify)	Progression was assessed over a 25 month period which exceeds the requirement by 1 month
03221	Sham Eye CXL	2009-05-15	Month 6 Follow-Up	Other (Specify)	Month 6 visit was not performed for the Crossover Eye OD

03222	Fellow Eye CXL	2009-04-06	Month 12 Follow-Up	Other (Specify)	Month 12 visit for study eye (OD), was out of window (24 days early).
03223	Sham Eye CXL	2009-01-13	Month 3 Follow-Up	Other (Specify)	Subject missed 3 month follow up appt. Note to File created in chart.
03225	Primary Eye Sham	2008-07-08	Screening	Did not obtain proper consent prior to performing study procedure	ICF was not signed at screening on 7/8/08, but instead signed at Treatment on 7/21/08.
03226	Primary Eye Sham	2008-07-16	Eligibility	Other (Specify)	Progression demonstrated over a 29 month period which exceeds the 24 month allowance. Email on file from previous CRO provides waiver for enrollment
03226	Sham Eye CXL	2008-10-29	Month 3 Follow-Up	Endothelial cell count not done	Source data states the site was unable to perform the exam
03227	Primary Eye Sham	2008-07-23	Screening	Patients questionnaire not done	Patient questionnaire not done on day of Screening Visit (2008-07-23); however, was done on Treatment Visit (2008-08-11)
03228	Fellow Eye CXL	2009-08-14	Month 12 Follow-Up	Other (Specify)	Month 12 visit for the crossover eye (OS) was 21 days out of window (early).
03229	Primary Eye Sham	2008-08-11	Screening	Patients questionnaire not done	Patient Questionnaires not done at Screening (2008-08-11); however, were done at Treatment (2008-08-20)
03230	Primary Eye CXL	2008-08-12	Screening	Did not obtain proper consent prior to performing study procedure	The subject was screened on 8/12/08, but did not sign consent until Treatment on 8/18/08.
03230	Primary Eye CXL	2008-08-12	Screening	Patients questionnaire not done	Questionnaire ND at Screening Visit (2008-08-12); however, was done at Treatment Visit (2008-08-18)
03232	Primary Eye Sham	2008-08-19	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed 14 days after screening on 9/2/08 instead of at or before screening which occurred on 8/19/08.
03233	Primary Eye CXL	2008-08-20	Screening	RSVP questionnaire not done	Patients RSVP Questionnaire was done on treatment day (9/17/08) instead of on screening day (8/20/08).
03233	Primary Eye CXL	2008-09-17	Treatment	IOP measurement not done	IOP not taken at treatment visit (study eye - OD).
03233	Primary Eye CXL	2008-11-03	Month 1 Follow-Up	Other (Specify)	Month 1 visit was 5 days out of window (late).
03234	Primary Eye CXL	2008-08-26	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (9/29/08) instead of on screening day (8/26/08).
03234	Primary Eye CXL	2008-08-26	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (9/29/08) instead of on screening day (8/26/08).
03234	Primary Eye CXL	2009-09-15	Month 12 Follow-Up	BSCVA not done	Reason was not given
03235	Primary Eye CXL	2008-09-02	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (9/15/08) instead of on screening day (9/2/08).
03235	Primary Eye CXL	2008-09-02	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (9/15/08) instead of on screening day (9/2/08).
03235	Primary Eye CXL	2008-09-02	Screening	Other (Specify)	The ICF was signed 15 days after screening on 9/15/08 instead of at or before screening which occurred on 9/2/08.
03237	Sham Eye CXL	2009-05-05	Month 6 Follow-Up	BSCVA not done	Procedure not performed, reason unknown
03238	Primary Eye Sham	2008-10-09	Treatment	IOP measurement not done	Procedure not done; no reason given.
03240	Primary Eye Sham	2008-09-16	Screening	Did not obtain proper consent prior to performing study procedure	Screening Visit began on 9/16/08, but the ICF was not signed until 9/23/08.
03240	Primary Eye Sham	2008-10-13	Eligibility	Did not meet inclusion/exclusion criteria	Progression shown over 28 months. Per inclusion criteria #2, progression should be shown over 24 months or less prior to randomization.
03240	Sham Eye CXL	2010-01-08	Month 12 Follow-Up	Other (Specify)	Month 12 visit for crossover eye (OD) was 16 days out of window (early).
03242	Primary Eye CXL	2008-11-25	Treatment	Other (Specify)	Time between Screening (10/07/08) and Treatment (11/25/08) was greater than 30 days.
03242	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	Other (Specify)	Month 12 visit was 21 days out of window (early).
03243	Primary Eye CXL	2008-10-14	Screening	Patients questionnaire not done	Patient questionnaire and RSVP completed by subject on 10/29/08 (Treatment) visit
03243	Primary Eye CXL	2008-10-14	Screening	Did not obtain proper consent prior to performing study procedure	ICF was signed at Treatment on 10/29/08 instead of at screening on 10/14/08.
03244	Primary Eye CXL	2008-10-14	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (11/13/08) instead of on screening day (10/14/08).
03244	Primary Eye CXL	2008-10-14	Screening	Did not obtain proper consent prior to performing study procedure	screening visit 10/14/08 ICF signed on 11/13/08 day of treatment
03244	Primary Eye CXL	2008-10-14	Eligibility	Other (Specify)	Progressive Keratoconus (MRSE) was measured over a 27 month period, instead of the 24 month period allowed by the protocol.

03244	Primary Eye CXL	2008-10-14	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (11/13/08) instead of on screening day (10/14/08).
03245	Primary Eye Sham	2008-10-20	Screening	Did not obtain proper consent prior to performing study procedure	The subject signed the ICF on 11/3/08 (Treatment Day) instead of signing at Screening on 10/20/08/
03245	Primary Eye Sham	2008-10-20	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (11/3/08) instead of on screening day (10/20/08).
03245	Primary Eye Sham	2008-10-20	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (11/3/08) instead of on screening day (10/20/08).
03245	Fellow Eye CXL	2009-04-13	Month 3 Follow-Up	BSCVA not done	BSCVA not performed OS at 3M follow-up visit with no reason given for not performing the assessment.
03246	Primary Eye Sham	2009-01-19	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed on 3/26/09 instead of at the screening visit on 1/19/09.
03246	Primary Eye Sham	2009-01-19	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (3/26/09) instead of on screening day (1/19/09).
03246	Primary Eye Sham	2009-01-19	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (3/26/09) instead of on screening day (1/19/09).
03246	Primary Eye Sham	2009-04-25	Month 1 Follow-Up	BSCVA not done	BSCVA not performed the 1M visit with no reason given.
03247	Primary Eye CXL	2009-03-03	Screening	RSVP questionnaire not done	The RSVP questionnaire was not completed at the screening visit (03/03/09) but was done at the treatment visit (03/05/09).
03247	Primary Eye CXL	2009-03-03	Screening	Patients questionnaire not done	The Patients Questionnaire was not completed at the screening visit (03/03/09) but was completed at the treatment visit (03/05/09).
03247	Primary Eye CXL	2009-03-03	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed at the treatment visit (3/5/09) instead of at the screening visit (3/3/09).
03247	Fellow Eye CXL	2010-03-08	Month 12 Follow-Up	BSCVA not done	The BSCVA was not performed at the 12M visit and no reason was given for not performing the assessment.
03248	Primary Eye CXL	2009-02-17	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed on 4/30/09 (Treatment Day) instead of 2/17/09, the Screening day.
03248	Primary Eye CXL	2009-04-30	Treatment	Other (Specify)	Treatment day not within 30 days of screening evaluation
03248	Primary Eye CXL	2009-04-30	Screening	Other (Specify)	RSVP questionnaire completed on day of treatment, not within preoperative visit window (-30 to -1 days)
03248	Primary Eye CXL	2009-04-30	Screening	Other (Specify)	Subjective complaint questionnaire completed on day of treatment, not within preoperative period (-30 to -1 days)
03248	Primary Eye CXL	2009-06-23	Month 1 Follow-Up	Other (Specify)	1 month follow-up visit was outside protocol visit window.
03248	Primary Eye CXL	2009-08-08	Month 3 Follow-Up	Other (Specify)	3 month follow-up visit was two days outside protocol visit window.
03248	Primary Eye CXL	2009-12-18	Month 6 Follow-Up	Other (Specify)	6 month follow-up visit was outside protocol visit window.
03248	Primary Eye CXL	2010-06-10	Month 12 Follow-Up	Other (Specify)	12 month visit was out of protocol visit window. Site sent subject certified letter to return for visit.
03250	Sham Eye CXL	2009-10-29	Week 1 Follow-Up	Other (Specify)	Patient missed 1 week follow-up visit for crossover treatment of primary eye.
03250	Fellow Eye CXL	2009-12-09	Week 1 Follow-Up	Other (Specify)	Patient missed 1 week follow up visit for fellow eye (OD)
03250	Fellow Eye CXL	2010-05-22	Month 6 Follow-Up	Other (Specify)	6 month F/U visit for crossover primary eye (OS) was done 23 days out of visit window.
03251	Primary Eye Sham	2009-03-27	Screening	Did not obtain proper consent prior to performing study procedure	Partial screening visit done on 3/27/09; patient questionnaires completed on 4/30/09 the day of treatment and ICF signing.
03252	Primary Eye CXL	2009-04-07	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed on 4/22/09 (treatment) instead of at screening on 4/7/09.
03252	Primary Eye CXL	2009-04-07	Screening	Patients questionnaire not done	Patients Questionnaire was done on treatment day (4/22/09) instead of on screening day (4/7/09).
03252	Primary Eye CXL	2009-04-07	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day (4/22/09) instead of on screening day (4/7/09).
03253	Primary Eye Sham	2009-04-07	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed on 4/22/09 at the treatment visit instead of screening on 4/7/09.
03253	Primary Eye Sham	2009-04-15	Screening	Patients questionnaire not done	Patient questionnaires completed on 2009-4-22 (Treatment) vs 2009-4-15 (Screening)
03254	Primary Eye Sham	2009-02-06	Screening	Patients questionnaire not done	Patient questionnaires completed 2009-5-4 (Treatment Visit) vs 2009-2-6 (Screen Visit)

03254	Primary Eye Sham	2009-02-06	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed on 5/4/09 (Treatment) instead of at screening on 2/6/09.
03254	Primary Eye Sham	2009-05-04	Treatment	Other (Specify)	Treatment visit occurred out of window (Screen Visit = 2009-2-6 and Treatment Visit = 2009-5-4)
03259	Primary Eye CXL	2009-04-27	Screening	RSVP questionnaire not done	RSVP questionnaire was not completed at screening visit but was completed at treatment visit (5/6/09).
03259	Primary Eye CXL	2009-04-27	Screening	Patients questionnaire not done	Patients questionnaire was not completed at the screening visit but was completed at the treatment visit (5/6/09).
03259	Primary Eye CXL	2009-04-27	Screening	Did not obtain proper consent prior to performing study procedure	Informed consent not obtained prior to screening procedures. It was obtained on the day of treatment
03261	Primary Eye Sham	2009-04-13	Screening	Did not obtain proper consent prior to performing study procedure	The ICF was signed on 5/31/09 (Treatment) instead of at Screening on 4/31/09.
04202	Fellow Eye CXL	2009-07-15	Month 12 Follow-Up	Other (Specify)	12 month visit randomized eye (OS) 40 days late outside visit window.
04204	Fellow Eye CXL	2009-06-26	Month 12 Follow-Up	Other (Specify)	Subject was seen for their 12 month post-op 3 days after the window closed.
04208	Primary Eye CXL	2008-07-18	Week 1 Follow-Up	Manifest refraction not done	Manifest refraction was Not Done during the 1 week post-op due to oversight.
04212	Primary Eye CXL	2008-12-01	Month 3 Follow-Up	Other (Specify)	Missed Month 3 Follow-up Visit
05201	Sham Eye CXL	2009-11-02	Month 6 Follow-Up	Other (Specify)	OD/Sham eye - out of window (42 days late).
05201	Fellow Eye CXL	2009-11-30	Treatment	BSCVA not done	OS/Fellow Eye - BSCVA not done.
05201	Fellow Eye CXL	2009-11-30	Treatment	Other (Specify)	After 3rd attempt to increase Pachymetry reading using Hypotonic Riboflavin, Site used BSS and waited 1 minute before getting a Pachymetry reading of 400.
05201	Fellow Eye CXL	2009-11-30	Month 1 Follow-Up	Other (Specify)	OD/Crossover eye - Pentacam Indices not done.
05201	Fellow Eye CXL	2010-01-15	Month 1 Follow-Up	Other (Specify)	OS/Fellow eye - out of window (4 days late).
05201	Fellow Eye CXL	2010-03-12	Month 6 Follow-Up	Other (Specify)	OS/Fellow eye - out of window (4 days late).
05201	Fellow Eye CXL	2010-03-12	Month 6 Follow-Up	Other (Specify)	OD/Crossover eye - out of window (10 days early).
05202	Primary Eye CXL	2009-02-23	Treatment	Other (Specify)	A Consent Form was signed at Screening and another Consent Form is in chart signed but not dated.
05202	Primary Eye CXL	2009-04-03	Month 1 Follow-Up	Patients questionnaire not done	M1 Patient questionnaire not done.
05202	Primary Eye CXL	2009-06-15	Month 3 Follow-Up	Other (Specify)	M3 was out of window - 14 days late.
05202	Primary Eye CXL	2009-08-25	Month 6 Follow-Up	Other (Specify)	Visit was not done. Subject cancelled the visit 1 day prior and did not reschedule.
05203	Primary Eye Sham	2009-05-01	Month 1 Follow-Up	Patients questionnaire not Done	OS/Sham - Patient questionnaire not done.
05203	Primary Eye Sham	2009-05-01	Month 1 Follow-Up	Other (Specify)	OS/Sham eye - out of window (4 days late).
05203	Primary Eye Sham	2009-08-04	Month 3 Follow-Up	Other (Specify)	OS/Sham - Subject missed 3 month follow up visit twice and returned on 11-Sep-2009.
05203	Fellow Eye CXL	2009-11-16	Treatment	Other (Specify)	OS Crossover eye - Riboflavin was given every 2 minutes some of the time and every 3 minutes some of the time.
05203	Fellow Eye CXL	2009-11-16	Treatment	BSCVA not done	OD/Fellow eye - BSCVA not done.
05203	Fellow Eye CXL	2010-02-14	Month 3 Follow-Up	Other (Specify)	OD/Fellow eye - Month 3 not done.
05203	Fellow Eye CXL	2010-02-14	Month 3 Follow-Up	Other (Specify)	OS/Crossover eye - Month 3 not done.
05203	Fellow Eye CXL	2011-04-22	Other	Other (Specify)	M6 and M12 OU not done. Patient withdrew from study due to moving and cost of transportation.
05204	Primary Eye CXL	2009-05-22	Month 1 Follow-Up	Patients questionnaire not Done	OS/CXL eye - Patient questionnaire not done.
05204	Primary Eye CXL	2009-07-21	Month 3 Follow-Up	Other (Specify)	OS/CXL eye - out of window (1 day late).
05204	Primary Eye CXL	2009-07-21	Month 3 Follow-Up	Endothelial cell count not Done	OS/CXL eye - Endothelial cell count not done.
05204	Fellow Eye CXL	2009-10-19	Treatment	Other (Specify)	OD/Fellow eye - Riboflavin gtts not given every 2 minutes per protocol.
05204	Fellow Eye CXL	2009-10-19	Treatment	BSCVA not done	OD/Fellow eye - BSCVA not done.
05204	Fellow Eye CXL	2009-12-07	Month 1 Follow-Up	Other (Specify)	OD/Fellow eye - out of window (7 days late).
05205	Primary Eye CXL	2009-04-27	Treatment	Other (Specify)	OS/CXL - Treatment day was > 30 days from screening. Manual K, UCVA, and BSCVA were not repeated.

05205	Primary Eye CXL	2009-06-01	Month 1 Follow-Up	Patients questionnaire not Done	OS/CXL - Patient questionnaire not done.
05205	Primary Eye CXL	2009-08-10	Month 3 Follow-Up	Other (Specify)	OS/CXL - out of window (7 days late).
05205	Fellow Eye CXL	2009-11-23	Treatment	Other (Specify)	OD/Fellow eye - Site used Hypotonic Riboflavin with BSS to achieve a Pachymetry reading of >/= 400.
05205	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	Other (Specify)	OS/CXL - out of window (14 days late).
05205	Fellow Eye CXL	2009-11-23	Treatment	BSCVA not done	OD/Fellow eye - BSCVA not done.
05205	Fellow Eye CXL	2009-12-23	Month 1 Follow-Up	Other (Specify)	OD/Fellow eye - Month 1 was not done.
05205	Fellow Eye CXL	2010-03-01	Month 12 Follow-Up	Endothelial cell count not Done	OS/CXL eye - Endothelial cell count not done.
05205	Fellow Eye CXL	2010-03-01	Month 3 Follow-Up	Endothelial cell count not Done	OD/Fellow eye - Endothelial cell count not done.
05205	Fellow Eye CXL	2010-06-14	Month 6 Follow-Up	Other (Specify)	OD/Fellow eye - out of window (7 days late).
05206	Primary Eye Sham	2009-03-13	Screening	Endothelial cell count not Done	OS/Sham - Endothelial cell count not done.
05206	Primary Eye Sham	2009-06-05	Month 1 Follow-Up	Patients questionnaire not Done	OS/Sham - Patient questionnaire not done.
05207	Primary Eye CXL	2009-06-08	Treatment	Other (Specify)	OS/CXL - There was > 30 days between screening and Treatment Day. UCVA, BSCVA, and Manual Keratometry were not repeated per protocol.
05207	Primary Eye CXL	2009-06-16	Week 1 Follow-Up	Other (Specify)	OS/CXL - Manifest Refraction, BSCVA, and IOP not done due to corneal haze.
05207	Primary Eye CXL	2009-07-07	Month 1 Follow-Up	Patients questionnaire not done	OS/CXL - Patient Questionnaire not done.
05207	Primary Eye CXL	2009-09-04	Month 3 Follow-Up	Endothelial cell count not done	OS/CXL - Endothelial Cell Count not done due to blurriness.
07201	Primary Eye Sham	2008-07-01	Screening	Did not obtain proper consent prior to performing study procedure	Informed consent process not documented. The signature page of the informed consent is missing. HIPPA signature page was signed 7/1/08 and is in patient's chart.
07201	Primary Eye Sham	2008-08-26	Screening	Manual keratometry not done	Screening Manual keratometry not done
07201	Primary Eye Sham	2008-09-21	Day 1 Follow-Up	Other (Specify)	Day 1 randomized -sham eye (OD) visit not done.
07201	Primary Eye Sham	2008-09-30	Week 1 Follow-Up	UCVA not done	Week 1 randomized sham eye (OD) UCVA not done. Only Snellen equivalent.
07201	Primary Eye Sham	2008-10-28	Month 1 Follow-Up	BSCVA not done	1 month randomized sham eye (OD) UCVA not done.
07201	Primary Eye Sham	2008-10-28	Month 1 Follow-Up	BSCVA not done	1 month randomized sham eye (OD) BSCVA not done.
07201	Primary Eye Sham	2008-10-28	Month 1 Follow-Up	Manual keratometry not done	Manual keratometry sham eye (OD) not done
07201	Primary Eye Sham	2008-10-28	Month 1 Follow-Up	RSVP questionnaire not done	RSVP sham eye (OD) not obtained
07201	Primary Eye Sham	2008-10-28	Month 1 Follow-Up	Patients questionnaire not done	Patient questionnaire sham eye (OD) not obtained
07201	Sham Eye CXL	2008-12-18	Treatment	Other (Specify)	Treatment day crossover eye (OD) pachymetry post riboflavin= 360. Hypotonic r boflavin was not given. Artificial tears were used and patient closed eye for 5 minutes. Pachymetry increased to 426.
07201	Sham Eye CXL	2008-12-18	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done at month 3 Sham eye (OD).
07201	Sham Eye CXL	2008-12-19	Day 1 Follow-Up	UCVA not done	Day 1 crossover eye (OD) UCVA not done.
07201	Sham Eye CXL	2008-12-22	Week 1 Follow-Up	Other (Specify)	Week 1 crossover eye (OD) visit is out of window, 1 day early.
07201	Sham Eye CXL	2009-04-21	Month 3 Follow-Up	Other (Specify)	Month 3 crossover eye (OD) out of window, 25 days late.
07201	Sham Eye CXL	2009-04-21	Month 3 Follow-Up	Endothelial cell count not done	Month 3 crossover eye (OD) endothelial cell count not done.
07201	Sham Eye CXL	2009-07-02	Month 6 Follow-Up	Other (Specify)	6 month crossover eye (OD) visit was missed
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	RSVP questionnaire not done	Month 12 crossover eye (OD) RSVP questionnaire not done.
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	UCVA not done	Month 12 crossover eye (OD) UCVA not done.
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	Other (Specify)	12 Month Pentacam crossover eye (OD) Kmax value not available.
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	Patients questionnaire not done	month 12 crossover eye (OD) patient questionnaire not done
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	Other (Specify)	12 month pentacam crossover eye (OD) 8 indices not available
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	Dilated fundus exam not done	month 12 crossover eye (OD) dilated fundus exam not done

07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	Endothelial cell count not done	Month 12 crossover eye (OD) endothelial cell count not done.
07201	Sham Eye CXL	2009-12-17	Month 12 Follow-Up	Manual keratometry not done	Month 12 crossover eye (OD) manual keratometry not done
07202	Primary Eye CXL	2008-07-08	Screening	UCVA not done	Missed exam OU
07202	Primary Eye CXL	2008-08-05	Week 1 Follow-Up	BSCVA not done	Missed exam
07202	Primary Eye CXL	2008-08-05	Week 1 Follow-Up	IOP measurement not done	Missed exam
07202	Fellow Eye CXL	2009-02-09	Month 3 Follow-Up	Endothelial cell count not done	Missed exam.
07202	Fellow Eye CXL	2009-08-07	Month 12 Follow-Up	BSCVA not done	missed exam
07202	Fellow Eye CXL	2009-08-07	Month 6 Follow-Up	BSCVA not done	missed exam
07202	Fellow Eye CXL	2009-08-07	Month 12 Follow-Up	Slit lamp exam not done	missed exam
07202	Fellow Eye CXL	2009-08-07	Month 6 Follow-Up	Other (Specify)	6 month visit performed at approximately 9 months from Tx day of fellow eye (out of window)
07202	Fellow Eye CXL	2009-08-07	Month 12 Follow-Up	UCVA not done	Missed exam.
07204	Primary Eye Sham	2008-09-18	Treatment	Slit lamp exam not done	Missing exam.
07204	Primary Eye Sham	2008-09-19	Day 1 Follow-Up	UCVA not done	Missed exam
07204	Primary Eye Sham	2008-09-30	Week 1 Follow-Up	UCVA not done	Missed exam
07204	Primary Eye Sham	2008-10-30	Month 1 Follow-Up	Other (Specify)	Missed visit
07204	Primary Eye Sham	2008-12-25	Month 3 Follow-Up	Other (Specify)	Missed visit
07204	Sham Eye CXL	2009-03-25	Month 6 Follow-Up	BSCVA not done	Missed exam.
07204	Sham Eye CXL	2009-03-25	Treatment	Other (Specify)	Crossover occurred one week later than allowable 3-6 month window
07204	Sham Eye CXL	2009-03-25	Month 6 Follow-Up	UCVA not done	Missed exam
07204	Sham Eye CXL	2009-03-26	Day 1 Follow-Up	UCVA not done	Missed exam
07204	Sham Eye CXL	2009-04-02	Week 1 Follow-Up	UCVA not done	Missed exam
07205	Primary Eye CXL	2008-09-04	Screening	Did not obtain proper consent prior to performing study procedure	Consented with the informed consent (ICF) for the Ectasia (UVX-003) study instead of the ICF for the Keratoconus (UVX-002) study. The ICF for the keratoconus study was never signed by subject.
07205	Primary Eye CXL	2008-09-18	Eligibility	Did not meet inclusion/exclusion criteria	Pt did not meet contact lens stability prior to treatment
07205	Primary Eye CXL	2008-09-23	Week 1 Follow-Up	Manifest refraction not done	per PI, this procedure could not be done
07205	Primary Eye CXL	2008-10-11	Month 1 Follow-Up	Other (Specify)	Month 1 pentacam was performed, Kmax value not available.
07205	Primary Eye CXL	2008-11-10	Month 1 Follow-Up	Other (Specify)	Visit occurred 10 days later than allowable window
08201	Primary Eye Sham	2008-05-12	Month 1 Follow-Up	Other (Specify)	OD Treatment Eye - visit out of window, 9 days late.
08201	Primary Eye Sham	2008-10-12	Month 1 Follow-Up	Other (Specify)	OD Treatment Eye - M1 MD exam done 05Dec2008, however; patient Questionnaire & RSVP Questionnaire completed on 10Dec2008 (5 days after clinic visit).
08201	Sham Eye CXL	2009-03-02	Month 3 Follow-Up	Other (Specify)	OD Treatment Eye - visit out of window, 13 days late.
08201	Sham Eye CXL	2009-03-24	Other	Did not meet inclusion/exclusion criteria	Patient became pregnant while participating in the study. Exclusion criteria #6.
08201	Sham Eye CXL	2010-01-03	Month 12 Follow-Up	Other (Specify)	OD Treatment Eye - visit out of window, 82 days late.
08203	Primary Eye CXL	2008-07-02	Treatment	Other (Specify)	Pre UV light riboflavin drops at 28 minute dosing time was done at 29 minutes randomized eye (OD).
08203	Primary Eye CXL	2008-07-02	Treatment	Manual keratometry not done	Manual Keratometry not done randomized eye (OD).
08203	Primary Eye CXL	2008-07-02	Treatment	Other (Specify)	Riboflavin dosing time during UV light treatment period was 33 minutes not 30 minutes per protocol.
08203	Fellow Eye CXL	2008-12-10	Treatment	BSCVA not done	BSCVA not done fellow eye (OS).
08203	Fellow Eye CXL	2008-12-17	Week 1 Follow-Up	IOP measurement not done	Doctor deferred IOP for fellow eye (OS).
08204	Fellow Eye CXL	2008-12-03	Treatment	Other (Specify)	OD/Fellow - repeat measurements (UCVA, BSCVA, Manifest Refraction and Manual Keratometry) not done day of treatment.
08204	Fellow Eye CXL	2008-12-03	Treatment	Other (Specify)	OD/Fellow - Illumination gtts, Dose #10 was given at 3 minutes instead of 2 minutes per protocol.
08204	Fellow Eye CXL	2009-05-15	Month 12 Follow-Up	Endothelial cell count not done	OD/Fellow - Endothelial cell count not done.

08205	Primary Eye CXL	2008-08-06	Treatment	Other (Specify)	OS/CXL - Isotonic Riboflavin Dosing procedure Dose 10 completed 1 min outside required every 2 min dosing window.
08205	Primary Eye CXL	2008-08-06	Treatment	Other (Specify)	OS/CXL - Illumination #15 and #16 for 28 and 30 min dosing drops not administered as required.
08205	Primary Eye CXL	2008-11-07	Month 3 Follow-Up	Endothelial cell count not done	OS/CXL - Endothelial cell count not done.
08205	Fellow Eye CXL	2009-01-27	Month 6 Follow-Up	Manifest refraction not done	OS/CXL - manifest refraction not done.
08205	Fellow Eye CXL	2009-02-02	Week 1 Follow-Up	IOP measurement not done	OD/Fellow - IOP measurement not done.
08205	Fellow Eye CXL	2009-05-01	Month 3 Follow-Up	Endothelial cell count not done	OD/Fellow - endothelial cell count not done.
08207	Primary Eye CXL	2008-09-10	Treatment	Other (Specify)	OS/CXL - Riboflavin isotonic drops the 22 minute dose was administered 1 minute outside the required 2 minute window.
08207	Fellow Eye CXL	2009-04-28	Month 3 Follow-Up	Manifest refraction not done	OD/Fellow - Manifest refraction not done.
08208	Sham Eye CXL	2008-11-17	Treatment	IOP measurement not done	OS/CRS-OVR - IOP not done.
08208	Sham Eye CXL	2008-11-17	Treatment	IOP measurement not done	OD/Fellow - IOP not done.
08209	Primary Eye Sham	2008-09-10	Treatment	Other (Specify)	OS/Sham - Riboflavin Dose 11 given at 3 minutes instead of 2 minutes as stated in protocol.
08209	Sham Eye CXL	2008-12-08	Week 1 Follow-Up	IOP measurement not done	OD/CRS-over - IOP deferred by doctor
08209	Sham Eye CXL	2009-02-23	Month 3 Follow-Up	Endothelial cell count not done	OD/CRS-OVR - Unable to get an image clear enough to count
08209	Sham Eye CXL	2009-02-23	Month 3 Follow-Up	Endothelial cell count not done	OD/CRS-OVR - Endothelial cell count not done.
08210	Primary Eye Sham	2008-09-17	Treatment	Other (Specify)	OD/Sham - illumination drops, Dose 4, given at 3 minutes instead of 2 per protocol.
08210	Sham Eye CXL	2009-02-10	Treatment	UCVA not done	OD/CRS-OVR - UCVA Not Done.
08210	Sham Eye CXL	2009-02-10	Treatment	Manifest refraction not done	OD/CRS-OVR - manifest refraction not done prior to treatment.
08210	Sham Eye CXL	2009-02-10	Treatment	Manual keratometry not done	OD/CRS-OVR - manual keratometry not done prior to treatment.
08210	Sham Eye CXL	2009-02-10	Treatment	BSCVA not done	OD/CRS-OVR - BSCVA not done prior to treatment.
08210	Sham Eye CXL	2009-02-16	Week 1 Follow-Up	IOP measurement not done	OD/CRS-OVR - W1 IOP measurement not done.
08210	Fellow Eye CXL	2009-07-28	Treatment	Other (Specify)	OS/Fellow - Isotonic Riboflavin Dose 2 was given 1 minute after dose 1 instead of 2 per protocol.
08210	Fellow Eye CXL	2009-08-25	Month 1 Follow-Up	Patients questionnaire not done	(OS) Fellow eye
08210	Fellow Eye CXL	2009-08-25	Month 1 Follow-Up	RSVP questionnaire not done	(OS) Fellow eye
08210	Fellow Eye CXL	2009-12-16	Month 12 Follow-Up	Endothelial cell count not done	OD unable to acquired image today
08211	Fellow Eye CXL	2009-06-05	Month 6 Follow-Up	Patients questionnaire not done	patient questionnaire for right eye not done at 6 month follow up
08212	Primary Eye Sham	2008-08-29	Treatment	Other (Specify)	Pretreatment 4-minute dose was administered less than 2 minutes (1 minute) from previous dose for the Sham Eye
08212	Primary Eye Sham	2008-08-29	Treatment	Other (Specify)	Pretreatment 12-minute dose was administered greater than 2 minutes (3 minute) from previous dose for the Sham Eye
08212	Primary Eye Sham	2008-09-19	Month 1 Follow-Up	RSVP questionnaire not done	Sham Eye, OS
08212	Primary Eye Sham	2008-09-19	Month 1 Follow-Up	Patients questionnaire not done	Sham Eye, OS
08212	Sham Eye CXL	2008-11-11	Treatment	Other (Specify)	Pretreatment 28-minute dose was administered greater than 2 minutes (3 minute) from previous dose for the Cross-over Eye
08212	Fellow Eye CXL	2008-11-12	Treatment	Other (Specify)	Pretreatment 22-minute dose was administered greater than 2 minutes (3 minute) from previous dose for the Fellow Eye
08212	Fellow Eye CXL	2008-11-17	Week 1 Follow-Up	IOP measurement not done	IOP dot done for Cross-over eye; OS
08212	Fellow Eye CXL	2008-11-17	Week 1 Follow-Up	IOP measurement not done	IOP dot done for Fellow eye; OD
08212	Fellow Eye CXL	2009-01-23	Month 3 Follow-Up	Endothelial cell count not done	Fellow eye OD ECC photo's not done
08212	Fellow Eye CXL	2009-01-23	Month 3 Follow-Up	Endothelial cell count not done	Cross-over eye ECC Photos not done
08213	Primary Eye CXL	2008-10-22	Treatment	Other (Specify)	OD/CXL - illumination drops at 24 minutes were given at 3 minutes after last drop instead of 2 minutes per protocol.
08213	Primary Eye CXL	2008-10-22	Treatment	Other (Specify)	OD/CXL - During 2nd set of Illumination drops, drops at 14 minutes were given at 3 minutes after last drop instead of 2 minutes per protocol.
08213	Primary Eye CXL	2008-10-27	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done - Dr. deferred.

08214	Primary Eye Sham	2009-01-06	Treatment	Other (Specify)	OS/Sham - Illumination drops, second set, Dose 6 was given 3 minutes after Dose 5 and Dose 7 was given 4 minutes after Dose 6 instead of 2 minutes apart per protocol.
08214	Primary Eye Sham	2009-04-30	Month 3 Follow-Up	Other (Specify)	OS/Sham - Month 3 out of window (16 days late).
08214	Sham Eye CXL	2009-06-02	Treatment	Other (Specify)	OS/CRS-OVR - illumination drops, first set, were not given at 2 minutes apart for every dose, some doses were 1 and 3 minutes apart.
08214	Sham Eye CXL	2009-11-09	Month 6 Follow-Up	Other (Specify)	OS/CRS-OVR - Month 6 not done. Lost to Follow-up.
08214	Sham Eye CXL	2010-06-02	Month 12 Follow-Up	Other (Specify)	OS/CRS-OVR - Month 12 not done. Lost to Follow-up.
08215	Primary Eye CXL	2008-12-17	Week 1 Follow-Up	IOP measurement not done	OS/CXL - IOP measurement deferred by MD.
08222	Primary Eye Sham	2009-05-12	Treatment	Other (Specify)	Treatment 12-minute dose was administered greater than 2 minutes (3 minute) from previous dose for the Sham Eye
08222	Primary Eye Sham	2009-05-12	Treatment	Other (Specify)	Pretreatment 2-minute dose was administered greater than 2 minutes (3 minute) from previous dose for the Sham Eye
08222	Fellow Eye CXL	2009-07-21	Month 3 Follow-Up	UCVA not done	no further information
08222	Fellow Eye CXL	2009-07-21	Treatment	Other (Specify)	Pretreatment 2-minute dose was administered greater than 2 minutes (3 minute) from previous dose for the Fellow Eye
08222	Fellow Eye CXL	2009-07-21	Treatment	Other (Specify)	Pachymetry after debridement was not done for the Fellow eye
09201	Primary Eye Sham	2009-03-18	Treatment	Other (Specify)	Treatment Day 0 and Screening visit occurred on the same day.
09201	Primary Eye Sham	2009-03-18	Screening	Other (Specify)	Screening visit I-S ratio not done randomized eye (OS).
09201	Primary Eye Sham	2009-03-18	Screening	Manual keratometry not done	Screening manual keratometry not done randomized eye (OS).
09201	Primary Eye Sham	2009-03-18	Screening	Other (Specify)	Progressive Keratoconus Assessment: MRSE randomized eye (OS) values taken 29 months apart, not within 24 months per protocol.
09201	Primary Eye Sham	2009-03-18	Screening	Did not meet inclusion/exclusion criteria	Patient did not meet inclusion/exclusion criteria as I-S ratio was not done randomized eye (OS).
09201	Primary Eye Sham	2009-03-18	Screening	Endothelial cell count not done	Screening endothelial cell count not done randomized eye (OS).
09201	Primary Eye Sham	2009-03-25	Week 1 Follow-Up	BSCVA not done	Week 1 BSCVA randomized eye (OS) not done.
09201	Primary Eye Sham	2009-04-21	Month 1 Follow-Up	Manual keratometry not done	1 Month Manual Keratometry not done randomized eye (OS).
09201	Primary Eye Sham	2009-07-07	Month 3 Follow-Up	Other (Specify)	Month 3 visit is out of window, 13 days late.
10202	Fellow Eye CXL	2008-10-04	Month 1 Follow-Up	Other (Specify)	Month 1 Follow-up Visit was not done for the Fellow Eye, OD
10202	Fellow Eye CXL	2008-10-04	Month 1 Follow-Up	Other (Specify)	Month 1 Follow-up Visit was not done for the Crossover Eye, OS
10203	Primary Eye Sham	2008-06-30	Eligibility	Other (Specify)	Contact Lens Recheck not done prior to subject treatment for study eye (OD).
10203	Primary Eye Sham	2008-06-30	Screening	Patients questionnaire not done	Patient questionnaire not done for the screening visit.
10203	Fellow Eye CXL	2009-03-30	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam was out of service and therefore not obtained - Month 6 visit for crossover eye (OD).
10203	Fellow Eye CXL	2009-03-30	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam was out of service and therefore not obtained - Month 6 visit for fellow eye (OS).
10204	Fellow Eye CXL	2009-11-25	Treatment	Other (Specify)	Fellow eye (right eye) was treated greater than 6 months after the study eye.
10205	Primary Eye CXL	2008-06-23	Screening	Patients questionnaire not done	Patient questionnaire not done for screening visit.
10205	Primary Eye CXL	2008-08-11	Month 1 Follow-Up	Manual keratometry not done	Manual Keratometry not done during the month 1 visit for the study eye (left eye).
10205	Primary Eye CXL	2008-08-31	Month 3 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam not done at 3 month Fellow Eye (OD) visit. Pentacam out of service.
10205	Fellow Eye CXL	2009-09-11	Month 6 Follow-Up	Patients questionnaire not done	Patient Questionnaire not done at 6 month Fellow Eye (OD) visit.
10205	Fellow Eye CXL	2009-09-11	Month 6 Follow-Up	RSVP questionnaire not done	RSVP not done 6 month Fellow Eye (OD) visit.
10206	Primary Eye Sham	2008-06-24	Screening	Patients questionnaire not done	Patient Questionnaire either not done or cannot be found
10206	Primary Eye Sham	2008-08-20	Treatment	Other (Specify)	The time between the Screening visit (6/30/08) and the Treatment visit (8/20/08) was greater than 30 days.
10207	Primary Eye CXL	2008-06-24	Screening	Endothelial cell count not done	OD
10207	Primary Eye CXL	2008-06-24	Screening	Patients questionnaire not done	Patient questionnaire not done at the screening visit.
10207	Primary Eye CXL	2008-06-24	Screening	Other (Specify)	I/S Ration not done for OD
10207	Fellow Eye CXL	2009-04-09	Month 3 Follow-Up	Endothelial cell count not done	Assessment was attempted several times without success for the fellow eye (OD).

10207	Fellow Eye CXL	2009-06-24	Month 6 Follow-Up	Endothelial cell count not done	Assessment was attempted several times without success for the fellow eye (OD).
10207	Fellow Eye CXL	2009-11-04	Month 12 Follow-Up	Endothelial cell count not done	Assessment was attempted several times without success for the fellow eye (OD).
10208	Primary Eye Sham	2008-08-14	Screening	Manual keratometry not done	Manual Keratometry values from previous visit Prior to study start, were used
10208	Primary Eye Sham	2008-09-10	Treatment	Did not meet inclusion/exclusion criteria	Multi Vitamin (Vitamin C) was not stopped for one week prior to treatment for the Sham Eye
10208	Primary Eye Sham	2008-09-10	Treatment	Did not meet inclusion/exclusion criteria	Pretreatment BSCVA was greater than 55 in the treated eye
10208	Sham Eye CXL	2008-11-19	Treatment	Did not meet inclusion/exclusion criteria	Multi Vitamin (Vitamin C)n was not stopped for one week prior to treatment of cross-over eye
10208	Sham Eye CXL	2008-11-24	Week 1 Follow-Up	IOP measurement not done	OD, crossover
10209	Primary Eye Sham	2008-08-13	Screening	Endothelial cell count not done	Unable to obtain cell count
10209	Primary Eye Sham	2008-08-13	Screening	Manual keratometry not done	Manual K Steep was done, however the values obtained were out of range
10209	Primary Eye Sham	2008-09-17	Month 1 Follow-Up	Manual keratometry not Done	Manual K values OD were not obtainable due to high distortion
10209	Primary Eye Sham	2008-11-17	Month 3 Follow-Up	Manual keratometry not Done	Manual Keratometry was done however the values were out of range due to distortions
10209	Primary Eye Sham	2008-11-17	Month 3 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam was done, however, the values were all out of range due to distortions OD
10209	Primary Eye Sham	2008-11-17	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count was done, however the values were out range
10209	Fellow Eye CXL	2008-12-19	Week 1 Follow-up	Manual keratometry not done	Steep measurements not done due to high distortions
10209	Fellow Eye CXL	2008-12-19	Week 1 Follow-up	BSCVA not done	OD BSCVA not done as manifest refraction was not done due to dark reflexes
10209	Fellow Eye CXL	2008-12-19	Week 1 Follow-up	Manifest refraction not done	Manifest refraction could not be completed due to dark reflexes
10209	Fellow Eye CXL	2009-01-19	Month 1 Follow-up	Pentacam pachymetry, keratometry not done	Pentacam could not be obtained following several attempts due to distortions
10209	Fellow Eye CXL	2009-01-19	Month 1 Follow-up	Manual keratometry not Done	Steep measurements could not be obtained due to distortions
10210	Primary Eye CXL	2008-08-18	Screening	Endothelial cell count not done	Unable to obtain image despite several attempts
10210	Primary Eye CXL	2008-09-29	Week 1 Follow-up	IOP measurement not done	IOP not done Randomized eye (OD), deferred, BSCL not removed.
10210	Primary Eye CXL	2008-10-06	Unscheduled Visit	IOP measurement not done	IOP not done Unscheduled Visit Randomized Eye (OD)small clump of epithelial cells in central cornea, sub-I not comfortable checking IOP as may be risk to healing epithelium
10210	Fellow Eye CXL	2009-01-05	Month 1 Follow-up	Slit lamp exam not done	Month1 slit lamp exam not done Fellow Eye (OS). Patient left clinic before seeing sub-investigator for slit lamp exam.
10210	Fellow Eye CXL	2009-01-05	Month 1 Follow-up	Other (Specify)	Month 1 Cornea exam not done Fellow eye (OS). Patient left clinic early before exam was performed
10211	Primary Eye Sham	2008-12-30	Month 1 Follow-up	Other (Specify)	RSVP was not done at the time of 1 Month Follow up Visit. It was done two weeks prior to the follow up visit
10211	Primary Eye Sham	2008-12-30	Month 1 Follow-up	Other (Specify)	Patient Questionnaire was not done at the time of 1 Month Follow up Visit. It was done two weeks prior to the follow up visit
10211	Sham Eye CXL	2009-04-15	Week 1 Follow-Up	IOP measurement not done	OD- crossover; IOP deferred as BSCL was not removed secondary to epithelial defect
10211	Sham Eye CXL	2009-09-02	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam out of service
10211	Sham Eye CXL	2010-08-04	Month 12 Follow-Up	Other (Specify)	Visit was conducted 2 months outside the allowed window
10216	Primary Eye CXL	2009-01-28	Screening	Dilated fundus exam not done	Dilated fundus exam results from visit prior to study start 1/09/09 was used
10216	Primary Eye CXL	2009-01-28	Screening	IOP measurement not done	IOP value from an exam done on 1/09/09, prior to study start was used
10217		****-**-**	Month 3 Follow-Up	Other (Specify)	Month 3 visit randomized treated eye (OD) missed.

10217		****-**-**	Month 6 Follow-Up	Other (Specify)	Month 6 visit randomized treated eye (OD) missed.
10217	Primary Eye CXL	2009-06-08	Week 1 Follow-Up	IOP measurement not done	Week 1 IOP not done randomized treated eye (OD). Deferred per PI.
10217	Primary Eye CXL	2009-06-08	Week 1 Follow-Up	Manifest refraction not done	Week 1 Manifest refraction not done Randomized treated eye (OD). Deferred per PI.
10217	Primary Eye CXL	2009-07-07	Month 1 Follow-Up	IOP measurement not done	Month 1 IOP not done randomized treated eye (OD). Deferred per PI due to epithelial irregularity.
10217	Primary Eye CXL	2009-07-07	Month 1 Follow-Up	Endothelial cell count not done	Month 1 endothelial cell count attempted, but not recordable randomized treated eye (OD).
10217	Primary Eye CXL	2010-03-10	Month 12 Follow-Up	Endothelial cell count not done	Month 12 endothelial cell count attempted, but not recordable randomized treated eye (OD).
10218	Primary Eye CXL	2009-04-15	Month 1 Follow-Up	Other (Specify)	Month 1 visit randomized treated eye (OS) is 8 days out of window late.
10218	Primary Eye CXL	2009-09-16	Month 6 Follow-Up	Other (Specify)	Month 6 visit randomized treated eye (OS) is 8 days out of window late.
10219		****-**-**	Month 3 Follow-Up	Other (Specify)	This visit was missed
10219	Sham Eye CXL	2009-10-28	Treatment	Other (Specify)	OS Cross-over treatment visit was conducted greater than 6 months from Sham Control treatment
10219	Fellow Eye CXL	2009-11-19	Day 1 Follow-Up	UCVA not done	OD
10219	Fellow Eye CXL	2010-05-03	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	Equipment was out of order for the OD exam
10219	Fellow Eye CXL	2010-05-03	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	Equipment was out of order for OS exam
10221	Primary Eye CXL	2009-05-27	Treatment	Other (Specify)	Pachymetry measurement prior to debridement was not done
10221		2009-06-22	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	Unable to obtain measurements for OS following several attempts
10221	Primary Eye CXL	2009-08-26	Month 3 Follow-Up	Pentacam pachymetry, keratometry not done	OS, Pentacam equipment out of order
10221	Fellow Eye CXL	2009-11-11	Week 1 Follow-Up	IOP measurement not done	OD, due to presence of bandage lens
11201	Primary Eye Sham	2008-11-17	Screening	Manual keratometry not done	Manual Keratometry Flat was not done due to distortion for OS Sham
11201	Primary Eye Sham	2008-11-17	Eligibility	Other (Specify)	I/S ratio was not done for primary eye; OS, unable to confirm elig bility
11201	Primary Eye Sham	2009-01-07	Treatment	Slit lamp exam not done	Post Op evaluation not done for Sham OS
11201	Primary Eye Sham	2009-01-07	Treatment	Other (Specify)	Treatment visit occurred more than 30 days from screening, repeat measurement were not done for OS Sham
11201	Primary Eye Sham	2009-02-09	Month 1 Follow-Up	Manual keratometry not done	OS Sham
11201	Primary Eye Sham	2009-04-15	Month 3 Follow-Up	Other (Specify)	Month-3 exam 35 days outside window for OS Sham
11201	Sham Eye CXL	2009-05-21	Month 3 Follow-Up	Manual keratometry not done	OS Sham
11201	Sham Eye CXL	2009-06-29	Month 1 Follow-Up	Manual keratometry not done	OS Cross-over
11201	Sham Eye CXL	2009-08-24	Month 3 Follow-Up	Manual keratometry not done	OS Cross-over
11201	Sham Eye CXL	2009-08-24	Month 3 Follow-Up	Endothelial cell count not done	OS Cross-over
11201	Sham Eye CXL	2010-05-24	Month 12 Follow-Up	Patients questionnaire not done	OS Cross-over
11201	Sham Eye CXL	2010-05-24	Month 12 Follow-Up	Endothelial cell count not done	OS Cross-over
11201	Sham Eye CXL	2010-05-24	Month 12 Follow-Up	RSVP questionnaire not done	Questions 1 thru 21 are presumed as not done as pages 58 thru 61 are missing and considered lost
11202	Primary Eye Sham	2009-01-29	Treatment	Slit lamp exam not done	The slip lamp exam was not performed at Treatment for Sham Control OS
11202	Primary Eye Sham	2009-02-09	Week 1 Follow-Up	UCVA not done	The UCVA was not performed at Week 1 Follow-up Visit for the Sham Control OS.
11202	Primary Eye Sham	2009-03-09	Month 1 Follow-Up	Manual keratometry not done	Manual keratometry was not performed at Month 1 Follow-up Visit for Sham Control OS.
11202	Sham Eye CXL	2009-05-11	Month 3 Follow-Up	Other (Specify)	Month 3 Follow-up Visit was conducted 4 days out of window per protocol visit schedule. Month 3 Follow-up should have occurred between 4/9/09 through 5/7/09.
11202	Sham Eye CXL	2009-05-11	Month 3 Follow-Up	Manual keratometry not done	Manual keratometry was not performed at Month 3 Follow-up Visit for Sham Control OS.

11202	Sham Eye CXL	2009-06-22	Month 1 Follow-Up	Manual keratometry not done	Manual keratometry was not performed at Month 1 Follow-up Visit for Non-Randomized CXL Treatment OS.
11202	Sham Eye CXL	2009-08-17	Month 3 Follow-Up	Manual keratometry not done	Manual keratometry was not performed at Month 3 Follow-up Visit for Non-Randomized CXL Treatment OS.
11202	Sham Eye CXL	2009-08-17	Month 3 Follow-Up	Endothelial cell count not done	Endothelial Cell Count was not performed at Month 3 Follow-up Visit for Non-Randomized CXL Treatment OS.
11202	Sham Eye CXL	2009-11-02	Month 6 Follow-Up	Manual keratometry not done	Manual keratometry was not performed at Month 6 Follow-up Visit for Non-Randomized CXL Treatment OS.
11202	Sham Eye CXL	2010-02-22	Month 12 Follow-Up	Manual keratometry not done	Manual keratometry was not performed at Month 12 Follow-up Visit for Non-Randomized CXL Treatment OS.
11202	Sham Eye CXL	2010-02-22	Month 12 Follow-Up	Endothelial cell count not done	Endothelial Cell Count was not performed at Month 12 Follow-up Visit for Non-Randomized CXL Treatment OS.
11203	Primary Eye CXL	2008-12-22	Screening	Endothelial cell count not done	OD
11203	Primary Eye CXL	2009-01-29	Treatment	Other (Specify)	Treatment visit is greater than 30 days(37) from screening visits, no repeat measurements were done
11203	Fellow Eye CXL	2009-05-21	Month 3 Follow-Up	Manual keratometry not done	OD
11203	Fellow Eye CXL	2009-07-06	Month 1 Follow-Up	Other (Specify)	OS Month-1 Visit was 4 days outside allowed window
11203	Fellow Eye CXL	2009-07-06	Month 1 Follow-Up	Manual keratometry not done	OS
11203	Fellow Eye CXL	2009-08-13	Month 6 Follow-Up	Other (Specify)	OD Month 6 visit was missed
11203	Fellow Eye CXL	2009-08-27	Month 3 Follow-Up	Other (Specify)	OS Month-3 visit was missed
11203	Fellow Eye CXL	2010-04-02	Month 12 Follow-Up	Manual keratometry not done	OD
11203	Fellow Eye CXL	2010-04-02	Month 12 Follow-Up	Endothelial cell count not done	OD
11203	Fellow Eye CXL	2010-04-02	Month 6 Follow-Up	Manual keratometry not done	OS
11203	Fellow Eye CXL	2010-04-02	Month 6 Follow-Up	Other (Specify)	OS Month-6 visit was conducted 4 months outside allowed window
11203	Fellow Eye CXL	2010-05-24	Month 12 Follow-Up	Endothelial cell count not done	OS
11203	Fellow Eye CXL	2010-05-24	Month 12 Follow-Up	Manual keratometry not done	OS
11204	Primary Eye CXL	2009-04-02	Treatment	Other (Specify)	The second dose of Medio-Cross Riboflavin 0.1% (Isotonic) was instilled 3 minutes after the first dose; therefore, the second dose was 1 minute out of window for the cross-linking OD.
11204	Primary Eye CXL	2009-04-06	Week 1 Follow-Up	Other (Specify)	Week 1 Follow-up Visit was conducted 1 day out of window for the Cross-linking OD. The Week 1 Follow-up Visit should have occurred between 4/7/09 through 4/16/09.
11204	Primary Eye CXL	2009-05-11	Month 1 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for Month 1 Follow-up Visit for the Cross-linking OD.
11204	Primary Eye CXL	2009-07-13	Month 3 Follow-Up	Other (Specify)	Month 3 Follow-up Visit occurred 4 days out of window for the cross-linking OD. The Month 3 Follow-up Visit should have occurred between 6/11/09 through 7/9/09.
11204	Primary Eye CXL	2009-07-13	Month 3 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for Month 3 Follow-up Visit for the Cross-linking OD.
11204	Primary Eye CXL	2009-10-12	Month 6 Follow-Up	Manual keratometry not done	CXL OD
11204	Fellow Eye CXL	2009-12-21	Month 1 Follow-Up	BSCVA not done	The BCVA was not done for Month 1 Follow-up Visit for the Non-Randomized CXL Treatment fellow eye OS.
11204	Fellow Eye CXL	2010-02-15	Month 3 Follow-Up	Endothelial cell count not done	The Endothelial Cell Count was not done for Month 3 Follow-up Visit for the Non-Randomized CXL Treatment fellow eye OS.
11204	Fellow Eye CXL	2010-05-10	Month 6 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for Month 6 Follow-up Visit for the Non-Randomized CXL Treatment fellow eye OS.
11204	Fellow Eye CXL	2010-05-10	Month 12 Follow-Up	Endothelial cell count not done	The Endothelial Cell Count was not done for Month 12 Follow-up Visit for the Cross-linking OD.
11204	Fellow Eye CXL	2010-05-10	Month 12 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for Month 12 Follow-up Visit for the Cross-linking OD.
11205	Primary Eye Sham	2009-03-02	Screening	UCVA not done	UCVA was not done on OD and OS at Screening Visit.
11205	Primary Eye Sham	2009-03-02	Screening	Other (Specify)	The RGP out 12 days and not 14 days. Exception was granted by sponsor.
11205	Primary Eye Sham	2009-04-16	Treatment	Other (Specify)	Treatment Visit was greater than 30 days and no repeat measures were performed.
11205	Primary Eye Sham	2009-04-16	Treatment	Pentacam pachymetry, keratometry not done	Pentacam and pachymetry was not done at Treatment Visit.

11205	Primary Eye Sham	2009-04-16	Treatment	Other (Specify)	Pre-Treatment: 4 minute dose was 6 minutes after the 2 minute dose.
11205	Primary Eye Sham	2009-05-18	Month 1 Follow-Up	Manual keratometry not done	Manual keratometry was not done OD

Appendix C- Protocol Deviations in Study UVX-003

Subject	Treatment	Violation/ Deviation Date	Associated Visit/Event	Violation/Deviation Reason	Violation/Deviation Reason/Details
01301	Primary Eye Sham	2008-06-16	Screening	Other (Specify)	ICF #1 signed on 6/16/08 is a copy of pages 19,24,25 only- no original, not complete, #2 ICF signed on 6/16/08 page 20 is a copy, pages 24, 25 are original all other pages are missing
01301	Primary Eye Sham	2008-08-29	Week 1 Follow-Up	Other (Specify)	Sham visit out of visit window for Week 1- 1 day out of window.
01301	Sham Eye CXL	2008-11-25	Week 1 Follow-Up	Other (Specify)	CXL OD-Week 1 out of the visit window by 1 day.
01301	Sham Eye CXL	2009-03-17	Month 3 Follow-Up	Patients questionnaire not done	RSVP questionnaire pages 52-58 not done, unable to locate.
01301	Sham Eye CXL	2009-11-27	Month 1 Follow-Up	RSVP questionnaire not done	RSVP pages 31-34 not done, unable to be located.
01302	Primary Eye CXL	2008-06-16	Screening	Other (Specify)	ICF #1- (5/7/08) pgs 20, 24, 25 copy-signed 6/16/08. ICF #2-(5/7/08) pgs 20,24 only, ICF #3-(5/16/08) pag # 19 only copy no original
01302	Primary Eye CXL	2008-10-03	Week 1 Follow-Up	Other (Specify)	Week I Follow up visit out of the visit window- early by 1 day.
01302	Primary Eye CXL	2009-04-21	Month 6 Follow-Up	Other (Specify)	Subject did not return for Month 6 Follow up visit.
01302	Primary Eye CXL	2009-10-13	Month 12 Follow-Up	Other (Specify)	Subject missed the Month 12 Follow up visit.
01302	Fellow Eye CXL	2009-10-23	Week 1 Follow-Up	IOP measurement not done	IOP result for Week 1 not done.
01302	Fellow Eye CXL	2010-01-12	Month 3 Follow-Up	Other (Specify)	Month 3 out of the visit window- late 2 days.
01303	Primary Eye CXL	2008-07-07	Screening	Other (Specify)	ICF is signed by subject on 7/7/08, original of pages 17, 20,21 only, all other pages missing.
01303	Primary Eye CXL	2008-07-31	Week 1 Follow-Up	Other (Specify)	Week 1 visit out of the visit window - early by 2 days
01303	Primary Eye CXL	2009-02-17	Month 6 Follow-Up	Other (Specify)	Month 6 out of the visit window - late by 8 days.
01304	Sham Eye CXL	2009-05-04	Month 1 Follow-Up	Patients questionnaire not done	Month 1 pt questionnaire not done.
01304	Sham Eye CXL	2009-09-30	Month 12 Follow-Up	Other (Specify)	Subject did not return for Month 12 Sham OD follow up visit.
02301	Primary Eye CXL	2008-03-01	Treatment	Ultrasound pachymetry not done	"Ultrasound pachymetry measurement before debridement" was not done.
02301	Primary Eye CXL	2008-03-01	Treatment	Other (Specify)	UV-A and Riboflavin treatment was started while the ultrasound pachymetry was only 263 microns. The hypotonic r boflavin was not instilled until after the treatment had been initiated.
02302	Primary Eye Sham	2008-03-05	Screening	Did not obtain proper consent prior to performing study procedure	Informed Consent for Study UVX-002 Progressive Keratoconus was used instead of UVX-003 Corneal Ectasia.
02302	Sham Eye CXL	2008-11-19	Treatment	Other (Specify)	Illumination only lasted for 28 minutes for the crossover eye.
02302	Sham Eye CXL	2008-11-19	Treatment	Other (Specify)	Crossover treatment was completed greater than 6 months after sham treatment.
02303	Primary Eye Sham	2008-03-21	Screening	Did not meet inclusion/exclusion criteria	Diff between the initial screen refraction 2/29/08 and corneal stability refraction on 3/21/08 was greater than .75D in MRSE (difference = 4.13 diopters) in the PRIMARY EYE
02304	Primary Eye CXL	2008-09-04	Screening	RSVP questionnaire not Done	RSVP not done for the treated fellow eye screening visit
02304	Fellow Eye CXL	2008-09-29	Treatment	Other (Specify)	Treatment for fellow eye OD dated 9/29/08 is after the 6-month follow-up visit for the treatment eye (OS).
02304	Fellow Eye CXL	2008-10-22	Month 1 Follow-Up	RSVP questionnaire not done	Month 1 RSVP questionnaire not done
02304	Fellow Eye CXL	2008-12-17	Month 3 Follow-Up	RSVP questionnaire not done	Month 3 RSVP questionnaire not done
02305	Sham Eye CXL	2008-10-31	Month 1 Follow-Up	Endothelial cell count not done	An ECC printout is present and indicates 3195 cells but, the eye is not specified. The monitor could not verify if the results were for OD or OS; the test is considered "not done"
02308	Primary Eye Sham	2008-04-28	Treatment	Did not meet inclusion/exclusion criteria	The subject took multi-vitamins containing Vitamin C within 1 week (6 days) of the screening visit.
02309	Primary Eye CXL	2008-02-17	Month 3 Follow-Up	RSVP questionnaire not done	Not done for treated fellow eye (OS)
02309	Fellow Eye CXL	2008-12-10	Month 1 Follow-Up	RSVP questionnaire not done	Not done for treated fellow eye (OS)
02309	Fellow Eye CXL	2009-10-30	Month 12 Follow-Up	RSVP questionnaire not done	Not done for treated fellow eye (OS).
02310	Primary Eye Sham	2008-06-09	Treatment	Other (Specify)	Pachymetry post riboflavin dosing not done sham eye
02310	Sham Eye CXL	2008-09-22	Treatment	Other (Specify)	Eight minutes elapsed between 4 minute and 6 minute doing intervals of Riboflavin pre-UV light crossover eye.
02310	Sham Eye CXL	2008-09-22	Treatment	Other (Specify)	Total riboflavin dosing time pre-UV light was 36 minutes crossover eye.

02310	Sham Eye CXL	2009-05-06	Month 6 Follow-Up	Other (Specify)	Visit performed out of window (30 days late) crossover eye.
02311	Primary Eye Sham	2008-08-13	Screening	Slit lamp exam not done	not done in untreated fellow eye (OS)
02311	Primary Eye Sham	2008-08-13	Screening	BSCVA not done	not done in untreated fellow eye (OS)
02311	Primary Eye Sham	2008-08-13	Screening	UCVA not done	not done in untreated fellow eye (OS)
02313	Primary Eye CXL	2009-03-25	Treatment	Other (Specify)	UV light duration 28 minutes, not 30 minutes per Protocol for primary study eye (OS).
02313	Fellow Eye CXL	2009-11-11	Treatment	Other (Specify)	Treatment of fellow eye (OD) greater than 6 months post primary eye treatment. No documentation of Sponsor authorization.
02313	Fellow Eye CXL	2009-11-11	Treatment	Other (Specify)	UV light duration 27 minutes, not 30 minutes per Protocol for fellow eye (OD).
02313	Fellow Eye CXL	2009-12-17	Month 1 Follow-Up	RSVP questionnaire not done	RSVP not done at Month 1 visit for fellow eye (OD).
02313	Fellow Eye CXL	2010-04-14	Month 6 Follow-Up	RSVP questionnaire not done	RSVP not done at Month 6 visit for fellow eye (OD)
02313	Fellow Eye CXL	2010-04-14	Month 6 Follow-Up	Endothelial cell count not done	Endothelial cell count not done Month 6 fellow eye (OD).
02313	Fellow Eye CXL	2010-11-17	Month 12 Follow-Up	RSVP questionnaire not done	RSVP not done Month 12 fellow eye (OD).
02314	Sham Eye CXL	2009-11-17	Treatment	Other (Specify)	Cross-over treatment of sham eye was greater than 6 months
03201	Primary Eye CXL	2008-01-03	Screening	Endothelial cell count not done	Endothelial cell count was done but could not be interpreted.
03201	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At treatment, PI used 5 drops of hypotonic r boflavin every 5 seconds for 3 doses, then brought dose back to 2 drops every 5 seconds, to increase corneal thickness.
03201	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At illumination time, PI alternated between hypotonic riboflavin and isotonic solution for the first half of treatment time to keep pachymetry above 400 microns.
03201	Primary Eye CXL	2008-04-18	Month 3 Follow-Up	Other (Specify)	Patient outside of window visit (3/15 to 4/12/2008)
03201	Primary Eye CXL	2008-07-10	Month 6 Follow-Up	IOP measurement not done	PI not aware of full protocol requirements
03201	Primary Eye CXL	2010-01-03	Screening	Other (Specify)	Contact Lens Stability not done prior to treatment
03202	Primary Eye CXL	2007-12-14	Screening	Endothelial cell count not done	Endothelial cell count was done but could not be computed. OD
03202	Primary Eye CXL	2007-12-14	Screening	Other (Specify)	Contact lens discontinue only 6 days prior to screening vs. 14 days for RGPs - discontinued 12/8/2007
03202	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At eight minutes into the illumination time, the PI switch from one drop of isotonic r boflavin to two drops of riboflavin and maintained this through the remainder of the illumination. OD
03202	Primary Eye CXL	2008-01-05	Treatment	Other (Specify)	At 8 minutes into the illumination time, PI added hypotonic riboflavin at each interval for the remainder of the time in order to maintain corneal thickness. OD
03202	Primary Eye CXL	2008-04-03	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done at month 3. OD
03202	Fellow Eye CXL	2008-07-30	Treatment	Other (Specify)	PI used artificial tears after administration of as opposed to hypotonic riboflavin to increase pachymetry reading from 361 to 420.
03202	Fellow Eye CXL	2008-10-15	Month 3 Follow-Up	IOP measurement not done	IOP not done on month 3 visit. OS
03202	Fellow Eye CXL	2008-12-17	Month 12 Follow-Up	IOP measurement not done	IOP not done on month 12 visit. OD
03202	Fellow Eye CXL	2009-09-22	Month 12 Follow-Up	Manual keratometry not done	Manual keratometry was not done at Month 12 Visit. OS
03203	Primary Eye Sham	2008-04-17	Month 1 Follow-Up	Other (Specify)	Visit out of range - 7 days late: OS Sham
03203	Sham Eye CXL	2008-05-28	Treatment	Other (Specify)	OS Cross-over: Error in administration or recording of time of illumination
03203	Sham Eye CXL	2008-08-07	Month 3 Follow-Up	Other (Specify)	OS Cross-over: Kmax value and TKC indices not measured due to use of different pentacam than normally used on study.
03204	Primary Eye Sham	2008-01-24	Screening	Manual keratometry not done	OS Fellow
03204	Primary Eye Sham	2008-01-24	Screening	Endothelial cell count not done	OD Sham
03204	Primary Eye Sham	2008-03-07	Screening	Other (Specify)	Subject treated although contact lens stability check demonstrated that based on topography the refraction was not stable. OD Sham
03204	Primary Eye Sham	2008-03-07	Treatment	Other (Specify)	Treatment occurred greater than 30 days from screening - OD Sham
03204	Sham Eye CXL	2008-05-27	Treatment	Other (Specify)	Artificial tears in addition to hypotonic riboflavin used to increase pachymetry prior to illumination - OD Cross-over
03204	Fellow Eye CXL	2009-07-22	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry instead of protocol specified hypotonic r boflavin - OS Fellow
03204	Fellow Eye CXL	2009-07-22	Treatment	Other (Specify)	Treatment occurred more than 6 months after initial eye was treated - OS Fellow
03204	Fellow Eye CXL	2010-05-27	Month 12 Follow-Up	Endothelial cell count not done	OS Fellow

03205	Fellow Eye CXL	2008-09-05	Month 1 Follow-Up	Other (Specify)	1 Month follow up visit out of window. Subject was seen 3 weeks out of window.
03205	Fellow Eye CXL	2008-11-06	Treatment	Other (Specify)	Protocol deviation: use of artificial tears instead of Hypotonic 0.1% Riboflavin drops to increase Pachymetry.
03206	Primary Eye CXL	2008-03-18	Screening	Other (Specify)	Obtained consent on consent version 7, dated 10.24.2007, updated consent version 8, dated 11.16.2007 should have been used.
03207	Primary Eye CXL	2008-04-16	Treatment	Other (Specify)	Artificial tears and distilled water drops were used to obtain Pachymetry measurement over 400.
03208	Primary Eye Sham	2008-04-23	Treatment	Other (Specify)	Subject didn't present with a stable refraction based on MRSE, but treatment occurred
03208	Primary Eye Sham	2008-06-04	Month 1 Follow-Up	Manual keratometry not done	OD Sham
03208	Sham Eye CXL	2008-07-30	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified hypotonic riboflavin. OD Cross-over.
03208	Sham Eye CXL	2008-07-30	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified hypotonic riboflavin. OS Fellow.
03208	Sham Eye CXL	2008-08-08	Week 1 Follow-Up	Slit lamp exam not done	OS Fellow
03209	Primary Eye CXL	2008-05-16	Eligibility	Other (Specify)	Site instilled sterile water in addition to riboflavin to assist in raising pachymetry values.
03209	Primary Eye CXL	2008-05-16	Screening	Other (Specify)	On the Consent, the subject indicated they wanted their PCP notified of study participation; however, the PCP's contact information was not completed.
03209	Primary Eye CXL	2008-12-12	Month 6 Follow-Up	Other (Specify)	Month 6 follow-up visit was conducted 14 days out of window. Visit should have occurred between 10/23/08 through 11/28/08.
03210	Primary Eye CXL	2008-06-12	Week 1 Follow-Up	IOP measurement not done	IOP not done at week 1 - Randomized Eye OS
03210	Fellow Eye CXL	2008-09-09	Treatment	Other (Specify)	PI used Artificial Tears rather than isotonic saline to increase corneal thickness. - Fellow OD
03210	Fellow Eye CXL	2008-09-18	Week 1 Follow-Up	IOP measurement not done	IOP not done at Week 1 - Fellow OD
03210	Fellow Eye CXL	2008-11-20	Month 6 Follow-Up	IOP measurement not done	IOP not done on Month 6 Visit - Randomized OS
03210	Fellow Eye CXL	2008-11-20	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 Visit - Fellow OD
03210	Fellow Eye CXL	2009-03-24	Month 6 Follow-Up	IOP measurement not done	IOP not done on Month 6 Visit - Fellow OD
03211	Primary Eye Sham	2008-05-29	Treatment	Other (Specify)	PI used artificial tears rather than hypotonic riboflavin in order to increase the corneal thickness (348 to 436).
03211	Primary Eye Sham	2008-06-03	Week 1 Follow-Up	IOP measurement not done	IOP not done at week 1 - Fellow OS
03211	Sham Eye CXL	2008-09-05	Treatment	Other (Specify)	PI used artificial tears rather than hypotonic riboflavin to increase corneal thickness (348 to 436). - OD
03211	Sham Eye CXL	2008-09-10	Week 1 Follow-Up	IOP measurement not done	IOP not done at Week 1 - Crossover OD
03211	Sham Eye CXL	2008-12-10	Month 3 Follow-Up	IOP measurement not done	IOP not done at Month 3 Visit - Crossover OD
03211	Sham Eye CXL	2008-12-10	Month 6 Follow-Up	IOP measurement not done	IOP not done at month 6 - Fellow - OS
03212	Primary Eye CXL	2008-06-24	Week 1 Follow-Up	IOP measurement not done	OS CXL
03212	Primary Eye CXL	2008-09-03	Month 3 Follow-Up	Corneal topography not done	OS CXL
03212	Primary Eye CXL	2008-11-20	Month 6 Follow-Up	IOP measurement not done	OS CXL
03212	Fellow Eye CXL	2009-07-29	Treatment	Other (Specify)	Fellow eye treated more than 6 months after first treated eye
03212	Fellow Eye CXL	2009-07-29	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified Hypotonic riboflavin - OD Fellow
03212	Fellow Eye CXL	2009-08-05	Week 1 Follow-Up	IOP measurement not done	OD Fellow
03212	Fellow Eye CXL	2009-10-14	Month 3 Follow-Up	RSVP questionnaire not done	OD Fellow
03212	Fellow Eye CXL	2009-10-14	Month 3 Follow-Up	Patients questionnaire not done	OD Fellow
03213	Primary Eye Sham	2008-09-04	Week 1 Follow-Up	IOP measurement not done	IOP not done at Week 1 Visit - Sham Eye - OD
03213	Primary Eye Sham	2008-09-17	Month 12 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 12 Visit as it was out of range - Crossover - OD
03213	Sham Eye CXL	2008-11-12	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness - OD
03213	Sham Eye CXL	2008-11-12	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness - OS
03213	Sham Eye CXL	2008-11-20	Week 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 Visit - Fellow - OS
03213	Sham Eye CXL	2008-11-20	Week 1 Follow-Up	IOP measurement not done	IOP not done on Week 1 Visit - Crossover - OD
03213	Sham Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - Fellow - OS
03213	Sham Eye CXL	2008-12-04	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - Crossover OD

03213	Sham Eye CXL	2008-12-04	Month 1 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 1 Visit as it was out of range - Crossover - OD
03213	Sham Eye CXL	2009-02-06	Month 3 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 3 Visit as it was out of range - Crossover - OD
03213	Sham Eye CXL	2009-05-21	Month 6 Follow-Up	Other (Specify)	Manual keratometry not recorded at Month 6 Visit as it was out of range - Crossover - OD
03214	Primary Eye Sham	2008-09-04	Week 1 Follow-Up	IOP measurement not done	OD
03214	Sham Eye CXL	2008-10-29	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic riboflavin (Crossover OD)
03214	Sham Eye CXL	2008-10-29	Month 3 Follow-Up	Other (Specify)	Visit out of range - 1 day early; OD Sham
03214	Sham Eye CXL	2008-10-29	Treatment	Other (Specify)	Illumination procedure was performed although pachymetry was not greater than or equal to 400.
03214	Sham Eye CXL	2008-11-20	Month 1 Follow-Up	IOP measurement not done	Crossover OD
03214	Sham Eye CXL	2009-01-28	Month 3 Follow-Up	IOP measurement not done	Crossover OD
03214	Fellow Eye CXL	2009-05-06	Treatment	Other (Specify)	Artificial Tears used to increase pachymetry instead of protocol specified Hypotonic Riboflavin
03214	Fellow Eye CXL	2009-05-06	Month 6 Follow-Up	IOP measurement not done	Crossover OD
03214	Fellow Eye CXL	2009-05-12	Week 1 Follow-Up	IOP measurement not done	fellow eye OS
03214	Fellow Eye CXL	2009-06-18	Month 1 Follow-Up	Other (Specify)	Visit out of range - 1 day late; OS Fellow
03214	Fellow Eye CXL	2009-06-18	Month 1 Follow-Up	IOP measurement not done	OS Fellow
03215	Primary Eye CXL	2008-08-19	Screening	Did not obtain proper consent prior to performing study procedure	Person obtaining consent did not sign and date the ICF.
03215	Primary Eye CXL	2008-08-26	Treatment	Other (Specify)	Eye was treated although eye did not meet stability criteria for MRSE. Difference was 1.62 and needed to be less than or equal to 0.75D - OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Other (Specify)	Failed to measure and/or record debridement diameter - OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Slit lamp exam not done	OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Ultrasound pachymetry not done	Failed to measure and/or record pachymetry before debridement OS CXL
03215	Primary Eye CXL	2008-08-26	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Riboflavin- OS CXL
03215	Primary Eye CXL	2008-09-30	Month 1 Follow-Up	IOP measurement not done	OS CXL
03215	Primary Eye CXL	2008-11-17	Month 3 Follow-Up	IOP measurement not done	OS CXL
03215	Fellow Eye CXL	2008-12-18	Month 1 Follow-Up	IOP measurement not done	OD Fellow
03215	Fellow Eye CXL	2009-02-24	Month 6 Follow-Up	IOP measurement not done	OS CXL
03215	Fellow Eye CXL	2009-02-24	Month 3 Follow-Up	IOP measurement not done	OD Fellow
03216	Primary Eye Sham	2008-08-13	Screening	Endothelial cell count not Done	Not performed on OD
03216	Primary Eye Sham	2008-08-13	Screening	Endothelial cell count not done	Not performed on OS
03216	Primary Eye Sham	2008-09-10	Week 1 Follow-Up	IOP measurement not done	Not performed on OS Sham Eye
03216	Primary Eye Sham	2008-09-30	Month 1 Follow-Up	IOP measurement not done	Not performed on OS Sham Eye
03216	Sham Eye CXL	2008-11-25	Month 3 Follow-Up	IOP measurement not done	Not performed on Sham OS
03216	Sham Eye CXL	2010-01-20	Month 12 Follow-Up	Other (Specify)	Visit was conducted 1 day out of window. Visit should have occurred between 9/1/09 through 1/19/10
03217	Primary Eye CXL	2008-01-29	Other	Other (Specify)	Site personnel who obtained consent did not properly sign and date the consent where indicated.
03217	Primary Eye CXL	2008-09-17	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic Riboflavin - OS CXL
03217	Primary Eye CXL	2008-09-17	Treatment	Other (Specify)	Subject was treated without verifying that refraction was stable. OS CXL
03217	Primary Eye CXL	2008-09-24	Week 1 Follow-Up	IOP measurement not done	Not performed on CXL Tx OS
03217	Primary Eye CXL	2008-12-12	Month 3 Follow-Up	IOP measurement not done	Not performed on CXL Tx OS
03218	Primary Eye CXL	2008-09-24	Treatment	Other (Specify)	Protocol deviation: use of artificial tears instead of Hypotonic 0.1% R boflavin drops to increase Pachymetry
03218	Primary Eye CXL	2008-12-23	Month 3 Follow-Up	Other (Specify)	Protocol Violation: Month 3 Follow up visit did not occur.
03218	Primary Eye CXL	2010-01-21	Month 12 Follow-Up	Other (Specify)	Month 12 visit was two months out of window. Visit windows were 07/01/2009 through 11/18/2009.
03219	Primary Eye CXL	2008-12-18	Month 3 Follow-Up	IOP measurement not done	Deviation

03219	Fellow Eye CXL	2009-01-29	Treatment	Other (Specify)	Deviation: Use of artificial tears to increase Pachymetry.
03219	Fellow Eye CXL	2009-03-06	Month 1 Follow-Up	Manual keratometry not done	Deviation
03219	Fellow Eye CXL	2009-04-22	Month 3 Follow-Up	Other (Specify)	Deviation: Pentacam Indices not obtained.
03219	Fellow Eye CXL	2009-09-26	Treatment	Other (Specify)	Deviation: Use of artificial tears to increase Pachymetry.
03220	Primary Eye Sham	2008-10-13	Week 1 Follow-Up	IOP measurement not done	OS Sham
03220	Sham Eye CXL	2008-12-19	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic Riboflavin - OS Cross-over
03220	Sham Eye CXL	2008-12-19	Month 3 Follow-Up	IOP measurement not done	OS Sham
03220	Sham Eye CXL	2008-12-23	Week 1 Follow-Up	Other (Specify)	Visit out of range - 1 day early - OS Cross-over
03220	Sham Eye CXL	2008-12-23	Week 1 Follow-Up	IOP measurement not done	OS Cross-over
03220	Sham Eye CXL	2009-01-23	Month 1 Follow-Up	IOP measurement not done	OS Cross-over
03220	Sham Eye CXL	2009-03-11	Month 3 Follow-Up	IOP measurement not done	OS Cross-over
03220	Sham Eye CXL	2009-06-18	Month 6 Follow-Up	IOP measurement not done	OS Cross-over
03221	Primary Eye Sham	2008-10-15	Week 1 Follow-Up	IOP measurement not done	Sham Eye – OD
03221	Primary Eye Sham	2009-01-08	Month 3 Follow-Up	IOP measurement not done	Sham Eye – OD
03221	Sham Eye CXL	2009-04-16	Treatment	Other (Specify)	PI used artificial tears versus hypotonic riboflavin to increase corneal thickness.
03221	Sham Eye CXL	2009-04-21	Week 1 Follow-Up	IOP measurement not done	Crossover – OD
03221	Sham Eye CXL	2009-05-21	Month 1 Follow-Up	IOP measurement not done	Crossover – OD
03221	Sham Eye CXL	2009-07-14	Month 3 Follow-Up	IOP measurement not done	Crossover – OD
03221	Sham Eye CXL	2009-10-28	Month 6 Follow-Up	IOP measurement not done	Crossover – OD
03222	Primary Eye Sham	2008-10-08	Screening	Endothelial cell count not done	OS
03222	Primary Eye Sham	2008-10-22	Week 1 Follow-Up	IOP measurement not done	OD Sham
03222	Primary Eye Sham	2008-11-19	Month 1 Follow-Up	IOP measurement not done	OD Sham
03222	Sham Eye CXL	2009-04-24	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic Riboflavin - OD Cross-over
03222	Sham Eye CXL	2009-04-24	Treatment	Other (Specify)	Non-randomized OD was treated outside of the acceptable window of greater than 3 months and less than 6 months by 10 days: OD Cross-over
03222	Sham Eye CXL	2009-04-29	Week 1 Follow-Up	IOP measurement not done	OD Cross-over
03222	Sham Eye CXL	2009-06-03	Month 1 Follow-Up	IOP measurement not done	OD Cross-over
03223	Primary Eye Sham	2008-11-25	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - Sham OD
03223	Sham Eye CXL	2009-02-27	Treatment	Other (Specify)	PI used artificial tears as opposed to hypotonic riboflavin to increase corneal thickness. Crossover OD
03223	Sham Eye CXL	2009-02-27	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - Sham OD
03223	Sham Eye CXL	2009-03-04	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - Crossover OD
03223	Sham Eye CXL	2009-03-25	Month 1 Follow-Up	IOP measurement not done	IOP was not done on Month 1 Visit - Crossover OD
03223	Sham Eye CXL	2009-05-14	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - Crossover OD
03224	Primary Eye CXL	2008-12-03	Treatment	Other (Specify)	Deviation: Use of artificial tears to increase Pachymetry.
03224	Primary Eye CXL	2008-12-03	Treatment	Other (Specify)	Deviation: Last three drops of Medio-Cross Riboflavin 0.1% (Isotonic) drops administered 1 minute apart instead of 2 minutes per protocol.
03224	Primary Eye CXL	2008-12-10	Week 1 Follow-Up	IOP measurement not done	Deviation
03224	Primary Eye CXL	2009-03-04	Month 3 Follow-Up	IOP measurement not done	Deviation
03225	Primary Eye Sham	2008-12-23	Week 1 Follow-Up	IOP measurement not done	Sham OS
03225	Primary Eye Sham	2009-01-27	Month 1 Follow-Up	IOP measurement not done	Sham OS
03225	Primary Eye Sham	2009-04-21	Month 3 Follow-Up	IOP measurement not done	Sham OS
03225	Sham Eye CXL	2009-07-07	Treatment	Other (Specify)	PI used Artificial Tears as opposed to hypotonic riboflavin to increase corneal thickness.
03225	Sham Eye CXL	2009-07-07	Month 6 Follow-Up	IOP measurement not done	Sham OS

03225	Sham Eye CXL	2009-07-16	Week 1 Follow-Up	IOP measurement not done	Crossover OS
03225	Sham Eye CXL	2009-08-18	Month 1 Follow-Up	IOP measurement not done	Crossover OS
03225	Sham Eye CXL	2009-10-13	Month 3 Follow-Up	Other (Specify)	After multiple calls the patient was a "no show" for Month 3 Visit.
03225	Sham Eye CXL	2010-01-08	Month 6 Follow-Up	IOP measurement not done	Crossover OS
03225	Sham Eye CXL	2010-05-22	Month 12 Follow-Up	Other (Specify)	After numerous call, the patient would not come in for 12 Month Visit, consequently, he was terminated on 8/1/8/2010 (mo. 6), as the IRB closed the study at the PI's request.
03226	Primary Eye Sham	2009-01-15	Treatment	IOP measurement not done	Deviation
03226	Primary Eye Sham	2009-01-20	Week 1 Follow-Up	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-04-16	Treatment	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-04-16	Treatment	Other (Specify)	Site used artificial tears instead of protocol specified hypotonic r boflavin to increase Pachymetry after debridement and before treatment -OS Cross-over
03226	Sham Eye CXL	2009-04-17	Week 1 Follow-Up	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-07-21	Month 3 Follow-Up	IOP measurement not done	Deviation
03226	Sham Eye CXL	2009-10-20	Month 6 Follow-Up	IOP measurement not done	Deviation
03227	Primary Eye Sham	2009-01-28	Week 1 Follow-Up	IOP measurement not done	Deviation
03227	Primary Eye Sham	2009-02-24	Month 1 Follow-Up	IOP measurement not done	Deviation
03227	Primary Eye Sham	2009-04-28	Month 3 Follow-Up	IOP measurement not done	Deviation
03227	Sham Eye CXL	2009-06-17	Month 6 Follow-Up	IOP measurement not done	Deviation
03227	Sham Eye CXL	2009-06-17	Treatment	Other (Specify)	Use of artificial tears to increase Pachymetry
03227	Sham Eye CXL	2009-06-24	Week 1 Follow-Up	IOP measurement not done	Deviation
03227	Sham Eye CXL	2009-09-09	Month 3 Follow-Up	IOP measurement not done	Deviation
03228	Primary Eye CXL	2009-01-22	Treatment	Other (Specify)	Patient used Artificial Tear in the place of Hypotonic Riboflavin to increase corneal thickness. CXL OD
03228	Primary Eye CXL	2009-03-05	Month 1 Follow-Up	IOP measurement not done	IOP not done at Month 1 Visit. CXL OD
03229	Primary Eye CXL	2009-02-03	Week 1 Follow-Up	IOP measurement not done	OS 1 Wk. Deviation IOP not obtained
03229	Primary Eye CXL	2009-02-24	Month 1 Follow-Up	IOP measurement not done	OS 1 Mo. Deviation IOP not obtained
03229	Primary Eye CXL	2009-08-04	Month 3 Follow-Up	IOP measurement not done	OS 6 Mo. Deviation IOP not obtained
03230	Primary Eye Sham	2009-01-08	Screening	Did not obtain proper consent prior to performing study procedure	Subject signed ICF in only one of two required places and didn't answer question regarding 'inform PCP'
03230	Primary Eye Sham	2009-01-08	Screening	Endothelial cell count not done	Machine was down. ECC collected on 1/29/09 treatment visit – OS Sham
03230	Primary Eye Sham	2009-02-03	Week 1 Follow-Up	IOP measurement not done	OS Sham
03230	Primary Eye Sham	2009-03-06	Month 1 Follow-Up	IOP measurement not done	OS Sham
03230	Primary Eye Sham	2009-04-24	Month 3 Follow-Up	IOP measurement not done	OS Sham
03230	Primary Eye Sham	2009-04-24	Month 3 Follow-Up	Endothelial cell count not done	OS Sham
03230	Sham Eye CXL	2009-07-01	Month 6 Follow-Up	IOP measurement not done	OS Sham
03230	Sham Eye CXL	2009-07-01	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic Riboflavin - OS Cross-over
03230	Sham Eye CXL	2009-07-08	Week 1 Follow-Up	IOP measurement not done	OS Cross-over
03230	Sham Eye CXL	2009-08-04	Month 1 Follow-Up	IOP measurement not done	OS Cross-over
03230	Fellow Eye CXL	2009-11-18	Treatment	Other (Specify)	Fellow eye treated later than the 6 month visit for the randomized eye by approximately 4 months: OD Fellow
03230	Fellow Eye CXL	2009-11-18	Month 6 Follow-Up	IOP measurement not done	OS Cross-over

03230	Fellow Eye CXL	2010-02-19	Month 3 Follow-Up	IOP measurement not done	OD Fellow
03231	Primary Eye CXL	2009-01-30	Treatment	Other (Specify)	PI used artificial tears rather than hypotonic riboflavin to increase corneal thickness.
03231	Primary Eye CXL	2009-02-03	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - CXL - OS
03231	Primary Eye CXL	2009-03-11	Month 1 Follow-Up	IOP measurement not done	IOP was not done on Month 1 Visit - CXL - OS
03231	Primary Eye CXL	2009-04-24	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - CXL - OS
03232	Primary Eye CXL	2008-12-09	Screening	Endothelial cell count not done	Endothelial cell count was not done at screen - Fellow OD
03232	Primary Eye CXL	2009-03-03	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic Riboflavin to increase corneal thickness. Tx - CXL - OS.
03232	Primary Eye CXL	2009-03-03	Treatment	Other (Specify)	Treatment Visit is outside 30 day window. Ocular measurements were done on this visit.
03232	Primary Eye CXL	2009-03-10	Week 1 Follow-Up	IOP measurement not done	IOP was not done on Week 1 Visit - CXL- OS
03232	Primary Eye CXL	2009-04-14	Month 1 Follow-Up	IOP measurement not done	IOP was not done on Month 1 Visit - CXL- OS
03232	Primary Eye CXL	2009-06-04	Month 3 Follow-Up	IOP measurement not done	IOP was not done on Month 3 Visit - CXL- OS
03233	Primary Eye Sham	2009-03-31	Week 1 Follow-Up	IOP measurement not done	OS Sham
03233	Primary Eye Sham	2009-05-08	Month 1 Follow-Up	IOP measurement not done	OS Sham
03233	Primary Eye Sham	2009-05-08	Month 1 Follow-Up	Other (Specify)	Visit out of range - 2 days late: OS Sham
03233	Primary Eye Sham	2009-06-17	Month 3 Follow-Up	IOP measurement not done	OS Sham
03234	Primary Eye Sham	2009-03-10	Screening	Endothelial cell count not done	OS Fellow
03234	Primary Eye Sham	2009-03-10	Screening	Other (Specify)	Subject failed to sign PHI release as part of the ICF
03234	Primary Eye Sham	2009-04-14	Treatment	Other (Specify)	Treatment occurred more than 30 days after screening: OD Sham
03234	Primary Eye Sham	2009-04-21	Week 1 Follow-Up	IOP measurement not done	OD Sham
03234	Primary Eye Sham	2009-05-21	Month 1 Follow-Up	IOP measurement not done	OD Sham
03234	Primary Eye Sham	2009-07-16	Month 3 Follow-Up	IOP measurement not done	OD Sham
03234	Sham Eye CXL	2009-09-01	Month 6 Follow-Up	IOP measurement not done	OD Sham
03234	Sham Eye CXL	2009-09-01	Treatment	Other (Specify)	Site used Artificial Tears to increase pachymetry instead of protocol specified Hypotonic Riboflavin: OD Cross-over
03234	Sham Eye CXL	2009-09-09	Week 1 Follow-Up	IOP measurement not done	OD Cross-over
03234	Sham Eye CXL	2009-10-07	Month 1 Follow-Up	IOP measurement not done	OD Cross-over
03234	Sham Eye CXL	2010-02-03	Month 6 Follow-Up	IOP measurement not done	OD Cross-over
03235	Primary Eye CXL	2009-04-29	Treatment	Other (Specify)	PI used Artificial Tears as opposed to isotonic Riboflavin to increase corneal thickness.
03235	Primary Eye CXL	2009-05-06	Week 1 Follow-Up	IOP measurement not done	IOP was not done at Week 1 Visit. CXL - OD
03235	Primary Eye CXL	2009-05-27	Month 1 Follow-Up	IOP measurement not done	IOP was not done at Month 1 Visit. CXL - OD
03235	Primary Eye CXL	2009-07-30	Month 3 Follow-Up	IOP measurement not done	IOP was not done at Month 3 Visit. CXL - OD
03235	Primary Eye CXL	2009-11-11	Month 6 Follow-Up	Manual keratometry not done	Manual Keratometry was not done on Month 6 Visit. CXL - OD
03236	Primary Eye Sham	2009-05-12	Week 1 Follow-Up	IOP measurement not done	OS SHAM 1 Wk. - Deviation IOP was not obtained.
03236	Primary Eye Sham	2009-06-17	Month 1 Follow-Up	IOP measurement not done	OS SHAM 1 Mo. Deviation IOP not obtained.
03236	Primary Eye Sham	2009-08-06	Month 3 Follow-Up	IOP measurement not done	OS 3 Mo Deviation-IOP not obtained
03236	Sham Eye CXL	2009-09-29	Week 1 Follow-Up	IOP measurement not done	OS Crossover 1 Wk. Deviation IOP not obtained.
03236	Sham Eye CXL	2009-10-30	Month 1 Follow-Up	IOP measurement not done	OS Crossover 1 Mo. Deviation IOP not obtained
03236	Sham Eye CXL	2009-12-31	Month 3 Follow-Up	IOP measurement not done	OS Crossover 3 Mo IOP not obtained
03237	Primary Eye CXL	2009-05-14	Treatment	Other (Specify)	Artificial tears used to increase pachymetry instead of protocol specified Hypotonic Riboflavin: OD CXL
03237	Primary Eye CXL	2009-05-19	Week 1 Follow-Up	IOP measurement not done	OD CXL
03237	Primary Eye CXL	2009-06-23	Month 1 Follow-Up	IOP measurement not done	OD CXL
03237	Primary Eye CXL	2009-08-12	Month 3 Follow-Up	IOP measurement not done	OD CXL

03238	Primary Eye CXL	2009-03-26	Screening	Endothelial cell count not done	OS Fellow
03238	Primary Eye CXL	2009-05-14	Treatment	Other (Specify)	Artificial tears was used to increase pachymetry instead of protocol specified Hypotonic Riboflavin: OS CXL
03238	Primary Eye CXL	2009-05-14	Treatment	Other (Specify)	Treatment was done more than 30 days after screening: OS CXL
03238	Primary Eye CXL	2009-05-20	Week 1 Follow-Up	IOP measurement not done	OS CXL
03238	Primary Eye CXL	2009-06-23	Month 1 Follow-Up	IOP measurement not done	OS CXL
03238	Primary Eye CXL	2009-08-18	Month 3 Follow-Up	IOP measurement not done	OS CXL
03239	Primary Eye Sham	2009-07-08	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done on Month 1 Visit - Sham - OS
03239	Primary Eye Sham	2009-09-08	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done on Month 3 Visit - Sham - OS
03239	Sham Eye CXL	2009-10-30	Month 6 Follow-Up	IOP measurement not done	IOP measurement not done on Month 6 Visit - Sham - OS
03239	Sham Eye CXL	2009-10-30	Treatment	Other (Specify)	PI used artificial tears as opposed to hypotonic riboflavin to increase corneal thickness. CRS-OVR - OS
03239	Sham Eye CXL	2009-11-03	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done on Week 1 Visit - CRS-OVR - OS
03239	Sham Eye CXL	2009-11-24	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done on Month 1 Visit - CRS-OVR - OS
03239	Sham Eye CXL	2010-01-19	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done on Month 3 Visit - CRS-OVR - OS
03240	Primary Eye CXL	2009-06-04	Treatment	Other (Specify)	OD Treatment Use of artificial tears to increase pachymetry
03240	Primary Eye CXL	2009-06-10	Week 1 Follow-Up	IOP measurement not done	OD 1 Wk. Deviation IOP Not obtained
03240	Primary Eye CXL	2009-07-17	Month 1 Follow-Up	Other (Specify)	OD 1 Mo. Deviation Visit took place 1 day out of window.
03240	Primary Eye CXL	2009-07-17	Month 1 Follow-Up	IOP measurement not done	OD 1Mo. Deviation IOP not obtained
03240	Primary Eye CXL	2009-12-01	Month 6 Follow-Up	IOP measurement not done	OD 6 Mo Deviation IOP not obtained
03241	Primary Eye Sham	2009-07-21	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done at Week 1 Visit - Sham - OD
03241	Primary Eye Sham	2009-08-25	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - Sham - OD
03241	Primary Eye Sham	2009-10-15	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done Month 3 - Sham OD
03241	Primary Eye Sham	2009-10-15	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done at Month 3 Visit - Sham - OD
03241	Sham Eye CXL	2010-01-15	Month 6 Follow-Up	IOP measurement not done	IOP measurement not done at Month 6 Visit - Sham - OD
03241	Sham Eye CXL	2010-01-15	Treatment	Other (Specify)	PI used Artificial Tears rather than hypotonic R boflavin to increase corneal thickness.
03241	Sham Eye CXL	2010-01-21	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done at Week 1 Visit - CRS-ORV
03241	Sham Eye CXL	2010-02-18	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done at Month 1 Visit - CRS-ORV
03241	Sham Eye CXL	2010-03-31	Month 3 Follow-Up	IOP measurement not done	IOP measurement not done at Month 3 Visit - CRS-ORV
03241	Sham Eye CXL	2010-07-27	Month 6 Follow-Up	IOP measurement not done	IOP measurement not done at Month 6 Visit - CRS-ORV
03242	Primary Eye Sham	2009-01-19	Week 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Week 1 Visit - CRS-OVR - OD
03242	Primary Eye Sham	2009-09-04	Week 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Week 1 Visit - Sham OD
03242	Primary Eye Sham	2009-10-07	Month 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 1 Visit - Sham OD
03242	Sham Eye CXL	2010-01-13	Treatment	Other (Specify)	PI used Artificial Tears as opposed to hypotonic Riboflavin in order to increase corneal thickness.
03242	Sham Eye CXL	2010-01-13	Month 6 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 6 Visit - Sham OD
03242	Sham Eye CXL	2010-02-17	Month 1 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 1 Visit - CRS-OVR - OD
03242	Sham Eye CXL	2010-03-29	Month 3 Follow-Up	IOP measurement not done	IOP measurement was not done on Month 6 Visit - CRS-OVR - OD
03243	Primary Eye CXL	2009-09-02	Treatment	Other (Specify)	PI used artificial tears as opposed to hypotonic riboflavin to increase corneal thickness. CXL - OS
03243	Primary Eye CXL	2009-09-09	Week 1 Follow-Up	IOP measurement not done	IOP measurement not done on Week 1 - CXL - OS
03243	Primary Eye CXL	2009-10-16	Month 1 Follow-Up	IOP measurement not done	IOP measurement not done on Month 1 - CXL - OS
03243	Primary Eye CXL	2009-11-20	Month 3 Follow-Up	Endothelial cell count not done	Endothelial cell count not done on Month 3 - CXL - OS
03243	Primary Eye CXL	2009-11-20	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry not done on Month 3 - CXL - OS
03244	Primary Eye CXL	2009-10-20	Treatment	Other (Specify)	Deviation- OS Artificial tears used to increase pachymetry.

03244	Primary Eye CXL	2009-10-28	Week 1 Follow-Up	IOP measurement not done	Deviation OS 1 Wk. IOP not obtained.
03244	Primary Eye CXL	2009-12-11	Month 1 Follow-Up	IOP measurement not done	Deviation OS 1 Mo. IOP not obtained
03244	Primary Eye CXL	2009-12-11	Month 1 Follow-Up	Other (Specify)	Deviation 1 Mo. OS follow up visit done 10 days out of window.
03244	Primary Eye CXL	2010-01-19	Month 3 Follow-Up	IOP measurement not done	Deviation 3 Mo OS IOP not obtained
03245	Primary Eye Sham	2009-11-17	Day 1 Follow-Up	IOP measurement not done	Deviation 1 week OS SHAM IOP not obtained.
03245	Primary Eye Sham	2009-12-16	Month 1 Follow-Up	IOP measurement not done	Deviation 1 Mo OS SHAM IOP not obtained
03245	Primary Eye Sham	2010-01-15	Month 3 Follow-Up	IOP measurement not done	Deviation Mo 3 OS SHAM IOP not obtained
03245	Primary Eye Sham	2010-01-15	Month 3 Follow-Up	Other (Specify)	Deviation Visit out of range - 4 days early
03245	Primary Eye Sham	2010-04-14	Month 6 Follow-Up	IOP measurement not done	Deviation Mo 6 OS SHAM IOP not obtained.
03246	Primary Eye CXL	2009-11-19	Week 1 Follow-Up	IOP measurement not done	OS CXL
03246	Primary Eye CXL	2009-11-19	Screening	Other (Specify)	Subject did not sign HIPAA release section of ICF
03246	Primary Eye CXL	2009-12-22	Month 1 Follow-Up	IOP measurement not done	OS CXL
03247	Primary Eye CXL	2009-11-24	Treatment	Other (Specify)	Treatment Deviation OS Artificial tears used to increase Pachymetry
03247	Primary Eye CXL	2009-12-01	Week 1 Follow-Up	IOP measurement not done	1 Wk OS Deviation IOP not obtained
03247	Primary Eye CXL	2009-12-30	Month 1 Follow-Up	IOP measurement not done	1 Mo OS Deviation IOP not obtained
03247	Primary Eye CXL	2010-03-02	Month 3 Follow-Up	IOP measurement not done	3 Mo OS Deviation IOP not obtained
03248	Primary Eye Sham	2009-11-05	Screening	Endothelial cell count not done	IOP not performed on OS
03248	Primary Eye Sham	2009-12-10	Treatment	Other (Specify)	Treatment Day was > 30 days after Screening day. Screening occurred on 11/05/09. TX Visit occurred on 12/10/09.
03248	Primary Eye Sham	2010-01-14	Month 1 Follow-Up	IOP measurement not done	IOP not performed on the Sham OD
03249	Primary Eye Sham	2009-12-09	Screening	IOP measurement not done	Screen OD Deviation IOP not obtained
03249	Primary Eye Sham	2009-12-31	Week 1 Follow-Up	IOP measurement not done	1 Wk OD Deviation IOP not obtained
03249	Primary Eye Sham	2009-12-31	Week 1 Follow-Up	Other (Specify)	1 Wk. OD scheduled visit out of window by one day.
03249	Primary Eye Sham	2010-01-27	Month 1 Follow-Up	IOP measurement not done	1 Mo OD Deviation IOP not obtained
03249	Primary Eye Sham	2010-03-16	Month 3 Follow-Up	Other (Specify)	3 Mo OD Deviation visit was not done.
03301	Primary Eye Sham	2008-01-29	Screening	RSVP questionnaire not done	RSVP Questionnaire was administered on 2/6/08 (Treatment Visit) instead of on 1/29/08 (Screening Visit).
03301	Primary Eye Sham	2008-01-29	Screening	Patients questionnaire not done	Patient Questionnaire was administered on 2/6/08 (Treatment Visit) instead of on 1/29/08 (Screening Visit).
03301	Primary Eye Sham	2008-01-29	Treatment	Did not obtain proper consent prior to performing study procedure	Screening visit was on 1/29/08 but the subject was not consented until 2/6/08 (Treatment Visit).
03303	Primary Eye Sham	2008-02-19	Week 1 Follow-Up	BSCVA not done	Protocol required BSCVA not measured.
03305	Primary Eye CXL	2008-02-18	Screening	RSVP questionnaire not done	Completed on day of treatment (4/2/08).
03305	Primary Eye CXL	2008-02-18	Screening	Patients questionnaire not done	Completed on treatment day (4/2/08).
03305	Primary Eye CXL	2008-04-02	Treatment	Other (Specify)	Treatment not within 1 to 30 days of screening visit (2/18/08).
03308	Primary Eye Sham	2008-03-14	Screening	Patients questionnaire not done	Patient questionnaire and RSVP completed on 2008-4-2 (Treatment) vs. 2008-3-14 (Screen).
03309	Primary Eye Sham	2008-04-08	Screening	Other (Specify)	Patient Questionnaire and RSVP completed (2009-4-23) Treatment vs. (2008-4-8) Screening.
03309	Sham Eye CXL	2008-12-09	Month 1 Follow-Up	Other (Specify)	1 Month Visit was completed on 2008-12-09 1 day out of study visit window.
03309	Sham Eye CXL	2009-12-21	Month 12 Follow-Up	Other (Specify)	12 month follow-up visit occurred 2009-12-28 seven days outside of visit window.
03310	Primary Eye Sham	2008-04-14	Screening	Did not obtain proper consent prior to performing study procedure	Screening visit was on 4/14/08 but the subject was not consented until 4/23/08 (Treatment Visit).
03310	Primary Eye Sham	2008-04-23	Treatment	Other (Specify)	Hypotonic 0.1% Riboflavin was not administered even though the Pachymetry (Ultrasound at thinnest point) was under 400 microns after the Pretreatment Medio-Cross Riboflavin
03310	Primary Eye Sham	2008-05-05	Month 12 Follow-Up	BSCVA not done	BSCVA ETDRS was not done at the Month 12 visit.

03312	Primary Eye CXL	2008-04-21	Screening	Patients questionnaire not done	Patients Questionnaire was administered on 6/2/08 (Treatment Visit) instead of on 4/21/08 (Screening Visit).
03312	Primary Eye CXL	2008-04-21	Screening	RSVP questionnaire not done	RSVP Questionnaire was administered on 6/2/08 (Treatment Visit) instead of on 4/21/08 (Screening Visit).
03312	Primary Eye CXL	2008-04-21	Screening	Did not obtain proper consent prior to performing study procedure	Screening visit was on 4/21/08 but the subject was not consented until 6/2/08 (Treatment Visit).
03313	Primary Eye CXL	2008-06-23	Treatment	Other (Specify)	Treatment performed more than 1 month after the screening examination.
03313	Primary Eye CXL	2008-10-07	Month 3 Follow-Up	Other (Specify)	3 month visit occurred (2008-9-29) 8 days out of window.
03313	Primary Eye CXL	2009-01-09	Month 6 Follow-Up	Other (Specify)	6 month visit occurred (2009-1-5) 4 days out of window.
03314	Primary Eye CXL	2008-07-01	Month 1 Follow-Up	IOP measurement not done	Missed exam.
03315	Primary Eye Sham	2008-03-14	Screening	Did not obtain proper consent prior to performing study procedure	Patient did not sign consent until Treatment Day 0 6/26/2008.
03315	Primary Eye Sham	2008-06-26	Screening	Other (Specify)	Screening RSVP Questionnaire was not done on Screening Day, but was done on Treatment Day 0 Sham eye (OD).
03315	Primary Eye Sham	2008-06-26	Screening	Other (Specify)	Screening Patient Questionnaire was not done on Screening Day, but was done on Treatment Day 0 Sham eye (OD).
03315	Sham Eye CXL	2009-04-07	Month 6 Follow-Up	Other (Specify)	Month 6 Cross-over eye (OD) was out of window 11 days late.
03317	Primary Eye Sham	2008-09-17	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam not done at Month 1 visit for OD
03319	Primary Eye CXL	2008-07-23	Screening	Other (Specify)	Consent was signed on treatment day instead of screening day.
03319	Primary Eye CXL	2008-07-23	Screening	Patients questionnaire not done	Patient Questionnaire was done on treatment day instead of screening day.
03319	Primary Eye CXL	2008-07-23	Screening	RSVP questionnaire not done	RSVP Questionnaire was done on treatment day instead of screening day.
03320	Primary Eye Sham	2008-08-19	Screening	Patients questionnaire not done	Patients Questionnaire was completed on day of treatment (9/15/08).
03320	Primary Eye Sham	2008-08-19	Screening	RSVP questionnaire not done	RSVP questionnaire was completed at treatment visit (9/15/08).
03320	Sham Eye CXL	2008-12-02	Week 1 Follow-Up	BSCVA not done	Missed exam.
03320	Sham Eye CXL	2008-12-02	Week 1 Follow-Up	IOP measurement not done	Missed exam.
03320	Sham Eye CXL	2008-12-02	Week 1 Follow-Up	Manifest refraction not done	Missed exam.
03321	Primary Eye CXL	2008-09-02	Screening	Did not obtain proper consent prior to performing study procedure	Screening visit 09/02/2008 with IC signed on 9/17/2008, screening of subject took place prior to obtaining IC for trial participation
03321	Primary Eye CXL	2008-09-02	Screening	RSVP questionnaire not done	RSVP Questionnaire was administered on 9/17/08 (Treatment Visit) instead of on 9/2/08 (Screening Visit).
03321	Primary Eye CXL	2008-09-02	Screening	Patients questionnaire not done	Patient Questionnaire was administered on 9/17/08 (Treatment Visit) instead of on 9/2/08 (Screening Visit).
03321	Primary Eye CXL	2008-12-02	Month 3 Follow-Up	Endothelial cell count not done	Endothelial Cell Count was attempted but measurement could not be read, considered not done.
03322	Primary Eye Sham	2008-09-29	Screening	RSVP questionnaire not done	RSVP Questionnaire was administered on 10/20/08 (Treatment Visit) instead of on 9/29/08 (Screening Visit).
03322	Primary Eye Sham	2008-09-29	Screening	Patients questionnaire not done	Patient Questionnaire was administered on 10/20/08 (Treatment Visit) instead of on 9/29/08 (Screening Visit).
03322	Primary Eye Sham	2008-10-20	Treatment	Other (Specify)	the 6 minute medio-cross riboflavin (Isotonic) dosing was administered at 8 minutes; all subsequent administrations were 2 minutes late
03323	Primary Eye CXL	2008-10-28	Screening	Patients questionnaire not done	Patient Questionnaire was completed at treatment day instead of screening day.
03323	Primary Eye CXL	2008-10-28	Screening	Other (Specify)	Consent was signed at treatment day and not at screening.
03323	Primary Eye CXL	2008-10-28	Screening	RSVP questionnaire not done	RSVP was completed at treatment day instead of screening day.
03324	Primary Eye CXL	2008-11-11	Screening	RSVP questionnaire not done	RSVP Questionnaire was administered on 12/11/08 (Treatment Visit) instead of on 11/11/08 (Screening Visit).
03324	Primary Eye CXL	2008-11-11	Screening	Patients questionnaire not done	Patient Questionnaire was administered on 12/11/08 (Treatment Visit) instead of on 11/11/08 (Screening Visit).
03324	Primary Eye CXL	2008-11-11	Screening	Did not obtain proper consent prior to performing study procedure	Screening visit was on 11/11/08 but the subject was not consented until 12/11/08 (Treatment Visit).
03324	Fellow Eye CXL	2009-06-08	Treatment	Other (Specify)	Treatment of the fellow eye was one week past the primary eyes six month visit. No permission was obtained from sponsor.
03325	Primary Eye Sham	2008-12-12	Screening	Patients questionnaire not done	Patient's questionnaire completed at treatment visit (1/8/09).

03325	Primary Eye Sham	2008-12-12	Screening	Did not obtain proper consent prior to performing study procedure	ICF was signed on treatment day (1/8/09) instead of screening day (12/12/08).
03325	Primary Eye Sham	2008-12-12	Screening	RSVP questionnaire not done	RSVP questionnaire completed at treatment visit (1/8/09).
03325	Primary Eye Sham	2009-03-20	Month 3 Follow-Up	Endothelial cell count not done	Missed exam.
03325	Sham Eye CXL	2010-01-15	Month 3 Follow-Up	Endothelial cell count not done	Missed exam.
03326	Primary Eye CXL	2009-01-13	Screening	Did not obtain proper consent prior to performing study procedure	ICF signed on 2009-02-13 a month after the original start of screening visit
03327	Primary Eye	2009-03-03	Screening	Other (Specify)	Consent was signed on treatment day instead of screening day.
03327	Sham Primary Eye	2009-03-03	Screening	Endothelial cell count not done	Site unable to obtain endothelial cell count OD (no reason given).
03328	Sham Primary Eye	2009-03-03	Screening	Other (Specify)	Patient signed consent at Treatment Visit instead of Screening Visit.
03328	Sham Primary Eye	2009-03-03	Screening	Other (Specify)	RSVP was completed at Treatment Visit instead of Screening Visit.
03328	Sham Primary Eye	2009-03-03	Screening	Other (Specify)	Patient Questionnaire was completed at Treatment Visit instead of Screening Visit.
03328	Sham Fellow Eye	2010-11-23	Month 12	Endothelial cell count not done	OS - Month 12 Endothelial cell count was not done.
03329	CXL Primary Eye	2009-03-27	Follow-Up Screening	Other (Specify)	Patient Questionnaire and RSVP completed 4/22/09 (Treatment) vs. 3/27/2009
03329	Primary Eye CXL	2009-03-27	Screening	Did not obtain proper consent prior to performing study procedure	Subject consented on 04/22/2009 (Treatment Visit) vs. 03/27/2009 (Screening)
03329	Fellow Eye CXL	2009-11-19	Month 6 Follow-Up	Other (Specify)	CXL OS Month 6 visit occurred 2009-11-19 which was 15 days out of window
03330	Primary Eye CXL	2008-04-14	Screening	RSVP questionnaire not done	Screening RSVP Questionnaire was not completed during screening visit. It was completed on Treatment Day 0 randomized eye OS 6/4/2009.
03330	Primary Eye CXL	2008-04-14	Screening	Patients questionnaire not done	Screening Patient Questionnaire was not completed during screening visit. It was completed on Treatment Day 0 randomized eye OS 6/4/2009.
03330	Primary Eye CXL	2008-04-14	Screening	Did not obtain proper consent prior to performing study procedure	Patient informed consent form was not signed by the patient on screening visit. It was signed 44 days after screen on 5/28/09.
03330	Primary Eye CXL	2009-06-04	Treatment	Other (Specify)	Dose #9 hypotonic r boflavin bath used with a 7mm zone ring held on eye (OS) for 2 minutes.
03330	Primary Eye CXL	2009-08-18	Month 3 Follow-Up	Endothelial cell count not done	Month 3 randomized eye (OS) endothelial cell count not done.
03330	Primary Eye CXL	2010-04-20	Month 12 Follow-Up	Endothelial cell count not done	Month 12 randomized eye (OS) endothelial cell count not done.
03331	Primary Eye CXL	2009-06-05	Screening	Other (Specify)	screening visit 4/28/2009 IC signed at treatment visit on 5/06/2009
03332	Primary Eye Sham	2009-04-20	Screening	Did not obtain proper consent prior to performing study procedure	Subject signed ICF at treatment visit (5/13/09).
03332	Primary Eye Sham	2009-04-20	Screening	RSVP questionnaire not done	RSVP questionnaire completed at treatment visit (5/13/09).
03332	Primary Eye Sham	2009-04-20	Screening	Patients questionnaire not done	Patient's questionnaire completed at treatment visit (5/13/09).
03334	Primary Eye CXL	2009-05-12	Screening	Did not obtain proper consent prior to performing study procedure	Screen Visit = 5/12/2009 vs. ICF signature / date = 5/18/2009
03334	Primary Eye CXL	2009-05-12	Screening	Other (Specify)	Patient Questionnaire & RSVP completed 5/18/2009 (Treatment Visit) vs. 5/12/2009 (Screen Visit)
04304	Sham Eye CXL	2009-08-21	Month 6 Follow-Up	Other (Specify)	Subject missed fellow eye 6M post-op
04307	Primary Eye Sham	2008-05-14	Month 1 Follow-Up	Other (Specify)	Out of visit window.
04308	Primary Eye CXL	2009-11-16	Month 12 Follow-Up	Other (Specify)	Subject was 3 months outside of 12 month visit window.
04310	Sham Eye CXL	2009-09-21	Month 12 Follow-Up	Other (Specify)	Subject voluntarily withdrew from the study prior to 12M post-op per taking a new job and not being able to take time off.
04320	Primary Eye Sham	2009-02-11	Screening	Other (Specify)	WIRB approved consent dated May 7, 2008 was signed and dated by patient with the date of 2/11/08. Screening was 2/11/09. Site to create NTF for the discrepancy in the dates
04323	Sham Eye CXL	2010-12-05	Month 12 Follow-Up	Other (Specify)	Voluntary Withdraw. Subject missed 12M visit.
05301	Primary Eye CXL	2009-01-23	Screening	RSVP questionnaire not done	Page #9 of RSVP questionnaire missing.
05301	Primary Eye CXL	2009-05-11	Month 1 Follow-Up	Patients questionnaire not done	Month 1 Patient Questionnaire not done.

05301	Primary Eye CXL	2009-07-14	Month 3 Follow-Up	Endothelial cell count not done	Month 3 Endothelial cell count not done for this visit as required.
05301	Primary Eye CXL	2009-07-14	Month 3 Follow-Up	Other (Specify)	Month 3 out of the visit window- late 8 days.
05302	Primary Eye CXL	2009-02-06	Screening	Endothelial cell count not done	Endothelial cell count was not conducted, no print out available
05302	Primary Eye CXL	2009-07-20	Month 12 Follow-Up	Other (Specify)	Month 12 visit out of the visit window- late 26 days.
05302	Primary Eye CXL	2009-08-31	Month 3 Follow-Up	Other (Specify)	Month 3 visit out of the visit window by 24 days.
05305	Primary Eye Sham	2009-06-29	Month 1 Follow-Up	Patients questionnaire not done	Questionnaire is not located in the subject's source document.
05305	Primary Eye Sham	2009-09-01	Month 3 Follow-Up	Other (Specify)	Month 3 visit out of the visit window- late 14days.
05305	Sham Eye CXL	2010-12-06	Month 12 Follow-Up	Other (Specify)	Month 12 visit out of the visit window- late 156 days.
05306	Primary Eye Sham	2009-05-22	Week 1 Follow-Up	Other (Specify)	Week 1 Visit is out of the visit window - 1 day early.
05306	Primary Eye Sham	2009-06-29	Month 1 Follow-Up	Patients questionnaire not done	Month 1 Patient Questionnaire not completed and not located in source.
05306	Primary Eye Sham	2009-08-25	Month 3 Follow-Up	Other (Specify)	Month 3 visit out of the visit window- late 1 day.
07301	Primary Eye Sham	2008-07-08	Screening	Manual keratometry not done	Axes not recorded for OD and OS measurements
07301	Primary Eye Sham	2008-07-08	Screening	UCVA not done	Missed exam OD.
07301	Primary Eye Sham	2008-07-08	Eligibility	Other (Specify)	Contact lens stability evaluation was not performed to determine eligibility.
07301	Primary Eye Sham	2008-08-05	Week 1 Follow-Up	IOP measurement not done	Missed exam.
07301	Primary Eye Sham	2008-08-05	Week 1 Follow-Up	BSCVA not done	Missed exam.
07301	Primary Eye Sham	2008-08-05	Week 1 Follow-Up	Manifest refraction not done	Missed exam.
07301	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	UCVA not done	Missed exam.
07301	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	Slit lamp exam not done	Missed exam.
07301	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	Endothelial cell count not done	Missed exam.
07301	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	BSCVA not done	Missed exam.
07301	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	Manual keratometry not done	Missed exam.
07301	Sham Eye CXL	2008-10-17	Day 1 Follow-Up	UCVA not done	Missed exam.
07301	Sham Eye CXL	2008-10-23	Week 1 Follow-Up	UCVA not done	Missed exam.
07301	Sham Eye CXL	2008-12-08	Month 1 Follow-Up	Manual keratometry not done	Steep K value missing.
07301	Sham Eye CXL	2008-12-08	Month 1 Follow-Up	Other (Specify)	Visit out of range, 11 days late.
07301	Sham Eye CXL	2009-02-26	Month 3 Follow-Up	RSVP questionnaire not done	Subject provided with incomplete questionnaire resulting in missing data.
07301	Sham Eye CXL	2009-02-26	Month 3 Follow-Up	Other (Specify)	Visit out of range, 35 days late.
07301	Fellow Eye CXL	2009-03-26	Day 1 Follow-Up	UCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-02	Week 1 Follow-Up	BSCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-02	Week 1 Follow-Up	UCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 1 Follow-Up	BSCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	IOP measurement not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 1 Follow-Up	UCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	RSVP questionnaire not done	Subject provided with incomplete questionnaire resulting in missing data.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	Slit lamp exam not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	Manifest refraction not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	UCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 6 Follow-Up	BSCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 3 Follow-Up	Patients questionnaire not done	Missed exam.

07301	Fellow Eye CXL	2009-04-21	Month 1 Follow-Up	RSVP questionnaire not done	Subject provided with incomplete questionnaire resulting in missing data.
07301	Fellow Eye CXL	2009-04-21	Month 1 Follow-Up	Manual keratometry not done	Missed exam.
07301	Fellow Eye CXL	2009-04-21	Month 1 Follow-Up	Corneal topography not done	Missed exam.
07301	Fellow Eye CXL	2009-06-24	Month 3 Follow-Up	BSCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-06-24	Month 3 Follow-Up	RSVP questionnaire not done	Missed exam.
07301	Fellow Eye CXL	2009-06-24	Month 3 Follow-Up	Endothelial cell count not done	Missed exam.
07301	Fellow Eye CXL	2009-06-24	Month 3 Follow-Up	UCVA not done	Missed exam.
07301	Fellow Eye CXL	2009-06-24	Month 3 Follow-Up	Pentacam pachymetry, keratometry not done	Missed exam.
07302	Primary Eye CXL	2008-07-22	Screening	UCVA not done	Screening visit UCVA randomized eye (OD) not done. Only Snellen equivalent was obtained. Site did not provide convention for conversion to ETDRS.
07302	Primary Eye CXL	2008-07-22	Screening	Manual keratometry not done	Screening visit randomized eye (OD) manual keratometry not done.
07302	Primary Eye CXL	2008-07-22	Eligibility	Did not meet inclusion/exclusion criteria	Patient did not meet inclusion criterion #4. BSCVA = 60 letters read.
07302	Primary Eye CXL	2008-11-17	Month 3 Follow-Up	Other (Specify)	3 month visit missed.
07302	Primary Eye CXL	2009-03-23	Month 6 Follow-Up	Other (Specify)	6 month visit was out of window, 30 days late.
07303	Primary Eye Sham	2008-07-31	Screening	Manual keratometry not done	Axis not recorded for manual k measurements OU
07303	Primary Eye Sham	2008-09-04	Month 1 Follow-Up	Manual keratometry not done	Missed exam.
07303	Primary Eye Sham	2008-09-04	Month 1 Follow-Up	IOP measurement not done	Missed exam.
07303	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	BSCVA not done	Missed exam.
07303	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	IOP measurement not done	Missed exam.
07303	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	Other (Specify)	Visit out of range, 4 days early
07303	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	UCVA not done	Missed exam.
07303	Sham Eye CXL	2008-10-16	Month 3 Follow-Up	Slit lamp exam not done	Missed exam.
07303	Sham Eye CXL	2008-10-17	Day 1 Follow-Up	UCVA not done	Missed exam.
07303	Sham Eye CXL	2008-12-08	Month 1 Follow-Up	Other (Specify)	Visit out of range, 11 days late.
07303	Sham Eye CXL	2009-01-22	Month 3 Follow-Up	RSVP questionnaire not done	Subject provided with incomplete questionnaire for completion (missing questions 10, 11, 12, 22-24)
07303	Sham Eye CXL	2009-05-11	Month 6 Follow-Up	Other (Specify)	Visit out of range, 11 days late.
07303	Sham Eye CXL	2009-05-11	Month 6 Follow-Up	UCVA not done	Missed exam.
07303	Sham Eye CXL	2009-05-11	Month 6 Follow-Up	BSCVA not done	Missed exam.
07303	Sham Eye CXL	2009-05-11	Month 6 Follow-Up	RSVP questionnaire not done	Incomplete questionnaire provided to subject resulting in missing data.
07303	Sham Eye CXL	2009-07-08	Month 12 Follow-Up	UCVA not done	Missed exam.
07303	Sham Eye CXL	2009-07-08	Month 12 Follow-Up	IOP measurement not done	Missed exam.
07303	Sham Eye CXL	2009-07-08	Month 12 Follow-Up	Manual keratometry not done	Missed exam.
07303	Sham Eye CXL	2009-07-08	Month 12 Follow-Up	Other (Specify)	Visit out of range, 15 days early.
07303	Sham Eye CXL	2009-07-08	Month 12 Follow-Up	BSCVA not done	Missed exam.
07304	Primary Eye CXL	2008-10-02	Screening	UCVA not done	Screening visit UCVA not done.
07304	Primary Eye CXL	2008-10-02	Screening	Did not meet inclusion/exclusion criteria	Patient did not meet elig bility as contact lens stability was not done.
07304	Primary Eye CXL	2008-10-16	Treatment	Other (Specify)	Contact Lens Stability not done
07304	Primary Eye CXL	2008-10-20	Week 1 Follow-Up	BSCVA not done	1 week BSCVA randomized eye (OD) not done.
07304	Primary Eye CXL	2008-11-27	Month 1 Follow-Up	Other (Specify)	1 month follow up missed visit.
07304	Primary Eye CXL	2009-01-28	Month 3 Follow-Up	Other (Specify)	3 month visit out of window, 6 days late.

07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	UCVA not done	Month 6 randomized eye (OD) UCVA not done. Snellen equivalent of 20/30. No conversion convention noted by site.
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	Endothelial cell count not done	6 month endothelial cell count not done.
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	Patients questionnaire not done	6 month patient questionnaire not done.
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	Slit lamp exam not done	6 month slit lamp not done.
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	Manual keratometry not done	6 month manual keratometry
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	IOP measurement not done	6 month IOP not done.
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	BSCVA not done	6 month BSCVA not done.
07304	Primary Eye CXL	2009-03-12	Month 6 Follow-Up	RSVP questionnaire not done	6 month RSVP questionnaire not done.
07304	Primary Eye CXL	2009-10-20	Week 1 Follow-Up	Other (Specify)	1 week visit out of window, 1 day early.
07305	Primary Eye CXL	2008-12-18	Screening	Did not obtain proper consent prior to performing study procedure	Patient signed the incorrect informed consent form (study UVX- 002) on 12/18/08 prior to screening visit on 3/25/08. Patient did sign UVX-003 on 4/21/09 on Treatment day.
07305	Primary Eye CXL	2009-04-21	Treatment	Other (Specify)	After the dose Regimen 1 of Hypotonic Riboflavin the Pachymetry was 383 microns. The subject was given Artificial tears x 5 and closed eye for 5 minutes and repeat pachymetry was 402
07305	Primary Eye CXL	2009-07-28	Month 3 Follow-Up	Endothelial cell count not done	3 month randomized eye (OS) endothelial cell count not done.
07305	Primary Eye CXL	2009-09-01	Month 6 Follow-Up	Patients questionnaire not done	6 month randomized eye (OS) patient questionnaire not done.
07305	Primary Eye CXL	2009-09-01	Month 6 Follow-Up	RSVP questionnaire not done	Month 6 randomized eye (OS) RSVP questionnaire was not done.
07305	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	IOP measurement not done	12 month IOP not done.
07305	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	Manual keratometry not done	12 month manual keratometry not done.
07305	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	Endothelial cell count not done	12 month endothelial cell count not done.
07305	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	BSCVA not done	12 month BSCVA not done.
07305	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	UCVA not done	12 month UCVA not done.
07305	Primary Eye CXL	2009-09-01	Month 12 Follow-Up	Other (Specify)	12 month out of window, 7 days late.
08302	Primary Eye CXL	2008-07-23	Treatment	Other (Specify)	Pachymetry after debridement was not done
08302	Primary Eye CXL	2008-07-23	Treatment	Did not meet inclusion/exclusion criteria	Multi Vitamin not stopped prior to treatment as most multi vitamins contain Vitamin C
08302	Primary Eye CXL	2008-12-10	Month 6 Follow-Up	Manifest refraction not done	Manifest Refraction not done or not documented for Month 6 f/u.
08302	Primary Eye CXL	2009-07-23	Treatment	Other (Specify)	Pretreatment 30-minute drop was administered greater than 2 minutes (3 minutes) from previous dosing.
08303	Primary Eye Sham	2008-08-05	Treatment	Other (Specify)	OD/Sham - Pre-dose illumination drops @ 14 minutes were given 3 minutes after the previous dose.
08303	Sham Eye CXL	2008-10-14	Treatment	Other (Specify)	OD/CRS-OVR - Pre-dose illumination drops @ 18 minutes were given 3 minutes after the previous dose.
08303	Sham Eye CXL	2008-10-14	Treatment	Other (Specify)	OD/CRS-OVR - Treatment illumination drops @ 28 minutes were given 3 minutes after the previous dose.
08303	Fellow Eye CXL	2008-10-15	Treatment	Other (Specify)	OS/Fellow eye - Treatment illumination drops @ 14 minutes were given 3 minutes after the previous dose.
08303	Fellow Eye CXL	2008-10-15	Treatment	Other (Specify)	OS/Fellow eye - Pre-dose illumination drops @ 6 minutes were given 3 minutes after the previous dose.
08304	Primary Eye CXL	2008-08-28	Screening	Other (Specify)	RSVP Questionnaire was completed at Contact re-check visit on 8/28/08. Questionnaire should have been completed at Screening Visit on 8/21/08.
08304	Primary Eye CXL	2008-09-10	Treatment	Did not meet inclusion/exclusion criteria	Subject's BCVA at Treatment Visit was 20/16; therefore, the subject does not meet Inclusion Criteria #4 (BCVA must be worst than 20/20)
08304	Primary Eye CXL	2008-09-10	Treatment	Ultrasound pachymetry not done	OS- not done after debridement
08304	Fellow Eye CXL	2009-03-10	Treatment	IOP measurement not done	OD
08304	Fellow Eye CXL	2009-03-10	Treatment	Ultrasound pachymetry not done	OD- not done after debridement
08305	Sham Eye CXL	2009-02-24	Treatment	Other (Specify)	Pachymetry measurement after debridement was not done for the cross-over eye
08305	Fellow Eye CXL	2009-05-05	Treatment	Other (Specify)	Pachymetry after debridement was not done for the fellow eye
08305	Fellow Eye CXL	2009-05-05	Treatment	Other (Specify)	Pre-treatment dose 3 was administered greater than 2 minutes (3 minutes) after previous dose
08305	Fellow Eye CXL	2009-05-12	Week 1 Follow-Up	Manifest refraction not done	(OS)

08305	Fellow Eye CXL	2009-05-12	Week 1 Follow-Up	IOP measurement not done	(OS)- deferred by doctor due to bandage contact having just been removed.
08306	Primary Eye Sham	2009-01-06	Treatment	Other (Specify)	OS/Sham eye - Treatment illumination drops, 6 minute dose, was given 3 minutes after the previous dose.
08306	Primary Eye Sham	2009-01-06	Treatment	Other (Specify)	OS/Sham eye - Treatment illumination drops, 26 minute dose, was given 3 minutes after the previous dose.
08306	Sham Eye CXL	2010-01-29	Month 12 Follow-Up	Patients questionnaire not Done	Month 12 Patient Questionnaire was not done.
09301	Primary Eye Sham	2008-05-20	Screening	Manual keratometry not Done	Screening manual Keratometry sham eye (OS) not done.
09301	Primary Eye Sham	2008-06-04	Treatment	Other (Specify)	Treatment day sham eye (OS) r boflavin drop not given at 30 minute time period pre-UV light.
09301	Primary Eye Sham	2008-07-02	Month 1 Follow-Up	Manual keratometry not Done	Month 1 sham eye (OS) manual keratometry not done.
09301	Primary Eye Sham	2008-12-19	Month 6 Follow-Up	Other (Specify)	Month 6 visit sham eye (OS) out of window, two days late.
09302	Primary Eye Sham	2008-06-17	Month 1 Follow-Up	Other (Specify)	Month 1 sham eye (OS) out of window, 12 days late.
09302	Sham Eye CXL	2008-09-16	Month 6 Follow-Up	Slit lamp exam not done	This 6 month sham eye (OS) visit was also the crossover treatment (OS) visit. Corneal exam was not done pre-treatment and therefore, not done for Month 6 sham eye.
09302	Sham Eye CXL	2008-09-16	Month 6 Follow-Up	Patients questionnaire not Done	Month 6 sham eye (OS) Patient Questionnaire not done.
09302	Sham Eye CXL	2008-09-16	Month 6 Follow-Up	RSVP questionnaire not Done	Month 6 sham eye (OS) RSVP Questionnaire not done.
09302	Sham Eye CXL	2008-12-23	Month 3 Follow-Up	Other (Specify)	Month 3 crossover eye (OS) not done, missed visit.
09303	Sham Eye CXL	2009-04-13	Month 6 Follow-Up	Manual keratometry not Done	Not done for Non-Randomized CXL Treatment OD
09304	Primary Eye CXL	2008-04-24	Screening	Manual keratometry not Done	CXL, OS
09304	Primary Eye CXL	2008-04-24	Screening	Manual keratometry not Done	Fellow eye, OD
09304	Primary Eye CXL	2008-05-23	Month 1 Follow-Up	Manual keratometry not Done	CXL, OS
09304	Primary Eye CXL	2008-05-23	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	CXL, OS
09304	Primary Eye CXL	2008-07-07	Month 3 Follow-Up	Manual keratometry not Done	CXL, OS
09304	Primary Eye CXL	2008-10-21	Month 6 Follow-Up	Manual keratometry not Done	CXL, OS
09304	Fellow Eye CXL	2009-03-24	Month 12 Follow-Up	Manual keratometry not Done	CXL, OS
09304	Fellow Eye CXL	2009-03-24	Month 1 Follow-Up	Manual keratometry not Done	Fellow Eye, OD
09304	Fellow Eye CXL	2009-05-26	Month 3 Follow-Up	Manual keratometry not Done	Fellow Eye, OD
09304	Fellow Eye CXL	2009-08-26	Month 6 Follow-Up	Manual keratometry not Done	Fellow eye, OD
09305	Primary Eye CXL	2008-04-11	Screening	Other (Specify)	Pupil size (bright and dim) was not performed by the site for OD and OS at screening.
09305	Primary Eye CXL	2008-08-19	Month 3 Follow-Up	Other (Specify)	Month 3 Visit was conducted out of window. Month 3 Visit should have occurred between 6/26/08 through 7/24/08.
09305	Primary Eye CXL	2008-11-19	Month 6 Follow-Up	Other (Specify)	Month 6 Visit was conducted out of window. Month 6 Visit ; should have occurred between 9/4/08 through 10/30/08.
09307	Primary Eye CXL	2008-06-19	Treatment	Other (Specify)	Time from screening to treatment was outside the 30 day protocol window.
09308	Primary Eye Sham	2008-04-08	Month 1 Follow-Up	Other (Specify)	1 month visit sham eye (OD) out of window, 4 days late.
09308	Primary Eye Sham	2008-05-19	Screening	Manual keratometry not Done	Screening sham eye (OD) manual keratometry not done.
09309	Primary Eye CXL	2008-10-24	Month 3 Follow-Up	Other (Specify)	Month 3 Visit was conducted 10 days out of window. Month 3 should have occurred between 9/16/09 through 10/14/09.
09309	Primary Eye CXL	2009-01-30	Month 6 Follow-Up	Other (Specify)	Month 6 Follow-Up VIsit was not done.
09309	Primary Eye CXL	2009-05-01	Month 12 Follow-Up	Manual keratometry not Done	Site did not perform the Manual Keratometry at Month 12 follow-up visit in error.
09310	Primary Eye CXL	2008-10-30	Month 3 Follow-Up	Other (Specify)	Month 3 visit randomized eye (OS) was out of window, 7 days late.
09311	Primary Eye Sham	2008-10-16	Treatment	BSCVA not done	Treatment 126 days after screen, (greater than 30 days) repeat BSCVA not done sham eye (OD).
09311	Primary Eye Sham	2008-10-16	Treatment	UCVA not done	Treatment 126 days after screen, (greater than 30 days) repeat UCVA not done sham eye (OD).
09311	Primary Eye Sham	2008-10-16	Treatment	Manifest refraction not done	Treatment 126 days after screen, (greater than 30 days) repeat Manifest refraction not done sham eye (OD).
09311	Sham Eye CXL	2009-02-11	Week 1 Follow-Up	BSCVA not done	Week 1 crossover eye (OD) BSCVA not done.
09311	Sham Eye CXL	2009-02-11	Week 1 Follow-Up	Manifest refraction not done	Week 1 crossover eye (OD) manifest refraction not done.
09311	Sham Eye CXL	2009-03-03	Month 1 Follow-Up	BSCVA not done	1 month crossover eye (OD) BSCVA not done.

09311	Sham Eye CXL	2009-05-13	Month 3 Follow-Up	Other (Specify)	3 month crossover eye (OD) out of window, 20 days late.
09312	Primary Eye Sham	2008-07-17	Screening	Manual keratometry not done	Site was unable to perform manual keratometry.
09312	Primary Eye Sham	2008-12-02	Month 1 Follow-Up	Other (Specify)	Mo 1 visit not done sham eye (OS). Scheduled for 11/19/08, but no-show. Rescheduled for 11/25/08, 11/26/08 & 05Jan09, but subj no-showed those days. Site spoke w/subj on 02Dec08 during this interval
09312	Primary Eye Sham	2009-02-20	Month 3 Follow-Up	Other (Specify)	Mo 3 visit not done Sham eye (OS).Scheduled for 12Jan2009. Cert letter mailed to subj 1/20/09. Subj called site on 2/20/09--returned from overseas. Too late for Mo 3, so subj to be seen for Mo 6 next.
09312	Primary Eye Sham	2009-03-24	Month 6 Follow-Up	BSCVA not done	No additional information
09312	Primary Eye Sham	2009-03-24	Month 6 Follow-Up	Manual keratometry not done	Sham OS
09312	Sham Eye CXL	2009-05-20	Treatment	Other (Specify)	Crossover treatment (OS) was done outside of 6 month visit window (Sham eye OS), 21 days late. No sponsor authorization given.
09312	Sham Eye CXL	2009-05-20	Treatment	Other (Specify)	The number of drops administered during irradiation is not recorded.
09312	Sham Eye CXL	2009-05-20	Treatment	Other (Specify)	Presence of Riboflavin in the chamber is not recorded/indicated in source.
09312	Sham Eye CXL	2009-05-20	Treatment	Other (Specify)	Pre-treatment number of drops administered is not recorded
09312	Sham Eye CXL	2009-06-03	Week 1 Follow-Up	BSCVA not done	No additional information
09312	Sham Eye CXL	2009-06-22	Month 1 Follow-Up	Manual keratometry not done	Cross-Over OS
09312	Sham Eye CXL	2009-08-24	Month 3 Follow-Up	Manual keratometry not done	Site stated it was unable to do manual keratometry.
09313	Primary Eye Sham	2008-08-28	Treatment	Slit lamp exam not done	Post Treatment Slit Lamp Exam was not done after the Sham Treatment
09313	Primary Eye Sham	2008-11-24	Month 3 Follow-Up	Manual keratometry not done	Manual keratometry was not done on the OS Sham Control
09313	Sham Eye CXL	2008-12-15	Week 1 Follow-Up	BSCVA not done	The BSCVA was not done at Week 1 follow-up visit on the Non-Randomized CXL Treatment OS.
09313	Sham Eye CXL	2008-12-15	Week 1 Follow-Up	Manifest refraction not done	Manifest refraction was not done at Week 1 follow-up visit on the Non-Randomized CXL Treatment OS.
09313	Sham Eye CXL	2008-12-15	Week 1 Follow-Up	IOP measurement not done	IOP was not done at Week 1 follow-up visit on the Non-Randomized CXL Treatment OS.
09313	Sham Eye CXL	2009-03-18	Month 3 Follow-Up	Other (Specify)	Month 3 follow-up visit on Non-Randomized CXL Treatment OS was conducted 1 day out of window. Visit should have occurred between 2/17/09 through 3/17/09.
09313	Sham Eye CXL	2009-06-03	Month 6 Follow-Up	Manual keratometry not done	Manual keratometry was not done at Month 6 follow-up visit on the Non-Randomized CXL Treatment OS.
09314	Primary Eye CXL	2008-11-21	Month 1 Follow-Up	Other (Specify)	1 month visit randomized eye (OS) out of window, 2 days late.
09314	Primary Eye CXL	2009-05-01	Month 6 Follow-Up	Other (Specify)	6 month visit randomized eye (OS) out of window, 9 days late.
09316	Primary Eye CXL	2008-10-16	Screening	Manual keratometry not done	OD
09316	Primary Eye CXL	2008-10-16	Treatment	Other (Specify)	Treatment visit was conducted on the same day as the screening visit
09316	Primary Eye CXL	2008-11-27	Month 1 Follow-Up	Other (Specify)	Month 1 Follow-Up Visit not Conducted - Patient out of the Country.
09316	Primary Eye CXL	2009-01-30	Month 3 Follow-Up	Manual keratometry not done	OD
09316	Primary Eye CXL	2009-04-24	Month 6 Follow-Up	Manual keratometry not done	OD
09319	Primary Eye CXL	2009-03-04	Week 1 Follow-Up	Manifest refraction not done	Manifest refraction not performed at Week 1 follow-up randomized eye (OS). Per PI this was due to removing Bandage contact lens.
09319	Primary Eye CXL	2009-03-04	Week 1 Follow-Up	IOP measurement not done	IOP not perform at Week 1 follow-up randomized eye (OS). Per PI this was due to removing Bandage contact lens.
09319	Primary Eye CXL	2009-03-04	Week 1 Follow-Up	BSCVA not done	BSCVA (OS) not perform at Week 1 follow-up. Per PI this was due to removing Bandage contact lens.
09319	Primary Eye CXL	2009-06-05	Month 3 Follow-Up	Other (Specify)	Month 3 Follow-up Visit was conducted 2 days out of window. Visit should have occurred between 5/6/09 through 6/3/09.
09320	Primary Eye Sham	2008-12-03	Eligibility	Did not meet inclusion/exclusion criteria	BSCVA at screening visit=59. BSCVA on treatment Day (0) was 57. Per protocol, BSCVA had to be worse than 55.
09320	Sham Eye CXL	2009-09-09	Month 3 Follow-Up	Other (Specify)	month 3 visit was missed
09321	Primary Eye CXL	2008-12-19	Screening	Manual keratometry not done	Screening manual keratometry not done randomized eye (OS)
09321	Primary Eye CXL	2008-12-26	Screening	Did not meet inclusion/exclusion criteria	Contact lens stability was not met for topography (OS). Difference=1.18
09321	Primary Eye CXL	2009-02-04	Treatment	Other (Specify)	Treatment day out of window, 39 days late and no repeat measure performed.
09321	Primary Eye CXL	2009-02-04	Treatment	UCVA not done	Treatment day UCVA not done randomized eye (OS).
09321	Primary Eye CXL	2009-02-10	Week 1 Follow-Up	BSCVA not done	Week 1 BSCVA not done randomized eye (OS).
09321	Primary Eye CXL	2009-02-10	Week 1 Follow-Up	Manifest refraction not done	Week 1 manual keratometry not done randomized eye (OS).

09321	Primary Eye CXL	2009-03-03	Month 1 Follow-Up	Manual keratometry not done	Month 1 manual keratometry not done randomized eye (OS).
09321	Primary Eye CXL	2009-05-08	Month 3 Follow-Up	Manual keratometry not done	Month 3 manual keratometry not done randomized eye (OS).
09321	Primary Eye CXL	2009-09-04	Month 6 Follow-Up	Other (Specify)	Month 6 visit randomized eye (OS) out of window, 15 days late.
09321	Primary Eye CXL	2009-09-04	Month 6 Follow-Up	Manual keratometry not done	Month 6 manual keratometry not done randomized eye (OS).
09321	Primary Eye CXL	2009-09-04	Month 6 Follow-Up	UCVA not done	Month 6 UCVA not done randomized eye (OS).
09322	Primary Eye Sham	2009-01-12	Screening	Manual keratometry not done	Manual keratometry was not done at screening for OU.
09322	Primary Eye Sham	2009-01-12	Screening	Other (Specify)	Site did not perform pupil size (bright & dim) at screening for OU.
09322	Primary Eye Sham	2009-05-15	Month 3 Follow-Up	Other (Specify)	Month 3 Follow-up Visit was conducted 9 days out of window per protocol schedule. Month 3 visit should have occurred between 4/15/09 through 5/6/09.
09323	Primary Eye CXL	2009-05-06	Treatment	BSCVA not done	Treatment visit was greater than 30 days after screening visit; therefore, the BSCVA should have been repeated for OD.
09323	Primary Eye CXL	2009-05-06	Treatment	UCVA not done	Treatment visit was greater than 30 days after screening visit; therefore, the UCVA should have been repeated for OD.
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	Endothelial cell count not done	The endothelial cell count was not performed for the CXL Treatment OD.
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	Manual keratometry not done	The manual keratometry was not performed for the CXL Treatment OD.
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	UCVA not done	12 Month UCVA not done OD
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	Patients questionnaire not done	The Patient questionnaire was not performed for Month 12 Follow-up Visit.
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	RSVP questionnaire not done	The RSVP questionnaire was not performed for Month 12 Follow-up Visit.
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	BSCVA not done	12 Month BSCVA not done OD
09323	Primary Eye CXL	2010-05-25	Month 12 Follow-Up	IOP measurement not done	12 Month IOP not done OD
10301	Fellow Eye CXL	2008-08-27	Treatment	Other (Specify)	OD/Fellow eye - no assessments done prior to treatment.
10301	Fellow Eye CXL	2008-09-10	Week 1 Follow-Up	IOP measurement not done	OD/Fellow eye - IOP measurement not done.
10304	Sham Eye CXL	2008-11-19	Treatment	Other (Specify)	OD/CRS-OVR eye was not evaluated prior to treatment.
10304	Sham Eye CXL	2009-03-03	Month 3 Follow-Up	Slit lamp exam not done	OD/CRS-OVR eye - slit lamp was not done. Patient left office before exam was done.
10304	Sham Eye CXL	2009-03-03	Month 3 Follow-Up	Other (Specify)	OD/CRS-OVR eye - visit was out of window (6 days late).
10304	Sham Eye CXL	2009-03-03	Month 3 Follow-Up	Endothelial cell count not done	OD/CRS-OVR eye - endothelial cell count was not done. Site was unable to obtain a clear image.
10306	Sham Eye CXL	2009-03-24	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	Pentacam was done, however unable to obtain required values for the study
10307	Primary Eye CXL	2008-10-09	Week 1 Follow-Up	IOP measurement not done	Week 1 F/U IOP was done for OD due to presence of Epi defect
10307	Fellow Eye CXL	2009-03-19	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	6 month randomized eye (OS) pentacam not done.
10307	Fellow Eye CXL	2009-03-19	Month 3 Follow-Up	Pentacam pachymetry, keratometry not done	3 month fellow eye (OD) pentacam not done.
10309	Primary Eye CXL	2008-11-20	Screening	Pentacam pachymetry, keratometry not done	Unable to obtain pentacam image after 5 tries. Unable to establish corneal thickness requirement
10309	Primary Eye CXL	2008-11-26	Week 1 Follow-Up	IOP measurement not done	IOP measurement deferred secondary to BSCL
10309	Primary Eye CXL	2009-04-20	Month 3 Follow-Up	Other (Specify)	Missed Visit
10309	Primary Eye CXL	2010-06-20	Month 12 Follow-Up	Other (Specify)	Month-12 follow-up visit was done 5 months outside window. Sponsor considered visit as missed visit.
10311	Sham Eye CXL	2009-03-18	Treatment	Other (Specify)	after six dosing with Hypotonic R boflavin, Optive was used to increase pachymetry prior to illumination
10313	Primary Eye Sham	2009-01-14	Screening	Endothelial cell count not done	OD
10313	Primary Eye Sham	2009-01-28	Eligibility	Other (Specify)	Contact lens recheck was not done
10313	Sham Eye CXL	2009-04-29	Month 3 Follow-Up	Endothelial cell count not done	OD Sham
10313	Sham Eye CXL	2009-07-14	Month 3 Follow-Up	Endothelial cell count not done	OD Cross-over
10313	Sham Eye CXL	2010-03-03	Month 12 Follow-Up	Endothelial cell count not done	OD Cross-over
10316	Primary Eye CXL	2009-03-26	Screening	Pentacam pachymetry, keratometry not done	OU

10316	Primary Eye CXL	2009-04-22	Week 1 Follow-Up	IOP measurement not done	OD
10316	Primary Eye CXL	2009-07-02	Month 3 Follow-Up	Endothelial cell count not done	OD
10317	Primary Eye CXL	2009-04-01	Screening	Other (Specify)	OS/CXL - Pentacam was performed, Kmax not available.
10317	Primary Eye CXL	2009-04-13	Week 1 Follow-Up	IOP measurement not done	OS/CXL - IOP not done.
10317	Primary Eye CXL	2009-09-14	Month 6 Follow-Up	Patients questionnaire not done	M6 Patient Questionnaire not done.
10317	Primary Eye CXL	2009-09-14	Month 6 Follow-Up	RSVP questionnaire not done	M6 RSVP questionnaire not done.
10319	Primary Eye CXL	2009-08-12	Month 3 Follow-Up	Endothelial cell count not done	OD/CXL - endothelial cell count not done.
10319	Fellow Eye CXL	2009-11-11	Week 1 Follow-Up	IOP measurement not done	OS/Fellow - IOP measurement not done.
10319	Fellow Eye CXL	2010-11-29	Month 12 Follow-Up	BSCVA not done	OS/Fellow - BSCVA not done.
11301	Primary Eye Sham	2008-10-29	Screening	Did not meet inclusion/exclusion criteria	Subject did not demonstrate stable refraction. Subject's MRSE difference was (2.5 D) greater than 0.75D
11301	Primary Eye Sham	2008-12-08	Month 1 Follow-Up	BSCVA not done	1 month sham eye (OS) BCVA not done.
11301	Sham Eye CXL	2009-03-12	Month 3 Follow-Up	Manual keratometry not done	3 month sham eye (OS) manual keratometry not done.
11301	Sham Eye CXL	2009-03-12	Month 3 Follow-Up	Other (Specify)	3 month visit sham eye (OS) out of window, 32 days late.
11301	Sham Eye CXL	2009-06-29	Month 3 Follow-Up	Other (Specify)	3 month visit crossover eye (OS) out of window, 11 days late.
11301	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	BSCVA not done	6 month crossover eye (OS) BSCVA not done.
11301	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	RSVP questionnaire not done	6 month crossover eye (OS) RSVP not done.
11301	Fellow Eye CXL	2009-11-23	Week 1 Follow-Up	BSCVA not done	1 week fellow eye (OD) BSCVA not done.
11301	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	Other (Specify)	6 month visit crossover eye (OS) out of window, 59 days late.
11301	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	Patients questionnaire not done	6 month visit crossover eye (OS) patient questionnaire not done.
11301	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	Pentacam pachymetry, keratometry not done	6 month crossover eye (OS) pentacam not done.
11301	Fellow Eye CXL	2009-11-23	Month 6 Follow-Up	Endothelial cell count not done	12 month crossover eye (OS) endothelial cell count not done.
11301	Fellow Eye CXL	2009-12-21	Month 1 Follow-Up	BSCVA not done	1 month fellow eye (OD) BSCVA not done.
11301	Fellow Eye CXL	2010-02-22	Month 3 Follow-Up	Manual keratometry not done	3 month fellow eye (OD) manual keratometry not done.
11301	Fellow Eye CXL	2010-02-22	Month 3 Follow-Up	Endothelial cell count not done	3 month fellow eye (OD) endothelial cell count not done.
11301	Fellow Eye CXL	2010-02-22	Month 3 Follow-Up	Other (Specify)	3 month fellow eye (OD) out of window, 5 days late.
11301	Fellow Eye CXL	2010-03-22	Month 12 Follow-Up	Manual keratometry not done	12 month crossover eye (OS) manual keratometry not done.
11301	Fellow Eye CXL	2010-06-07	Month 6 Follow-Up	Other (Specify)	6 month visit fellow eye (OD) out of window, 12 days late.
11302	Primary Eye CXL	2008-10-19	Treatment	Other (Specify)	Treatment day randomized eye (OS) repeat measures not done. Therefore, no baseline Kmax value is available.
11302	Primary Eye CXL	2008-10-20	Screening	Pentacam pachymetry, keratometry not done	Screening pentacam randomized eye (OS) not done.
11302	Primary Eye CXL	2008-12-15	Month 1 Follow-Up	Other (Specify)	The Month 1 Follow-up Visit was conducted 5 days out of window per protocol visit schedule for the CXL Treatment OS. The visit should have occurred between 11/19/08 through 12/10/08.
11302	Primary Eye CXL	2009-02-16	Month 3 Follow-Up	Other (Specify)	The Month 3 Follow-up Visit was conducted 12 days out of window per protocol visit schedule for the CXL Treatment OS. The visit should have occurred between 1/7/09 through 2/4/09.
11302	Primary Eye CXL	2009-02-16	Month 3 Follow-Up	Manual keratometry not done	The Manual keratometry was not done for the CXL Treatment OS.
11302	Primary Eye CXL	2009-03-18	Month 6 Follow-Up	Other (Specify)	Month 6 Follow-up Visit was not done for the CXL Treatment OS.
11302	Primary Eye CXL	2009-11-02	Month 12 Follow-Up	Endothelial cell count not done	The Endothelial Cell Count was not done for the CXL Treatment OS.
11302	Primary Eye CXL	2009-11-02	Month 12 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for the CXL Treatment OS.
11302	Fellow Eye CXL	2010-01-04	Month 1 Follow-Up	Other (Specify)	The visit was conducted 5 days out of window per protocol visit schedule for the Non-Randomized CXL Treatment Fellow OD. The visit should have occurred between 12/9/09 through 12/30/09
11302	Fellow Eye CXL	2010-01-04	Month 1 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for the Non-Randomized CXL Fellow Eye OD.
11302	Fellow Eye CXL	2010-03-22	Month 3 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for the Non-Randomized CXL Fellow Eye OD.

11302	Fellow Eye CXL	2010-03-22	Month 3 Follow-Up	Other (Specify)	The visit was conducted 26 days out of window per protocol visit schedule for the Non-Randomized CXL Treatment Fellow OD. The visit should have occurred between 1/27/10 through 2/24/10.
11302	Fellow Eye CXL	2010-03-22	Month 3 Follow-Up	Endothelial cell count not done	The Endothelial Cell Count was not done for the Non-Randomized CXL Fellow Eye OD.
11302	Fellow Eye CXL	2010-06-21	Month 6 Follow-Up	Other (Specify)	The visit was conducted 19 days out of window per protocol visit schedule for the Non-Randomized CXL Treatment Fellow OD. The visit should have occurred between4/7/10 through 6/2/10.
11302	Fellow Eye CXL	2010-06-21	Month 6 Follow-Up	Manual keratometry not done	The Manual Keratometry was not done for the Non-Randomized CXL Fellow Eye OD.
11302	Fellow Eye CXL	2011-01-10	Month 12 Follow-Up	Endothelial cell count not done	The Endothelial Cell Count was not done for the Non-Randomized CXL Fellow Eye OD.
11304	Primary Eye Sham	2009-01-07	Treatment	Other (Specify)	Treatment was greater than 30 days from screening, no repeat measurements were done
11304	Primary Eye Sham	2009-02-16	Month 1 Follow-Up	Manual keratometry not done	OD Sham
11304	Sham Eye CXL	2009-04-16	Month 3 Follow-Up	Slit lamp exam not done	OD Sham
11304	Sham Eye CXL	2009-04-16	Month 3 Follow-Up	Manual keratometry not done	OD Sham
11304	Sham Eye CXL	2009-08-03	Month 3 Follow-Up	Manual keratometry not done	OD Cross-over
11304	Sham Eye CXL	2009-11-09	Month 6 Follow-Up	Manual keratometry not done	OD Cross-over
11304	Sham Eye CXL	2010-05-10	Month 12 Follow-Up	Endothelial cell count not done	OD Cross-over
11304	Sham Eye CXL	2010-05-10	Month 12 Follow-Up	Manual keratometry not done	OD Cross-over
11306	Primary Eye CXL	2009-04-20	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry was not done for the Month 3 Follow-up Visit on the CXL Treatment OS.
11306	Fellow Eye CXL	2010-01-25	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry was not done for the Month 3 Follow-up Visit on the Non-Randomized CXL Fellow OD.
11306	Fellow Eye CXL	2010-01-25	Month 3 Follow-Up	Endothelial cell count not done	Endothelial Cell Count was not done for the Month 3 Follow-up Visit on the Non-Randomized CXL Fellow OD.
11306	Fellow Eye CXL	2010-02-08	Month 12 Follow-Up	Manual keratometry not done	Manual Keratometry was not done for the Month 12 Follow-up Visit on the CXL Treatment OS.
11306	Fellow Eye CXL	2010-02-08	Month 12 Follow-Up	Endothelial cell count not done	Endothelial Cell Count was not done for the CXL Treatment OS.
11306	Fellow Eye CXL	2010-04-20	Month 6 Follow-Up	Other (Specify)	Month 6 Follow-Up Visit was not done for the Non-Randomized CXL Fellow OD
11307	Primary Eye CXL	2009-03-12	Treatment	Other (Specify)	Hypotonic dose regimen #2, number of drops not recorded.
11307	Primary Eye CXL	2009-03-12	Treatment	Other (Specify)	Hypotonic dose regimen #2, start time not recorded.
11307	Primary Eye CXL	2009-03-12	Treatment	Other (Specify)	Hypotonic dose regimen #2, duration between drops not recorded.
11307	Primary Eye CXL	2009-04-09	Month 1 Follow-Up	Pentacam pachymetry, keratometry not done	1 month randomized eye (OS) pentacam not done.
11307	Primary Eye CXL	2009-06-12	Month 3 Follow-Up	Manual keratometry not done	3 month manual keratometry randomized eye (OS) not done.
11307	Primary Eye CXL	2009-06-12	Month 3 Follow-Up	Other (Specify)	3 month endothelial cell count not done at 3 month visit (6/12/09).Patient returned on 6/23/09 for endothelial cell count only. Therefore, 3 month cell count was performed out of window, 5 days late.
11307	Primary Eye CXL	2009-11-30	Month 6 Follow-Up	Manual keratometry not done	6 month manual keratometry not done.
11307	Primary Eye CXL	2009-11-30	Month 6 Follow-Up	Other (Specify)	6 month visit out of window, 36 days late.
11307	Primary Eye CXL	2010-04-05	Month 12 Follow-Up	Endothelial cell count not done	12 month endothelial cell count not done.
11307	Primary Eye CXL	2010-04-05	Month 12 Follow-Up	Manual keratometry not done	12 month manual keratometry not done.
11308	Primary Eye CXL	2009-03-05	Screening	Endothelial cell count not done	OS
11308	Primary Eye CXL	2009-03-05	Screening	Endothelial cell count not done	OD
11308	Primary Eye CXL	2009-06-04	Screening	Did not meet inclusion/exclusion criteria	Contact Lens stability requirement was not met. Subject has Sim K difference of 2.5 D for the CXL OS.
11308	Primary Eye CXL	2009-07-07	Month 1 Follow-Up	Manual keratometry not done	OS
11308	Primary Eye CXL	2009-07-07	Month 1 Follow-Up	Slit lamp exam not done	OS, CXL
11308	Fellow Eye CXL	2009-11-23	Month 3 Follow-Up	RSVP questionnaire not done	OS CXL
11308	Fellow Eye CXL	2009-11-23	Month 3 Follow-Up	Patients questionnaire not done	OS CXL
11308	Fellow Eye CXL	2009-11-23	Month 3 Follow-Up	Manual keratometry not done	OS CXL
11308	Fellow Eye CXL	2009-12-17	Month 6 Follow-Up	Other (Specify)	Missed Visit OS CXL

11308	Fellow Eye CXL	2009-12-21	Month 1 Follow-Up	Manual keratometry not done	OD, Fellow Eye
11308	Fellow Eye CXL	2010-02-22	Month 3 Follow-Up	Patients questionnaire not done	OD Fellow Eye
11308	Fellow Eye CXL	2010-02-22	Month 3 Follow-Up	RSVP questionnaire not done	OD Fellow Eye
11308	Fellow Eye CXL	2010-02-22	Month 3 Follow-Up	Manual keratometry not done	OD Fellow Eye
11308	Fellow Eye CXL	2010-06-28	Month 6 Follow-Up	Manual keratometry not done	OD Fellow Eye
11308	Fellow Eye CXL	2010-06-28	Month 12 Follow-Up	Manual keratometry not done	OS CXl
11309	Primary Eye Sham	2009-03-23	Screening	BSCVA not done	BSCVA was not done at screening for OD
11309	Primary Eye Sham	2009-05-28	Treatment	Pentacam pachymetry, keratometry not done	Pretreatment Pachymetry was not done at Treatment Visit for the Sham Control OD
11309	Primary Eye Sham	2009-05-29	Day 1 Follow-Up	Other (Specify)	Day 1 Follow-up Visit was not done due to missed appointment by the subject.
11309	Primary Eye Sham	2009-08-31	Month 3 Follow-Up	Endothelial cell count not done	Endothelial Cell Count was done on the Month 3 Follow-up Visit for the Sham Control OD
11309	Primary Eye Sham	2009-08-31	Month 3 Follow-Up	BSCVA not done	BSCVA was not done for the Month 3 Follow-up Visit for the Sham Control OD
11309	Primary Eye Sham	2009-08-31	Month 3 Follow-Up	Manual keratometry not done	Manual Keratometry was done for the Month 3 Follow-up Visit for the Sham Control OD
11309	Sham Eye CXL	2009-11-06	Week 1 Follow-Up	BSCVA not done	The BSCVA was not done for the Week 1 Follow-Up Visit on the Non-Randomized CXL Treatment Sham Control OD
11309	Sham Eye CXL	2010-01-04	Month 1 Follow-Up Follow-Up	Other (Specify)	The Month 1 Follow-up visit was conducted 19 days out of window. The visit should have occurred between 11/25/09 through 12/16/09.
11309	Sham Eye CXL	2010-02-02	Month 3 Follow-Up	Other (Specify)	Month 3 Follow-Up Visit was not completed. Subject was lost to follow-up.

Appendix D – cross-reference to Section 7.2

A. Subject Disposition – cross-over to UVX treatment with Clinical Trial device

1. Progressive Keratoconus Subjects, UVX-001, ITT Population

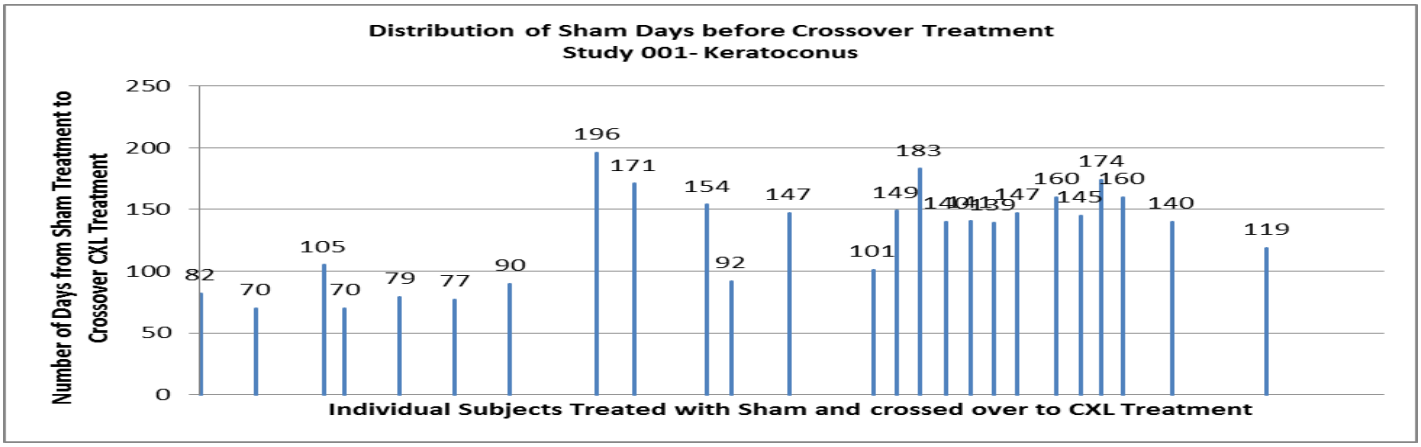
As noted in the protocol, sham patients were eligible to receive UVX-treatment of their sham study eye after the 3 month visit. Both arms were eligible to have the fellow eye (non-study eye) receive UVX-treatment. The table below shows that 12/29 CXL-arm patients received CXL-treatment in the fellow eye, 25/29 sham study eyes received CXL-treatment of the sham study eye and 4/29 did not. Eight fellow eyes also received CXL-treatment.

Treatments Administered: Primary (Study) Eyes and Secondary Eyes or Sham Study Eye Cross-Over (ITT: Progressive Keratoconus Subjects)

Randomization:	Primary (Study Eye)		Secondary Eye/Sham Study Eye			Total
	CLX	Sham	Fellow Eye CLX	None	Sham Eye UVX	
Subjects Randomized to CXL	29	---	12	17	---	---
Subjects Randomized to Sham	---	29	8	4	25	---
Total UVX	29	---	20	---	25	74

Source: Table 14.1.2.1 (Section 14.1.1)

The graph below displays for each of the 25 patients that crossed over from sham treatment to CXL treatment, the number of days between sham treatment and the crossover to CXL.



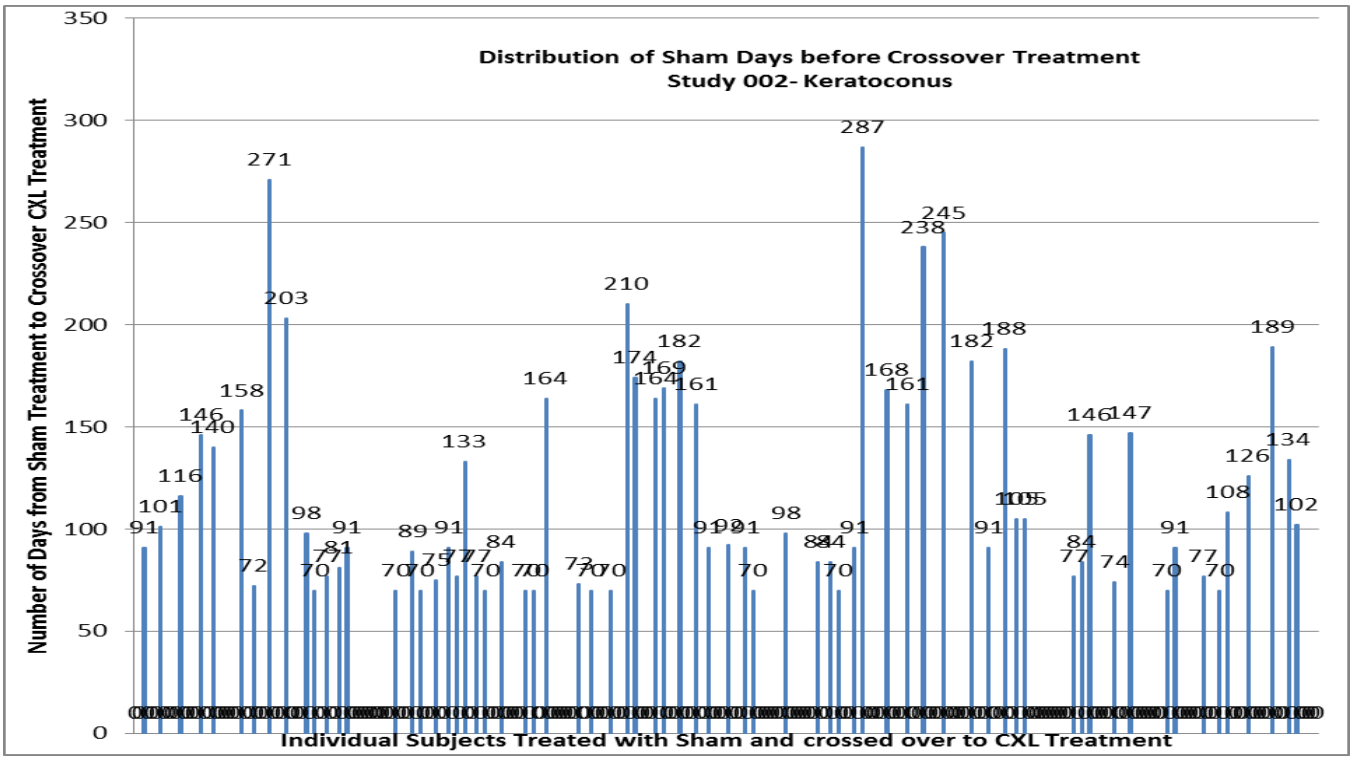
2. Progressive Keratoconus Subjects, UVX-002, ITT Population

The table shows that 44/73 CXL-treated patients had CXL treatment of their fellow eye; 69/74 sham-eyes crossed-over to CXL treatment and 33 fellow eyes also received CXL treatment.

Treatments Administered: Primary (Study) Eyes and Secondary Eyes/Sham Eye Cross-Over (ITT: CXL-002)

Randomization:	**Primary (Study Eye)**		**Secondary Eyes/ Sham Study Eye**			**Total**
	CLX	**Sham**	**Fellow Eye CLX**	**None**	**Sham Eye CLX**	
Subjects Randomized to CXL	73	---	44	29	**---**	---
Subjects Randomized to Sham	---	74	33	5	69	---
Total UVX	73	---	77	---	69	219

The graph below displays for each of the 69 patients that crossed over from sham treatment to CXL treatment, the number of days between sham treatment and the crossover to CXL.



3. Corneal Ectasia Subjects, UVX-001, ITT Population

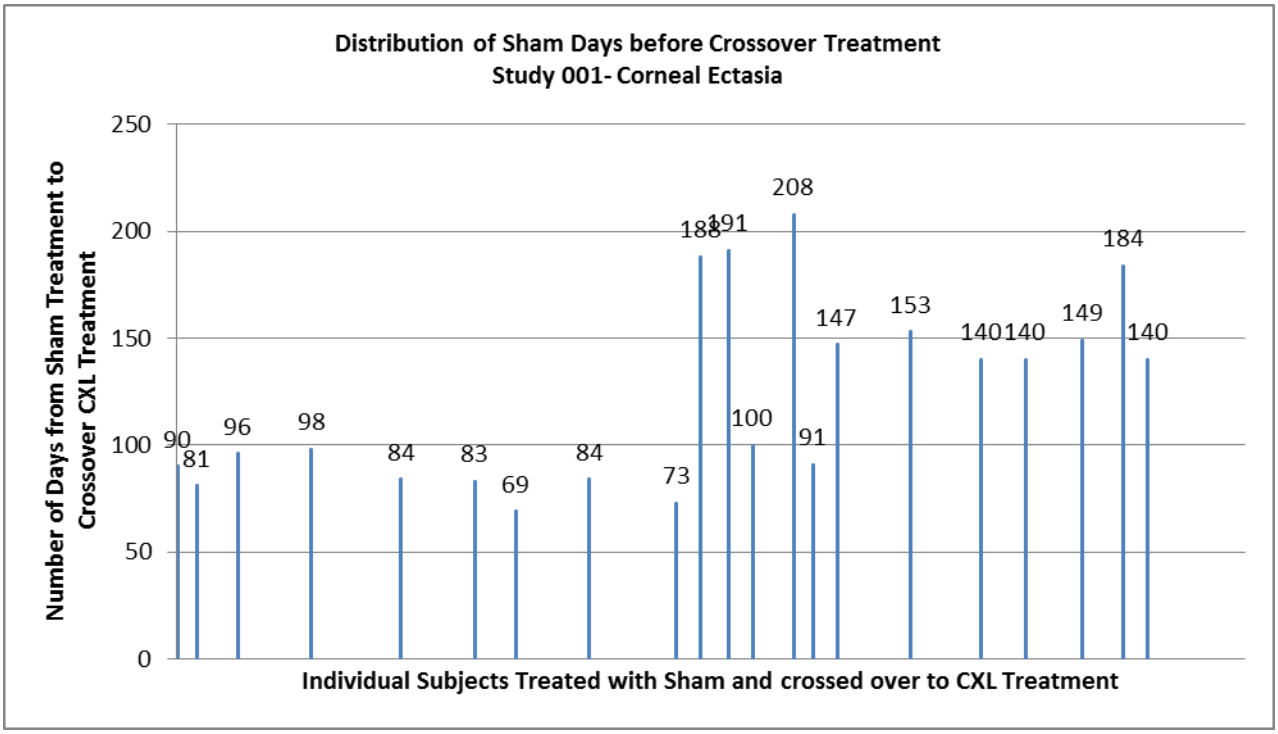
The table shows 5/24 CXL-arm patients received CXL-treatment in the fellow eye, 21/25 sham study eyes received CXL-treatment of the sham study eye and 4/29 did not. Seven fellow eyes also received CXL-treatment.

Treatments Administered: Primary (Study) Eyes and Secondary Eyes/Sham Eyes Cross-Over (ITT: Corneal Ectasia Subjects)

Randomization:	Primary (Study Eye)		Secondary Eyes			Total
	CLX	Sham	Fellow Eye CLX	None	Sham Eye UVX	
Subjects Randomized to UVX	24	---	5	19	---	---
Subjects Randomized to Sham	---	25	7	4	21	---
Total UVX	24	---	12	---	21	57

Source: Table 14.1.2.1 (Section 14.1.2)

The graph below displays for each of the 21 patients that crossed over from sham treatment to CXL treatment, the number of days between sham treatment and the crossover to CXL.



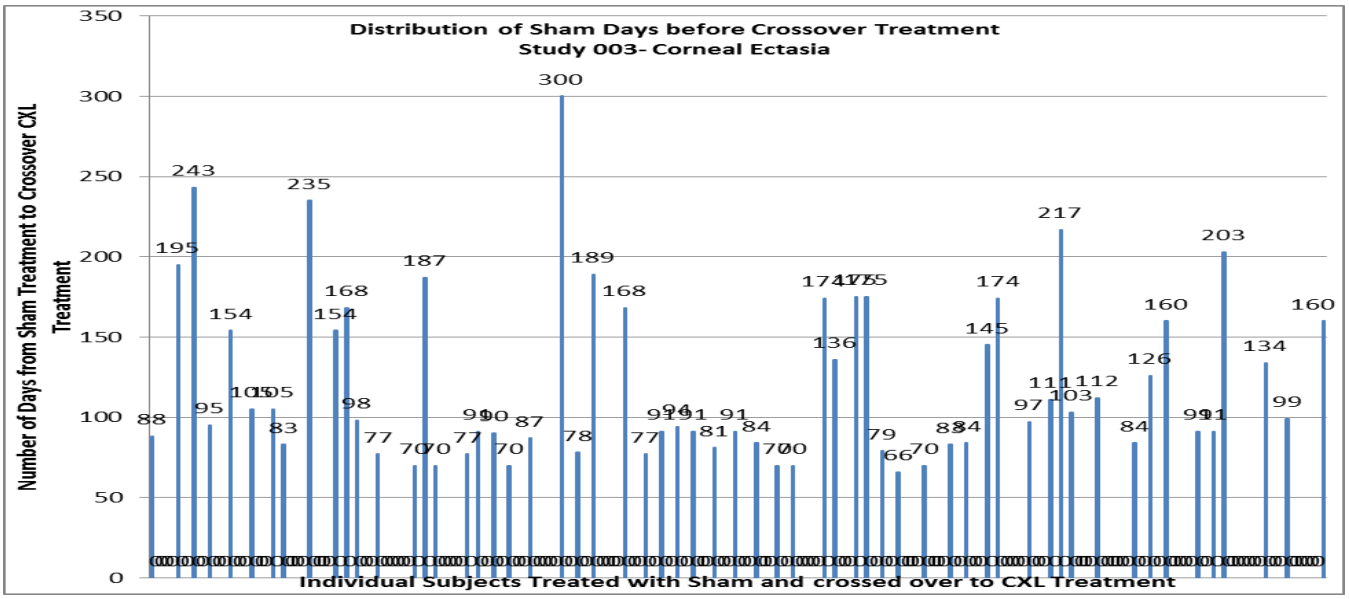
4. Corneal Ectasia Subjects, UVX-003, ITT Population

The table shows 21/67 CXL-arm patients received CXL-treatment in the fellow eye; 59/63 sham study eyes received CXL-treatment of the sham study eye and 4/29 did not. Fifteen fellow eyes also received CXL-treatment.

Treatments Administered: Primary (Study) Eyes and Secondary Eyes /Sham Eyes Cross-Over (ITT: CXL-003)

Randomization:	**Primary (Study Eye)**		**Secondary Eyes/Sham Study Eye**			**Total**
	CLX	**Sham**	**Fellow Eye CLX**	**None**	**Sham CLX**	
Subjects Randomized to CXL	67	---	21	46	**---**	---
Subjects Randomized to Sham	---	63	15	4	59	---
Total UVX	67	---	36	---	59	162

The graph below displays for each of the 59 patients that crossed over from sham treatment to CXL treatment, the number of days between sham treatment and the crossover to CXL.

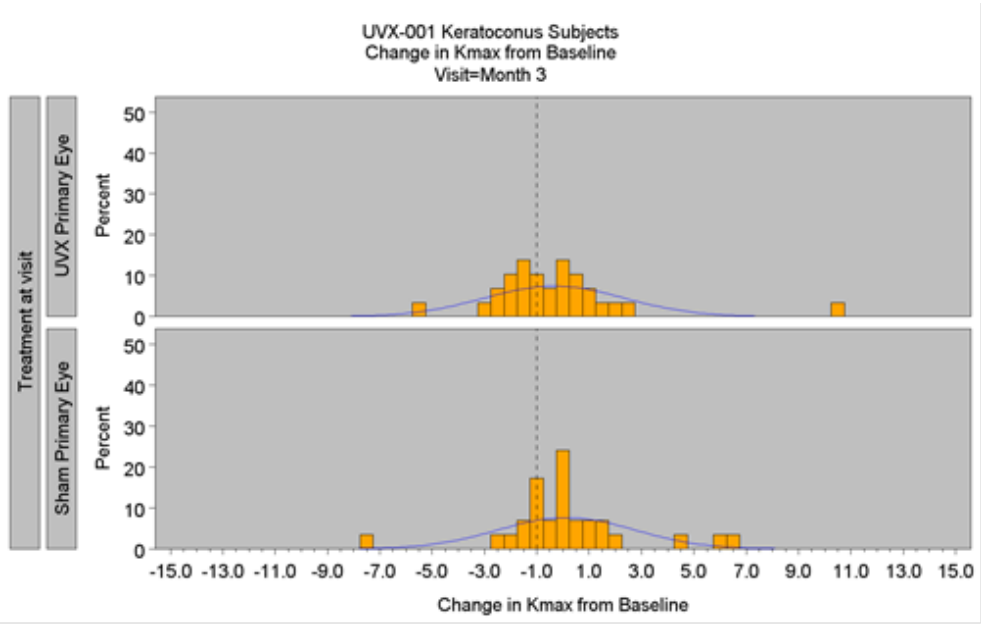


Appendix E – Cross Reference Section 8.1 and 8.2

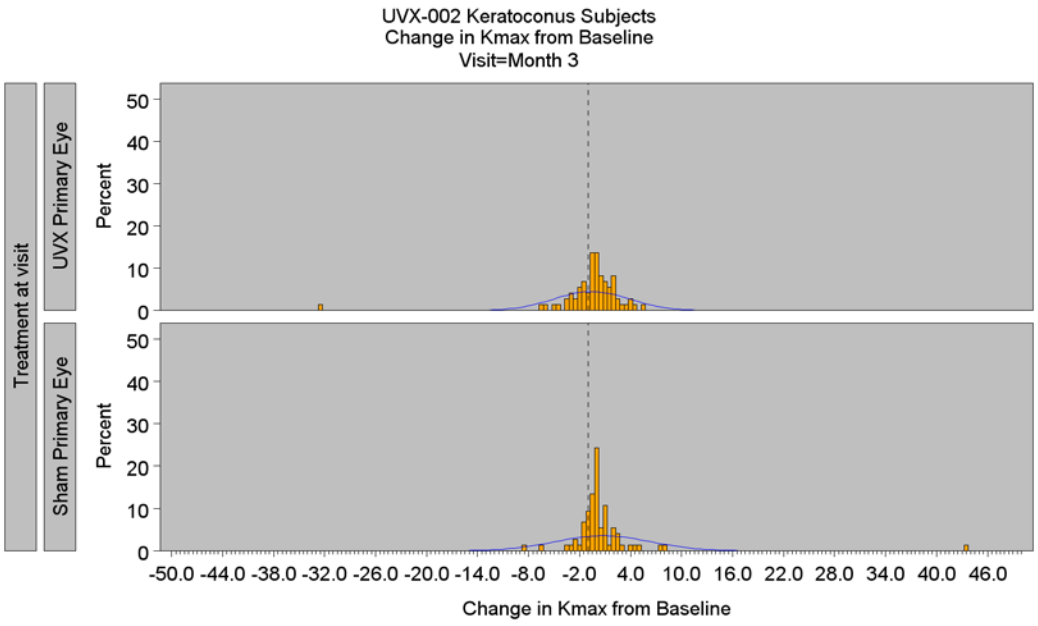
Primary Analysis Results:

The histograms below show the change in Kmax from baseline at Month 3 visit for each population and each study

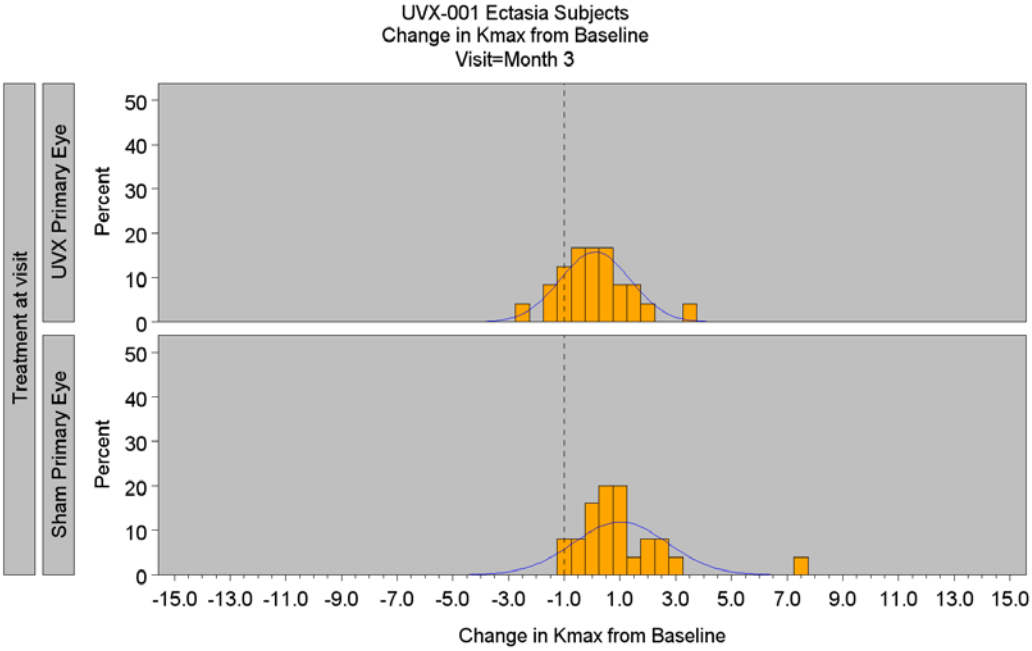
1. Progressive Keratoconus Subjects, UVX-001



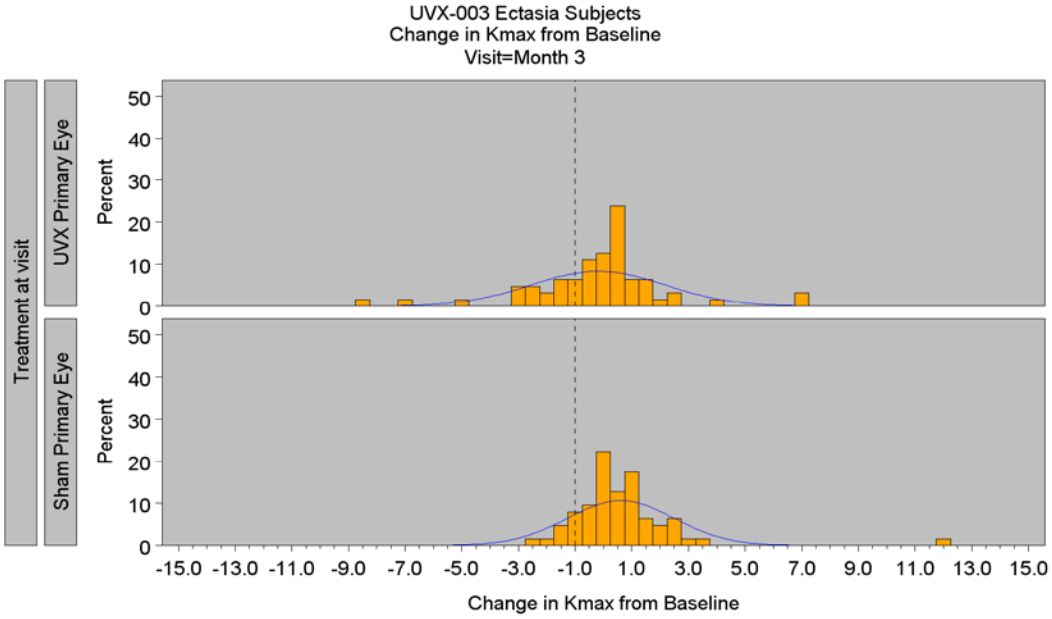
2. Progressive Keratoconus Subjects, UVX-002



3. Corneal Ectasia Subjects UVX-001



4. Corneal Ectasia Subjects UVX-003



B. Additional Analysis – Cross reference to section 8.3/Observed values

The tables below show the mean change in Kmax from baseline in randomized study eyes, based on observed values. In these tables, there is generally less values available for the later visits, compared to the 3 month visit and for the sham-control eyes, these is essentially 0% observed data available, although 100% of sham-control arms did not cross-over to CXL treatment (see Appendix D).

1. Progressive Keratoconus Subjects, UVX-001

Mean Changes from Baseline K_{max} in the Randomized Study Eye (Observed Values)

				Change from Baseline		
Visit	**Statistic**	**CXL Group (N=29)**	**Control Group (N=29)**	**CXL Group (N=29)**	**Control Group (N=29)**	**P-value**
Baseline	n	29	29			
	Mean	60.6	61.9			
	SD	7.3	8.3			
	Median	59.2	62.0			
	Min, Max	50, 79	48, 81			
Month 3	n	29	29	29	29	
	Mean	60.3	62.0	-0.3	0.1	0.5085
	SD	8.2	9.4	2.7	2.6	
	Median	58.3	60.8	-0.7	-0.1	
	Min, Max	48, 86	48, 87	-5, 11	-7, 7	
Month 6	N	28	18	28	18	
	Mean	59.3	62.6	-1.0	0.2	0.1517
	SD	7.9	10.2	2.6	3.2	
	Median	57.7	59.9	-1.2	0.1	
	Min, Max	48, 83	50, 84	-5, 7	-7, 8	
Month12	N	20	0	20	0	
	Mean	58.5		-1.6		
	SD	6.7		2.4		
	Median	58.7		-0.9		
	Min, Max	49, 72		-8, 1		

2. Progressive Keratoconus Subjects, UVX-002

Mean Changes from Baseline K_{max} in the Randomized Study Eye (Observed Values)

				Change from Baseline		
Visit	**Statistic**	**CXL Group (N=73)**	**Sham Control Group**	**CXL Group (N=73)**	**Sham Control Group**	**P-value**
Baseline	n	73	74			
	Mean	61.1	59.7			
	SD	9.8	9.2			
	Median	58.4	57.2			
	Min, Max	48, 96	48, 90			
Month 3	n	67	67	67	67	
	Mean	60.8	60.6	-0.7	0.8	0.1080
	SD	9.1	11.1	4.6	5.8	
	Median	58.5	58.0	-0.1	0.0	
	Min, Max	48, 90	49, 108	-33, 6	-9, 44	
Month 6	N	67	20	67	20	
	Mean	60.1	62.7	-1.4	2.0	0.0089
	SD	8.5	11.9	5.1	3.9	
	Median	58.3	58.7	-0.8	0.3	
	Min, Max	47, 88	50, 91	-36, 12	-2, 14	
Month12	N	69	1	69	1	
	Mean	59.4	62.6	-1.9	1.8	0.4428
	SD	8.7		4.7		
	Median	58.3	62.6	-1.2	1.8	
	Min, Max	47, 91	63, 63	-32, 7	2, 2	

Progressive Keratoconus: UVX-001 and UVX-002 Combined

Mean Changes from Baseline K_{max} in the Randomized Study Eye (Observed Values) –

				Change from Baseline		
Visit	**Statistic**	**CXL Group (N=102)**	**Sham Control Group**	**CXL Group (N=102)**	**Sham Control Group**	**P-value**
Baseline	n	102	103			
	Mean	60.9	60.3			
	SD	9.1	8.9			
	Median	58.8	58.4			
	Min, Max	48, 96	48, 90			
Month 3	n	96	96	96	96	
	Mean	60.6	61.0	-0.6	0.6	0.0820
	SD	8.8	10.6	4.1	5.1	
	Median	58.5	58.1	-0.3	-0.1	
	Min, Max	48, 90	48, 108	-33, 11	-9, 44	
Month 6	N	95	38	95	38	
	Mean	59.9	62.6	-1.3	1.1	0.0040
	SD	8.3	11.0	4.5	3.6	
	Median	58.1	59.2	-1.1	0.1	
	Min, Max	47, 88	50, 91	-36, 12	-7, 14	
Month12	N	89	1	69	1	
	Mean	59.2	62.6	-1.9	1.8	0.4075
	SD	8.3		4.7		
	Median	58.4	62.6	-1.2	1.8	
	Min, Max	47, 91	63, 63	-32, 7	2, 2	

3. Corneal Ectasia Subjects UVX-001

Mean Changes from Baseline K_{max} in the Randomized Study Eye (Observed Values)

				Change from Baseline		
Visit	**Statistic**	**CXL Group (N=67)**	**Sham Control Group**	**CXL Group (N=67)**	**Sham Control Group**	**P-value**
Baseline	n	24	25			
	Mean	56.3	55.0			
	SD	6.3	5.4			
	Median	56.2	55.2			
	Min, Max	47, 72	47, 68			
Month 1	n	24	25	24	25	
	Mean	57.4	55.8	1.1	0.8	0.6408
	SD	7.6	6.0	2.1	1.7	
	Median	57.2	55.5	0.9	0.5	
	Min, Max	43, 77	48, 67	-5, 6	-3, 7	
Month 3	n	23	24	23	24	
	Mean	56.6	55.6	0.1	0.9	0.0511
	SD	7.1	6.2	1.3	1.7	
	Median	55.1	55.5	0.0	0.7	
	Min, Max	48, 74	48, 70	-3, 3	-1, 7	
Month 6	N	22	13	22	13	
	Mean	55.6	57.0	-0.8	1.6	0.0002
	SD	6.2	6.1	1.4	2.0	
	Median	53.2	57.5	-0.9	1.3	
	Min, Max	48, 70	49, 70	-5, 1	-0, 7	
Month12	N	20	0	20	0	
	Mean	55.5		-1.4		
	SD	6.4		1.5		
	Median	54.7		-1.0		
	Min, Max	47, 71		-5, 1		

4. Corneal Ectasia Subjects UVX-003

Mean Changes from Baseline K_{max} in the Randomized Study Eye (Observed Values)

				Change from Baseline		
Visit	**Statistic**	**CXL Group (N=67)**	**Sham Control Group**	**CXL Group (N=67)**	**Sham Control Group**	**P-value**
Baseline	n	63	63			
	Mean	55.1	54.7			
	SD	7.1	6.8			
	Median	53.9	52.9			
	Min, Max	45, 75	43, 76			
Month 1	n	64	61	60	61	
	Mean	55.8	54.7	1.1	0.1	0.0005
	SD	7.1	6.7	1.9	1.1	
	Median	55.0	53.4	0.8	0.2	
	Min, Max	45, 76	43, 75	-3, 6	-2, 2	
Month 3	n	65	61	62	61	
	Mean	55.1	54.9	-0.2	0.7	0.0397
	SD	7.0	6.5	2.4	1.9	
	Median	53.4	53.6	0.1	0.5	
	Min, Max	45, 77	43, 78	-9, 7	-3, 12	
Month 6	N	62	19	59	19	
	Mean	54.4	53.0	-0.5	0.1	0.2901
	SD	6.6	5.8	1.8	2.6	
	Median	53.2	53.1	-0.2	0.5	
	Min, Max	45, 71	43, 65	-8, 2	-9, 6	
Month12	N	56	2	54	2	
	Mean	54.5	56.9	-0.6	0.4	0.5571
	SD	7.0	3.5	2.3	1.8	
	Median	53.0	56.9	-0.3	0.4	
	Min, Max	45, 74	54, 59	-10, 4	-1, 2	

Corneal Ectasia Subjects: UVX-001 and UVX-003 Combined

Mean Changes from Baseline K_{max} in the Randomized Study Eye (Observed Values)

				Change from Baseline		
Visit	**Statistic**	**CXL Group (N=91)**	**Sham Control Group**	**CXL Group (N=91)**	**Sham Control Group**	**P-value**
Baseline	n	87	88			
	Mean	55.4	54.8			
	SD	6.86	6.40			
	Median	54.1	53.9			
	Min, Max	45, 75	43, 76			
Month 1	n	88	86	84	86	
	Mean	56.2	55.0	1.1	0.3	0.0022
	SD	7.24	6.46	1.91	1.36	
	Median	55.5	54.0	0.9	0.2	
	Min, Max	43, 77	43, 75	-5, 6	-3, 7	
Month 3	n	88	85	85	85	
	Mean	55.5	55.1	-0.1	0.7	0.0073
	SD	7.03	6.41	2.13	1.82	
	Median	54.3	54.2	0.1	0.6	
	Min, Max	45, 77	43, 78	-9, 7	-3, 12	
Month 6	N	84	32	81	32	
	Mean	54.7	54.6	-0.6	0.7	0.0021
	SD	6.49	6.14	1.69	2.47	
	Median	53.2	53.6	-0.5	0.6	
	Min, Max	45, 71	43, 70	-8, 2	-9, 7	
Month 1 !	n	76	2	74	2	
	Mean	54.7	56.9	-0.8	0.4	0.4388
	SD	6.86	3.54	2.15	1.84	
	Median	53.6	56.9	-0.5	0.4	
	Min, Max	45, 74	54, 59	-10, 4	-1, 2	

Appendix F - Proposed labeling for Photrexa Viscous/Photrexa

Proposed package insert submitted 9/29/2014

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Photrexa Viscous™ (riboflavin ophthalmic solution) 20% dextran, Photrexa™ (riboflavin ophthalmic solution) with the KXL™ System for corneal collagen cross-linking safely and effectively.

See full prescribing information for Photrexa Viscous™ (riboflavin ophthalmic solution) 20% dextran, Photrexa™ (riboflavin ophthalmic solution) with the KXL™ System.

For topical ophthalmic use
Initial U.S. Approval: <<xxxx>>

INDICATIONS AND USAGE

Corneal collagen cross-linking is indicated for the treatment of progressive keratoconus or corneal ectasia following refractive surgery. (1)

DOSAGE AND ADMINISTRATION

Using topical anesthesia, debride the epithelium using standard aseptic technique. Post epithelial debridement, instill 1 drop of Photrexa Viscous topically on the eye every 2 minutes for 30 minutes.

At the end of the 30 minute soaking period, examine the eye under the slit lamp for the presence of a yellow flare in the anterior chamber. If the yellow flare is not detected, instill 1 drop of Photrexa Viscous every 2 minutes for an additional 2 to 3 drops and recheck for the presence of a yellow flare. This process can be repeated as necessary. Once the yellow flare is observed, perform ultrasound pachymetry. If corneal thickness is less than 400 microns, instill 2 drops of Photrexa every 5 to 10 seconds until the corneal thickness increases to at least 400 microns. Irradiation should not be performed unless this 400 micron threshold is met.

Irradiate the eye for 30 minutes at 3mW/cm^2 using the KXL System as per the instructions in the KXL manual. Avoid direct illumination of the limbus. During irradiation, continue topical instillation of Photrexa onto the eye every 2 minutes for the 30 minute irradiation period.

Please refer to the KXL Operator's manual for specific device instructions. [see Dosage and Administration (2)]

DOSAGE FORMS AND STRENGTHS

Photrexa Viscous™ (riboflavin ophthalmic solution) in a 3 mL glass syringe containing sterile 0.12% riboflavin ophthalmic solution with 20% dextran for topical administration. (3)

Photrexa™ (riboflavin ophthalmic solution) in a 3 mL glass syringe containing sterile 0.12% riboflavin ophthalmic solution for topical administration. (3)

CONTRAINDICATIONS

Photrexa Viscous and Photrexa for use with the KXL System in corneal collagen cross-linking are contraindicated in patients with: (4)

- A known hypersensitivity to any of the formulation components
- Intacs® in the eye(s) to be treated
- A history of chemical injury or delayed epithelial healing in the eye(s) to be treated
- Pregnancy
- Over 65 years of age
- History of herpes simplex, herpes zoster keratitis, recurrent erosion syndrome, corneal melt, corneal dystrophy, or any other corneal disease for which the physician feels may predispose a patient to complications

WARNINGS AND PRECAUTIONS

Corneal ulcer was reported in one patient [see Adverse Reactions (6)]. This TEAE was not related to corneal collagen cross-linking but related to epithelial defect. While this is rare, caution should be taken to monitor for corneal ulcer. [see Patient Counseling Information (17)].

Contact lens (other than bandage contact lens) use must be avoided for at least 5 days following corneal collagen cross-linking.

Photrexa Viscous and Photrexa are for use with the KXL™ system only.

For topical ophthalmic use only. Do not inject.

Single use only.

Discard syringe after use.

ADVERSE REACTIONS

The most frequently reported TEAEs reported for ≥2% of subjects, considered of mild intensity, were the expected sequelae following epithelial debridement of the cornea reported as corneal haze, corneal epithelium defect, corneal striae, punctate keratitis and eye pain. [see Adverse Reactions (6)].

To report SUSPECTED ADVERSE REACTIONS, contact Avedro at 1-800-xxx-xxxx or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

No adverse drug interactions have been identified. [see Drug Interactions (7)].

USE IN SPECIFIC POPULATIONS

The safety and effectiveness of corneal collagen cross-linking with Photrexa Viscous™ (riboflavin ophthalmic solution) 20% dextran, Photrexa™ (riboflavin ophthalmic solution) with the KXL™ System has not been established in patients less than 14 years of age. [see Use in Specific Populations (8)].

See 17 for PATIENT COUNSELING INFORMATION

Revised: <<insert month/year

FULL PRESCRIBING INFORMATION: CONTENTS*

1. INDICATIONS AND USAGE
2. DOSAGE AND ADMINISTRATION
3. DOSAGE FORMS AND STRENGTHS
4. CONTRAINDICATIONS
5. WARNINGS AND PRECAUTIONS
6. ADVERSE REACTIONS
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8. USE IN SPECIFIC POPULATIONS
- 8.1. Pregnancy
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10. OVERDOSAGE
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12. CLINICAL PHARMACOLOGY
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***Sections or subsections omitted from the full prescribing information are not listed.**

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

Corneal collagen cross-linking with Photrexa Viscous™ (riboflavin ophthalmic solution) 20% dextran, Photrexa™ (riboflavin ophthalmic solution)/KXL™ System is indicated for the treatment of progressive keratoconus or corneal ectasia following refractive surgery.

2. DOSAGE AND ADMINISTRATION

Using topical anesthesia, debride the epithelium using standard aseptic technique. Post epithelial debridement, instill 1 drop of Photrexa Viscous topically on the eye every 2 minutes for 30 minutes.

At the end of the 30 minute soaking period, examine the eye under the slit lamp for the presence of a yellow flare in the anterior chamber. If the yellow flare is not detected, instill 1 drop of Photrexa Viscous every 2 minutes for an additional 2 to 3 drops and recheck for the presence of a yellow flare. This process can be repeated as necessary. Once the yellow flare is observed, perform ultrasound pachymetry. If corneal thickness is less than 400 microns, instill 2 drops of Photrexa every 5 to 10 seconds until the corneal thickness increases to at least 400 microns. Irradiation should not be performed unless this 400 micron threshold is met.

Irradiate the eye for 30 minutes at 3mW/cm^2 using the KXL System as per the instructions in the KXL manual. Avoid direct illumination of the limbus. During irradiation, continue topical instillation of Photrexa onto the eye every 2 minutes for the 30 minute irradiation period.

PLEASE REFER TO THE KXL OPERATOR'S MANUAL FOR SPECIFIC DEVICE INSTRUCTIONS.

3. DOSAGE FORMS AND STRENGTHS

Photrexa Viscous™ (riboflavin ophthalmic solution) 20% dextran in a 3 mL glass syringe containing sterile 0.12% riboflavin ophthalmic solution with 20% dextran for topical administration.

Photrexa™ (riboflavin ophthalmic solution) in a 3 mL glass syringe containing sterile 0.12% riboflavin ophthalmic solution for topical administration.

4. CONTRAINDICATIONS

Photrexa Viscous and Photrexa for use with the KXL System in corneal collagen cross-linking is contraindicated in patients with:

- A known hypersensitivity to any of the formulation components.
- Intacs in the eye(s) to be treated.
- A history of chemical injury or delayed epithelial healing in the eye(s) to be treated.
- Pregnancy.
- Over 65 years of age.
- History of herpes simplex, herpes zoster keratitis, recurrent erosion syndrome, corneal melt, corneal dystrophy, or any other corneal disease for which the physician feels may predispose a patient to complications.

5. WARNINGS AND PRECAUTIONS

Corneal ulcer was reported in one patient [see Adverse Reactions (6)]. This TEAE was not related to corneal collagen cross-linking but related to epithelial defect. While this is rare, caution should be taken to monitor for corneal ulcer. [see Patient Counseling Information (17)].

Contact lens (other than bandage contact lens) use must be avoided for at least 5 days following corneal collagen cross-linking.

Photrexa Viscous and Photrexa are for use with the KXL™ system only.

For topical ophthalmic use only. Do not inject.

Single use only.

Discard syringe after use.

6. ADVERSE REACTIONS

The safety of the corneal collagen cross-linking procedure was evaluated in 3 randomized, parallel-group, open-label, sham-controlled, 12-month trials. Study UVX-001 enrolled subjects with progressive keratoconus or corneal ectasia following refractive surgery. Study UVX-002 enrolled only subjects with progressive keratoconus, and Study UVX-003 enrolled only subjects with corneal ectasia following refractive surgery. In each study, eligible subjects were randomized in a 1:1 ratio into 1 of 2 treatment groups: the corneal cross-linking (CXL) group and the control (sham) group. At Month 3 or later, subjects whose eye(s) had not developed any contraindications for performing the CXL treatment were given the option of having CXL performed on their sham treated control eyes and their untreated fellow eyes.

Safety data were obtained from 512 eyes that received any CXL treatment (293, keratoconus; 219, corneal ectasia): 193 randomized study eyes (102, keratoconus; 91, corneal ectasia) and 319 non-study eyes (191, keratoconus; 128, corneal ectasia).

The CXL procedure was safe and well tolerated in both populations. In keratoconus subjects, the most common ocular treatment-emergent adverse events (TEAEs) in any CXL-treated eye were corneal opacity (haze), punctate keratitis, corneal striae, corneal epithelium defect, eye pain, reduced visual acuity, and blurred vision (Table 1). In corneal ectasia subjects, the most common ocular TEAEs were corneal opacity (haze), corneal epithelium defect, corneal striae, dry eye, eye pain, punctate keratitis, photophobia, reduced visual acuity, and vision blurred. These events are expected sequelae following epithelial corneal debridement and occurred at a higher incidence than observed in control subjects, who did not undergo debridement or exposure to UVA light. For both indications, most ocular events were mild or moderate in intensity, with most being mild. Few systemic events were reported.

Table 1: Most Common (≥2%) Ocular Adverse Events in Any CXL-Treated Eye in the Pooled Keratoconus and Corneal Ectasia Studies (Safety Population)

	Pooled Keratoconus Studies			Pooled Corneal Ectasia Studies		
Preferred Term	**CXL Group (N=102)[1]**	**Control Group (N=103)[1]**	**Any CXL Eye (N=293)[2]**	**CXL Group (N=91)[1]**	**Control Group (N=88)[1]**	**Any CXL Eye (N=219)[2]**
Anterior chamber cell	2 (2.0)	0	5 (1.7)	2 (2.2)	1 (1.1)	3 (1.4)
Anterior chamber flare	4 (3.9)	0	9 (3.1)	5 (5.5)	2 (2.3)	9 (4.1)
Asthenopia	1 (1.0)	1 (1.0)	1 (0.3)	2 (2.2)	0	3 (1.4)
Blepharitis	0	0	4 (1.4)	0	1 (1.1)	7 (3.2)
Conjunctival hyperaemia	10 (9.8)	1 (1.0)	19 (6.5)	4 (4.4)	3 (3.4)	16 (7.3)
Corneal abrasion	1 (1.0)	0	2 (0.7)	2 (2.2)	0	4 (1.8)
Corneal disorder	3 (2.9)	1 (1.0)	7 (2.4)	3 (3.3)	0	7 (3.2)
Corneal epithelium defect	23 (22.5)	1 (1.0)	69 (23.5)	24 (26.4)	3 (3.4)	53 (24.2)
Corneal oedema	3 (2.9)	0	3 (1.0)	3 (3.3)	0	6 (2.7)
Corneal opacity[3]	58 (56.9)	4 (3.9)	178 (60.8)	62 (68 1)	7 (8.0)	148 (67.6)
Corneal scar	7 (6.9)	5 (4.9)	22 (7.5)	3 (3.3)	1 (1.1)	9 (4.1)
Corneal striae	24 (23.5)	12 (11.7)	70 (23.9)	8 (8.8)	6 (6.8)	27 (12.3)
Corneal thinning	1 (1.0)	2 (1.9)	8 (2.7)	0	0	1 (0.5)
Diplopia	2 (2.0)	1 (1.0)	4 (1.4)	1 (1.1)	0	3 (1.4)
Dry eye	6 (5.9)	2 (1.9)	18 (6.1)	13 (14 3)	4 (4.5)	27 (12.3)
Eye complication associated with device	2 (2.0)	0	2 (0.7)	1 (1.1)	0	1 (0.5)
Eye discharge	2 (2.0)	1 (1.0)	4 (1.4)	0	0	1 (0.5)
Eye irritation	10 (9.8)	1 (1.0)	18 (6.1)	8 (8.8)	1 (1.1)	15 (6.8)
Eye oedema	7 (6.9)	0	9 (3.1)	0	0	2 (0.9)
Eye pain	17 (16.7)	3 (2.9)	58 (19.8)	24 (26.4)	0	43 (19.6)
Eye pruritus	2 (2.0)	0	8 (2.7)	0	0	2 (0.9)
Eyelid oedema	5 (4.9)	0	10 (3.4)	5 (5.5)	1 (1.1)	11 (5.0)

	Pooled Keratoconus Studies			Pooled Corneal Ectasia Studies		
Preferred Term	**CXL Group (N=102)[1]**	**Control Group (N=103)[1]**	**Any CXL Eye (N=293)[2]**	**CXL Group (N=91)[1]**	**Control Group (N=88)[1]**	**Any CXL Eye (N=219)[2]**
Foreign body sensation in eyes	5 (4.9)	0	10 (3.4)	5 (5.5)	1 (1.1)	15 (6.8)
Glare	4 (3.9)	1 (1.0)	8 (2.7)	2 (2.2)	0	3 (1.4)
Halo vision	1 (1.0)	0	1 (0.3)	2 (2.2)	0	5 (2.3)
Keratitis	1 (1.0)	0	3 (1.0)	3 (3.3)	0	5 (2.3)
Lacrimation increased	5 (4.9)	0	18 (6.1)	9 (9.9)	1 (1.1)	20 (9.1)
Meibomian gland dysfunction	1 (1.0)	1 (1.0)	5 (1.7)	3 (3.3)	2 (2.3)	12 (5.5)
Ocular discomfort	0	0	8 (2.7)	8 (8.8)	0	19 (8.7)
Ocular hyperaemia	4 (3.9)	1 (1.0)	6 (2.0)	3 (3.3)	1 (1.1)	8 (3.7)
Photophobia	11 (10.8)	0	28 (9.6)	17 (18.7)	0	42 (19.2)
Punctate keratitis	25 (24.5)	8 (7.8)	62 (21.2)	18 (19.8)	3 (3.4)	51 (23.3)
Vision blurred	16 (15.7)	2 (1.9)	42 (14.3)	15 (16 5)	4 (4.5)	36 (16.4)
Visual acuity reduced	10 (9.8)	9 (8.7)	48 (16.4)	10 (11.0)	1 (1.1)	37 (16.9)
Visual impairment	3 (2.9)	2 (1.9)	6 (2.0)	4 (4.4)	1 (1.1)	11 (5.0)
Vitreous detachment	2 (2.0)	0	2 (0.7)	0	0	0

1)Results are presented as the number (%) of subjects with an event from baseline to Month 3.
2) Results are presented as the number (%) of CXL-treated eyes with an event from baseline to Month 12.
3) Almost all cases of corneal opacity were reported as haze.

Deaths, Other Serious Adverse Events, and Discontinuations

No subjects died or discontinued due to a TEAE. Two subjects developed a serious ocular adverse event in a CXL-treated eye: ulcerative keratitis (verbatim: corneal ulcer) and corneal epithelium defect (verbatim: epithelial ingrowth). Both events resolved. Neither event was considered by the investigator to be related to riboflavin or UVA light; both were attributed to epithelial defect due to corneal debridement.

To report Suspected Adverse Reactions, contact Avedro at 1-800-xxx-xxxx or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

7. DRUG INTERACTIONS

No adverse drug interactions have been identified. No specific drug interaction studies have been performed.

8. USE IN SPECIFIC POPULATIONS

8.1. Pregnancy

Pregnancy Category C: There are no adequate and well-controlled studies of corneal collagen cross-linking in pregnant women. Corneal collagen cross- linking should not be performed on pregnant women.

8.3. Nursing Mothers

Patients should notify their healthcare professional if they are breast-feeding or plan to breast-feed.

8.4. Pediatric Use

The safety and effectiveness of corneal collagen cross-linking has not been established in patients less than 14 years of age.

In the Phase III studies, there were 33 patients between 14-21 years of age.

8.5. Geriatric Use

No subjects enrolled in the clinical studies were 65 years of age or older.

10. OVERDOSAGE

Photrexa Viscous and Photrexa are administered topically to the eye by a physician as part of corneal collagen cross-linking. There is no experience with overdose of Photrexa Viscous or Photrexa.

11. DESCRIPTION

Photrexa Viscous (riboflavin ophthalmic solution) 20% dextran and Photrexa (riboflavin ophthalmic solution) are intended for topical ophthalmic administration as part of corneal collagen cross-linking with the KXL System.

Photrexa Viscous and Photrexa are supplied as:

- Photrexa Viscous in a 3 mL glass syringe containing sterile 0.12% riboflavin ophthalmic solution with 20% dextran for topical administration.
- Photrexa in a 3 mL glass syringe containing sterile 0.12% riboflavin ophthalmic solution for topical administration.

Photrexa Viscous (riboflavin ophthalmic solution) 20% dextran is a yellow solution containing 0.12% riboflavin, 20% dextran, 0.31% sodium chloride, 79% water for injection, 0.38% disodium phosphate, .02% sodium phosphate.

Photrexa (riboflavin ophthalmic solution) is a yellow solution containing 0.12% riboflavin, 0.31% sodium chloride, 99% water for injection, 0.38% disodium phosphate, .02% sodium phosphate.

The chemical formula for Riboflavin 5-Phosphate Sodium (Vitamin B2) is $C_{17}H_{20}N_4NaO_9P$ with a molecular mass of 478.33 g/mol.

Please refer to the KXL System Operator's Manual for a specific device description and instructions.

12. CLINICAL PHARMACOLOGY

No clinical pharmacology studies were conducted.

12.1. Mechanism of Action

Riboflavin (Vitamin B2) is a water-soluble vitamin that is the parent of two coenzymes, flavin adenine dinucleotide and flavin mononucleotide, which catalyze many oxidation/reduction reactions in the body that involve combining oxygen or removing hydrogen, including glucose oxidation, amino acid deamination, and fatty acid breakdown.

Under the conditions used for corneal collagen cross-linking, riboflavin functions as a photosensitizer.

13. NONCLINICAL TOXICOLOGY

13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility

A photocarcinogenicity study was undertaken to examine the effect of topical and oral administration of riboflavin on UV light-induced tumorigenesis in hairless mice. In this study, the auricle was "painted" daily with 15 mg/mL riboflavin solution in propylene glycol. A second group of hairless mice was provided riboflavin in drinking water at a concentration of 15 mg/mL. Controls were untreated. All groups were exposed to UV light for 5 min/day, 6 days/week for 11 months. No difference in tumor formation or latency of tumor formation was observed between controls and riboflavin-treated mice.

In an initiation-promotion study, mice were treated with riboflavin via the diet at concentrations of 0.2% or 0.6% for 27 weeks. Benzo(a)pyrene (0.2 mL, 0.025%) was topically applied twice weekly for 23 weeks, 4 weeks after initiation of the riboflavin administration. No increase in tumor development occurred in the riboflavin-treated group compared with controls, i.e., riboflavin was not a tumor promoter.

The genotoxicity of riboflavin has been examined *in vitro* in bacterial reverse mutation assays, sister chromatid exchange assay and chromosomal aberration assays. An *in vivo* mouse micronucleus study also has been reported. The overall weight of evidence indicates that riboflavin is not genotoxic.

In a 3-generation reproduction study with rats treated at a dose 10 mg (calculated dose ~50 mg/kg) for about 140 days from weaning, no effect on growth and development were reported.

13.2. Animal Toxicology and/or Pharmacology

Riboflavin has very low toxicity following single doses by the oral, intravenous and intraperitoneal routes of administration to rats and dogs. The LD50 for riboflavin by the oral route of administration to the mouse and rat was >40,000 and >10,000 mg/kg, respectively, and 2000 mg/kg in the dog, and by the intravenous route of administration to rats was about 560 mg/kg

Rats were treated via the diet with riboflavin produced from fermentation or chemical synthesis (purity 96-98%) at doses of 20-200 mg/kg for 13 weeks. No effects were observed on body weights, food or water consumption, clinical chemistry, urinalysis or gross or anatomic pathology. Dogs were treated with riboflavin at 25 mg/kg via the diet for 5 months. No adverse toxicity was reported.

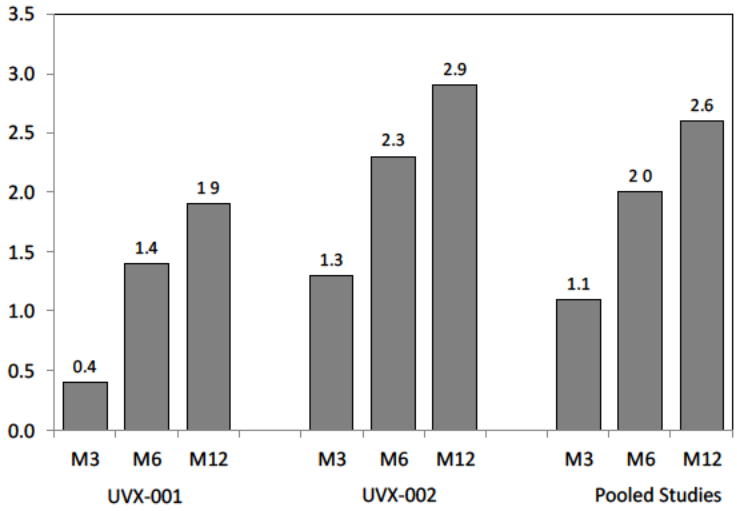
14. CLINICAL STUDIES

As described in Section 6 (Adverse Reactions), 3 prospective, randomized, parallel-group, open-label, sham-controlled, 12-month trials were conducted to evaluate the safety and effectiveness of riboflavin ophthalmic solution/UVA irradiation for performing CXL in the eyes of subjects with progressive keratoconus or corneal ectasia following refractive surgery: Study UVX-001 (keratoconus or corneal ectasia following refractive surgery); Study UVX-002 (keratoconus only); and Study UVX-003 (corneal ectasia only).

In each study, the primary efficacy endpoint was corneal curvature, as measured by maximum corneal curvature (K_{max}). Study success was defined as a difference of ≥1 diopter (D) in the mean change in K_{max} from baseline to Month 12 between the randomized CXL group and the control group. Using last observation carried forward, observations at Month 12 were obtained from 384 subjects: 205 keratoconus (102, CXL; 103, control) and 179 corneal ectasia (91, CXL; 88, control).

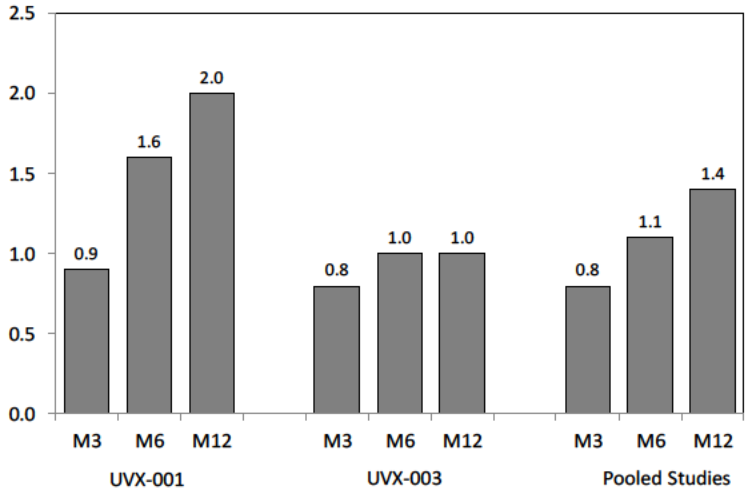
In both the individual studies and pooled analysis for keratoconus, the difference between the CXL and control groups in mean change from baseline K_{max} progressively improved, in favor of CXL, from Month 3 through Month 12 (Figure 1). In each analysis, the definition of success was met for the primary efficacy endpoint. Furthermore, the differences between treatment groups were statistically significant at Month 12, the only prospectively-defined time point for statistical inference. Absolute differences between the CXL and control groups in mean change from baseline K_{max} at Month 12 were 1.9 D ($p=0.0175$), 2.9 D ($p=0.0010$), and 2.6 D ($p<0.0001$) in UVX-001, UVX-002, and the pooled studies, respectively.

Figure 1: **Differences (Control minus CXL) between Treatment Groups in Mean Changes from Baseline K_{max} (D) in the Randomized Study Eye of Keratoconus Subjects (LOCF)**



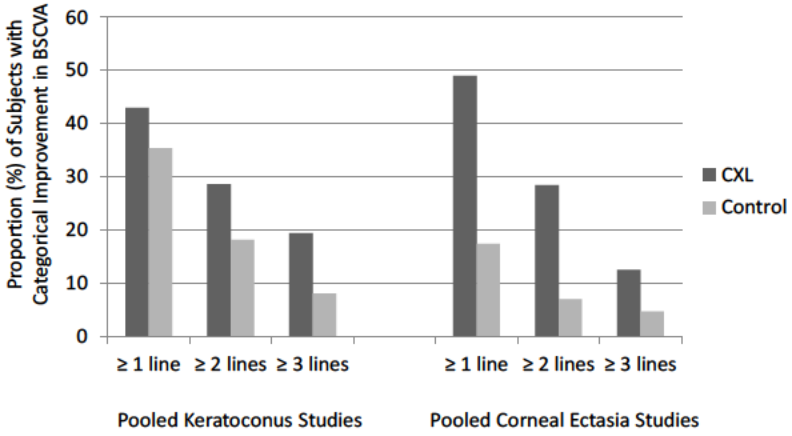
In both the individual studies and pooled analysis for corneal ectasia following refractive surgery, the difference between the CXL and control groups in mean change from baseline K_{max} increased, in favor of CXL, from Month 3 through Month 12 (Figure 2). In each analysis, the definition of success was met for the primary efficacy endpoint, and the differences between treatment groups were statistically significant at Month 12. Absolute differences between the CXL and control groups in mean change from baseline K_{max} at Month 12 were 2.0 D (p=0.0001), 1.0 D (p=0.0080), and 1.4 D (p<0.0001) in UVX-001, UVX-003, and the pooled studies, respectively.

Figure 2: **Differences (Control minus CXL) between Treatment Groups in Mean Changes from Baseline K_{max} (D) in the Randomized Study Eye of Corneal Ectasia Subjects (LOCF)**



CXL was associated with clinically meaningful improvements in best spectacle-corrected visual acuity (BSCVA). The proportion of subjects with a ≥2-line improvement in BSCVA was numerically higher in the CXL group compared with the control group at Month 12 for both indications (Figure 3). Further, the proportion of subjects with a ≥3-line improvement in BSCVA, the magnitude of which is widely accepted as being clinically relevant, was >2-fold higher in the CXL group compared with the control group at Month 12.

Figure 3: **Categorical Improvements from Baseline in BSCVA at Month 12 (LOCF): Pooled Keratoconus and Corneal Ectasia Studies**



16. HOW SUPPLIED/STORAGE AND HANDLING

Photrexa Viscous (riboflavin ophthalmic solution) 20% dextran and Photrexa (riboflavin ophthalmic solution) are provided in a bulk pack of 10 (ten), single-use foil pouches. Each foil pouch contains a 3 mL glass syringe of Photrexa Viscous or Photrexa contained within a Tyvek® pouch.

The entire bulk pack should be stored at room temperature and care should be taken to minimize exposure of the syringe to light once removed from its protective packaging. Discard syringe after use.

For topical ophthalmic use only.

Photrexa Viscous and Photrexa should be used with the KXL System only.

17. PATIENT COUNSELING INFORMATION

Important Reminders for the Patient

DO NOT RUB YOUR EYES for the first 5 days

Follow post-proceudre care recommended by your doctor.

You may be sensitive to light and have a feeling that something is in your eye. You may feel some discomfort in the treated eye. Sunglasses may make you more comfortable.

If you experience severe pain in the eye or any sudden decrease in your vision you should contact your doctor immediately.

If the contact lens that was placed on your eye on the day of treatment falls out or becomes dislodged, do not replace it and contact your doctor immediately.

Keep all appointments so the doctor can check on the healing of the cornea and the treatment results.

Regular contact lens use must be avoided for at least 5 days following corneal collagen cross-linking.

It is normal for your vision to be blurry and fluctuate for the first few days and to gradually improve in the next few weeks.

If you are not comfortable driving or operating hazardous equipment, avoid doing so until your vision is satisfactory. You should refrain from these activities if you are taking certain medications for pain.

Do not go swimming or go in a hot tub for at least 7 days following the treatment. Normal showering and washing of your hair is satisfactory.

Do not apply any form of make-up or other cosmetics to the treated eye(s) until the cornea is healed.

You should be able to resume most normal activities almost immediately, but the time may vary depending on the healing process. Please check with your doctor to confirm it is ok to resume such activities.

Please Distribute the Enclosed Patient Information Sheet.

Photrexa Viscous™ (riboflavin ophthalmic solution) 20% dextran, Photrexa ™ (riboflavin ophthalmic solution) and the KXL™ System are marketed by: Avedro, 230 Third Avenue, Waltham, MA, 02451.

This labeling text has been approved by the U.S. Food and Drug Administration.

Version:

Issued Month/Year

Avedro, Inc.
KXL™ System

Operator's Manual

ML-00006 Revision D

Printed in U.S.A.

Patents, Trademarks, Copyrights

The KXL System may be covered by one or more patent applications issued or pending in the United States and worldwide.

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

For more information, contact: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1 Forward

1.1 Intended Use of Manual

This manual is designed to serve the operators of the Avedro, Inc. KXL System. All operating instructions, product illustrations, screen graphics, troubleshooting/error messages, and other relevant information are contained in this manual. It is the operator's responsibility to ensure that all safety instructions in this manual are applied strictly.

1.2 Intended Use / Indications for Use

The KXL™ System is indicated for use in corneal collagen cross-linking for the treatment of keratoconus and corneal ectasia following refractive surgery. The KXL™ System is used in conjunction with Photrexa™ and Photrexa ZD™ (riboflavin ophthalmic solution).

1.3 Design Change Disclaimer

- Avedro assumes no responsibility for any errors that may appear in this manual. Avedro will make every reasonable effort to ensure that this manual is up to date and corresponds with the shipped KXL System.
- The computer display screens depicted in this manual are representative only. Depending on the software version of the system, minor differences may appear between the actual computer displays and those shown in this manual.
- All patient data appearing in this document, including the sample screen graphics, are fictitious and representative only. No patient's confidentiality has been violated, with or without permission.

1.4 Reproduction Disclaimer

Neither this manual nor any part of it may be reproduced, photocopied, or electronically transmitted in any way without the advanced written permission of Avedro, Inc.

1.5 User Operation Assistance Statement

Should you experience any difficulty in running your KXL System, please contact your local Avedro authorized representative.

1.6 Contraindications, Warnings and Cautions

1.6.1 Contraindications

This section describes situations in which the device should not be used because the risk of use clearly outweighs any possible benefit. Conditions that may contraindicate the use of the device include:

- Intacs in the eye(s) to be treated
- A history of chemical injury or delayed epithelial healing in the eye(s) to be treated
- Pregnancy (including plan to become pregnant) or lactating at time of treatment
- History of herpes simplex, herpes zoster keratitis, recurrent erosion syndrome, corneal melt, corneal dystrophy, or any other corneal disease for which the physician feels may predispose a patient to complications
- Corneal thickness, with epithelium < 400 microns
- Aphakic patients
- Pseudophakic patients without UV blocking lens implanted

1.6.2 Warnings

- Corneal ulcer as a result of epithelial debridement prior to corneal collagen cross-linking was reported in one patient. While this is rare, caution should be taken to monitor for corneal ulcer.

1.6.3 Precautions

- Contact lens use must be avoided for at least 5 days following corneal collagen cross-linking.
- The KXL System is for use in conjunction with Photrexa and Photrexa ZD (riboflavin ophthalmic solution).

1.6.4 Electrical Safety Warnings

This equipment requires special precautions regarding electromagnetic compatibility (EMC). Installation and use should be carried out according to the EMC information provided in this manual.

Portable and mobile RF communications equipment (remote) may affect other medical electrical equipment. Proper precautions should be taken prior to using the remote.

For Equipment Classifications please refer to chapter 5.0 Equipment Classifications

WARNING: To avoid the risk of shock this equipment must only be connected to a supply mains with protective earth.

Even with the power cord removed, there is the potential for an electrical shock from the 12VDC internal power source.

The system is designed for continuous operation using the external connector or its internal rechargeable battery.

WARNING: This equipment is operated with hazardous voltages that can shock, burn, or cause death. To reduce the possibility of electrical shock, and inadvertent UVA exposure do not remove any fixed panels. Ensure that all service to the system, beyond what is described in this manual, including to the rechargeable battery, is performed only by qualified Avedro service personnel.

WARNING: Remove the wall plug and turn off the power switch before servicing or cleaning (disinfecting) the equipment.

Never pull cords to remove the power cord from the outlet. Grasp the power cord plug and pull it from the outlet to disconnect.

WARNING: Do not operate the equipment with a damaged power cord.

WARNING: Position the power cord so that it cannot be tripped over, walked on, rolled over, crimped, bent, pinched, or accidentally pulled from the wall outlet.

WARNING: Do not use the instrument near water and be careful not to spill liquids on any part of it.

WARNING: The USB port can only be used when the system is not in treatment mode, do not connect to the USB during treatment.

WARNING: Do not operate the KXL System in the presence of flammable mixtures or anesthetics.

WARNING: Never look directly into the UV light beam. Never direct the beam towards a person except for therapeutic purposes.

WARNING: The remote contains replaceable batteries; if system is not going to be used for an extended period of time remove the batteries.

WARNING: Do not use adjacent to or stack with other equipment; if it is used adjacent to or stacked with other equipment, verify that the equipment behaves normally as intended.

WARNING: No modification of this equipment is allowed.

WARNING: MR Unsafe – Keep away from magnetic resonance imaging equipment.

1.7 Patient Safety

- The treatment should take place in a quiet and relaxed atmosphere in order not to distract the attention of the patient. The patient should lie on a table or patient's chair. The patient's head should rest comfortably in a headrest. It is imperative that the table or patient's chair or the system not be moved during the treatment procedure.

CAUTION: The KXL System is a medical device. It may be operated, therefore, only in health care facilities or medical areas under the supervision of medically trained personnel.

1.8 Additional Safety Considerations

- UV irradiance of the KXL System is calibrated by the manufacturer and must be checked annually. Any modification of the system's external light beam by means of optical elements is strictly prohibited.

- Plastic instrumentation such as speculums or eye shields may be damaged when impacted by the UV beam, possibly resulting in product degradation. Therefore, only Avedro recommended accessories or stainless steel surgical instruments should be used.

- Smooth metallic surfaces can reflect despite the effort to blank them. Therefore, only laser grade instruments should be used.

1.9 FCC Compliance Notice

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential environment. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instruction manual, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off

and on, the user is encouraged to try to correct the interference by one or more of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Connect the equipment into an electrical outlet on a circuit different from that to which the receiver is connected.
- Consult Avedro Customer Service for help.

Properly shielded and grounded cables and connectors must be used in order to meet FCC emission limits. Proper cables and connectors are available from Avedro. Avedro is not responsible for any radio or television interference caused by unauthorized changes or modifications to this equipment. Unauthorized changes or modifications could void the user's authority to operate the equipment.

2 Introduction

2.1 System Overview

The KXL System is an electronic medical device which delivers ultraviolet light (365 nm wavelength) in a circular pattern onto the cornea after Photrexa and Photrexa ZD (riboflavin ophthalmic solution) has been applied. Irradiating the Photrexa and Photrexa ZD (riboflavin ophthalmic solution) creates singlet oxygen, which forms intermolecular bonds in corneal collagen, stiffening the cornea through cross-linking. UV flux and irradiation time (that is, fluence) at the cornea are controlled by an onboard computer system.

The ***Optics Head*** houses the UVA irradiation mechanism. The LED emits UVA radiation at a wavelength of 365 nm at an intensity of 3 mW/cm^2.

A fixed aperture mounted in the UVA irradiation beam path is used to produce a uniform circular area of irradiation at the treatment plane with an approximate diameter of 9 mm. Alignment lasers are used to aid the user in focusing the beam on the patient's cornea. Fine alignment of the UV beam through observation of the alignment lasers is controlled through a wireless remote and an internal drive system. Treatment parameters are entered using a touch screen user interface.

The KXL is a portable system with an articulating arm to allow movement of the system for alignment of the UV Beam to the patient's cornea. An internal battery powers the system; the battery is recharged by a system internal charger from any standard AC outlet. The treatment parameters (Riboflavin Induction Period, Total UV Energy and UV Power) are selected and confirmed through the user interface touch screen computer.

The KXL System is used in conjunction with Photrexa and Photrexa ZD (riboflavin ophthalmic solution) and an RFID activation card.

2.1.1 Major Components

The major components of the KXL System include the following:

- **Optics Head with UV source**
- **KXL console with user interface**
- **Wireless remote control** (with replaceable batteries)

Figure 2-1. Overview Illustration of System

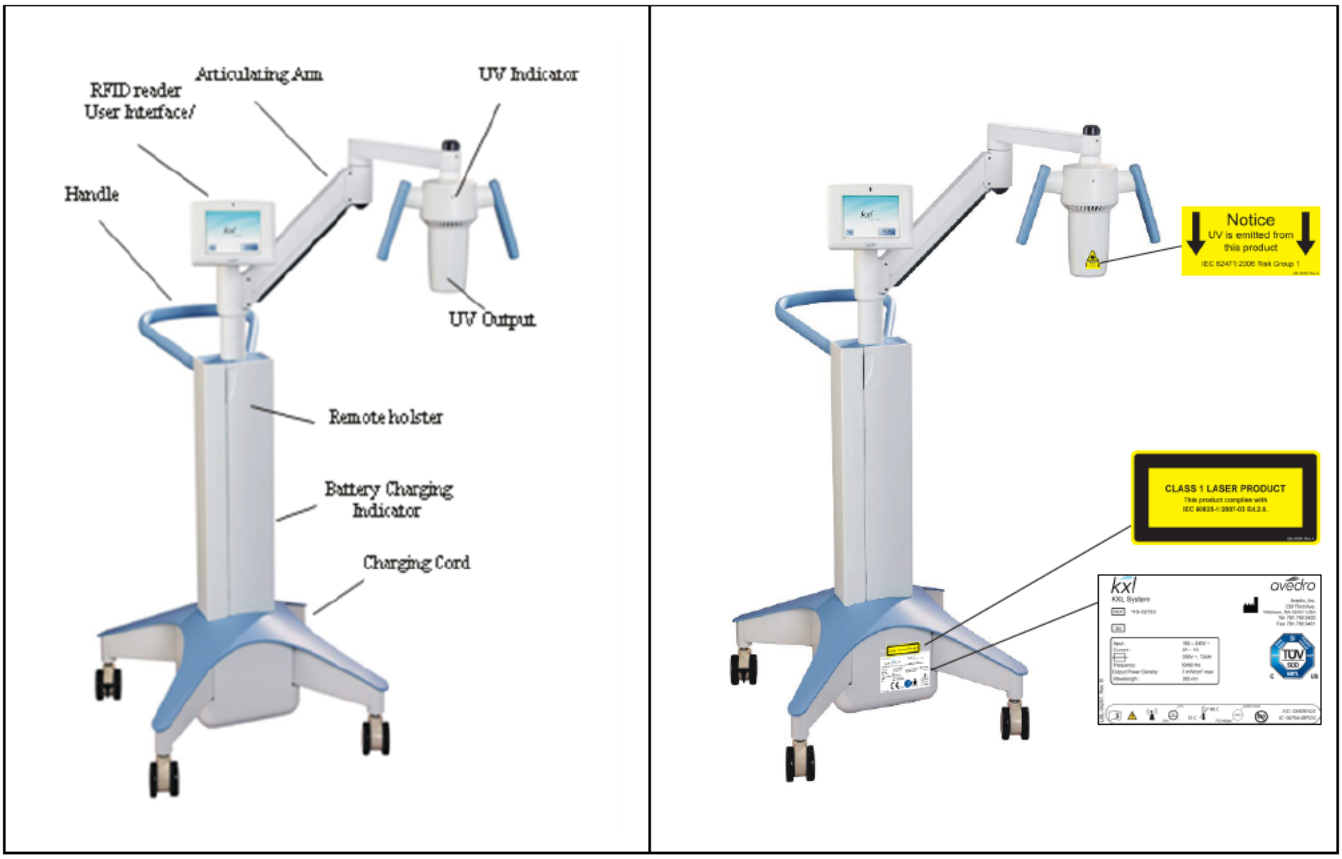


Figure 2-2. System Illustrations with Callouts

Figure 2-3. Wireless Remote

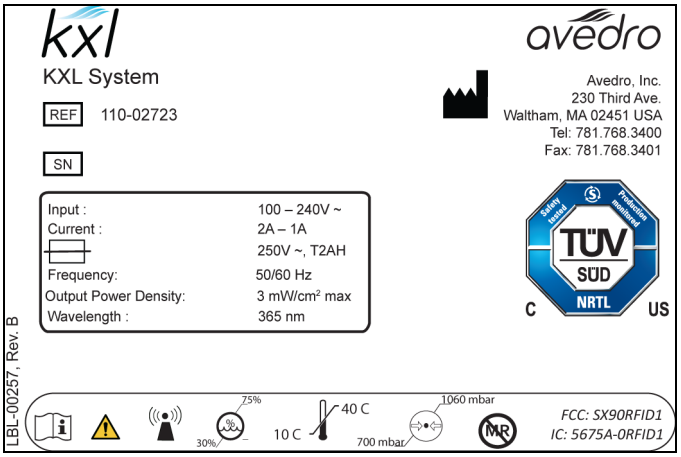


Figure 2-4. KXL Label

Figure 2-5. UV emitting Label

Figure 2-6. Alignment Laser Classification Label

3 System Operation

3.1 Charging the KXL Battery

NOTE: Prior to initial use, the internal battery pack of the KXL must be charged overnight.

- In order to maintain battery charge, it is recommended that the KXL be connected to a grounded supply mains at the end of each business day or when not in use.

- The charging status of the battery is identified by the color of the light located on the column of the KXL.
    - Orange – low, charging
    - Yellow – charging
    - Green – fully charged
      NOTE: if the battery does not appear to be charging or retaining its charge, please contact your local Avedro Service Representative.

NOTE: the KXL battery should last for 16 hours during normal operation. The system software will notify the user when the battery needs to be charged. The KXL system prohibits a treatment if there is insufficient battery power to perform a treatment. (See Chapter 4 Maintenance for more information on troubleshooting battery problems.)

3.2 Touchpad/Keyboard Use

The table below identifies and describes important touchpad keys and icons unique to KXL System operation. Chapter 2 identifies and describes the system's major components.

Touchpad Key	Icon	Description/Function
Power Off button (Initial screen)		Turns OFF electric power to the personal computer.
Start New Treatment button (Initial screen)		Directs the system to repeat the entire clinical treatment protocol so the physician can treat another patient.

Touchpad Key	Icon	Description/Function
UP arrow (various Clinical Protocol screens)		Increases the value of the current field.
DOWN arrow (various Clinical Protocol screens)		Decreases the value of the current field.
X button (various Device Settings screens)		Cancels all the entries on a particular screen and returns to the previous screen.
Checkmark button (various Clinical Protocol screens and Device Settings screen)		Directs the system to accept the current screen entries and to proceed to the next step.
Cancel Session button (various Clinical Protocol screens)		Cancels a treatment session for a particular patient. A prompt is then displayed to confirm your decision.
Return button (various Device Settings screen)		Returns to the Device Settings menu.

CAUTION: Only qualified and experienced personnel shall operate the KXL System.

3.3 UV Dose

- The UV Energy (Dose) is the product of the UV Power (Intensity) and the UV Irradiation Time. The UV Energy, the UV Power and the UV Irradiation Time are displayed.

- The system tracks UV Energy, UV Power, UV Irradiation Time and Total Treatment Time during the treatment.

NOTE - The system's parameters are:

Induction Period:	30 minutes
UV Energy:	5.4 J/cm^2
UV Power Density:	3 mW/cm^2

Please reference Photrexa and Photrexa ZD (riboflavin ophthalmic solution) package insert for formulation information.

3.4 Preparing the System

- Position the KXL System adjacent to the treatment table or chair. Lock the casters to secure the device's position.

- Make sure the system is turned ON.

- Check glass window of beam aperture for dust and dirt. See sections 4.8 and 4.9 for cleaning instructions.

3.5 Important Steps before Turning on the System

- The user is responsible for assuring that the KXL System is functioning properly and is in good-working condition before starting a treatment.

- To ensure the system is functioning properly, consider the following mandatory points:

    - Inspect the device, accessories, and connecting cables for visible damage.

    - Take local regulations for use of portable electro-optical medical devices into consideration.

3.6 Powering Up the System

- Turn ON the single power switch on the front of the KXL console. This switch turns on all the system components.

Figure 3-1. Power Switch

- The KXL System begins a power-up sequence, loading the operating system and all configuration and reference files.

Figure 3-2. Startup Screen

- Please see section 3.16 for Power Down sequence instructions.

NOTE: If there is a Start-up error, please note any error messages and contact your distributor or Customer Service immediately.

3.7 Confirm Riboflavin Induction Period

- To begin patient treatment, press the Start New Treatment button.
- Confirm the length of the induction period (30 min) for the patient.
- To proceed, press the Checkmark button.

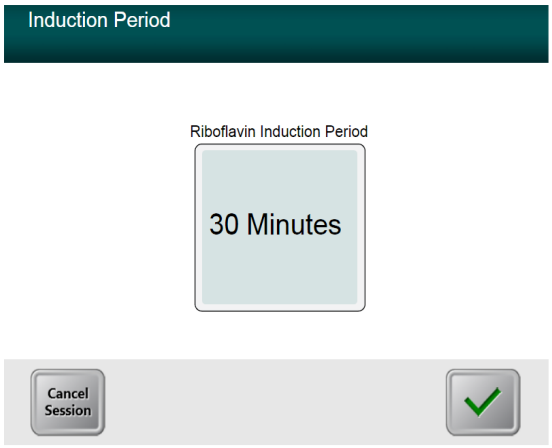


Figure 3-3. Induction Period Screen

3.8 Confirm UV Treatment

3.8.1 Confirm UV Dose

- Confirm the desired UV treatment parameters:
  - Total Energy (5.4 J/cm^2)
  - UV Power (3 mW/cm^2)

  NOTE: UV irradiation time is displayed in the orange box.

WARNING: The Treatment Activation Card is pre-programmed with above parameters and will only confirm the above energy and power dose.

- When finished, press the **Checkmark** button.

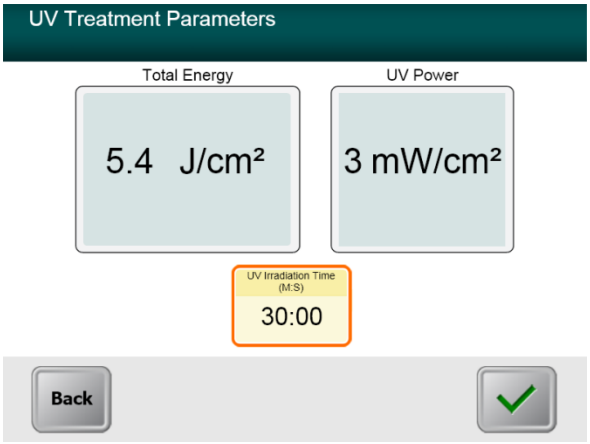


Figure 3-4. UV Energy Dose

- Confirm the specified treatment parameters by pressing the Checkmark; if the treatment parameters are not correct press the X and then re-enter the desired treatment parameters.

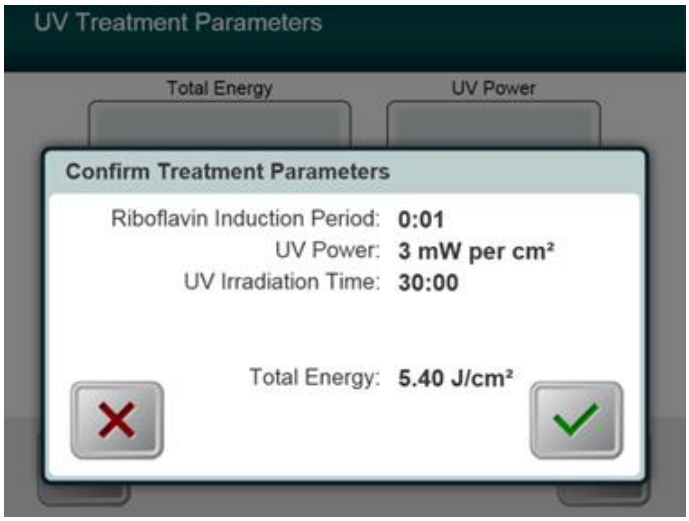


Figure 3-5. Confirm Treatment Parameters Screen

3.9 Starting Treatment

- Place the activation card on the RFID reader and hold in place until the system emits a beep.

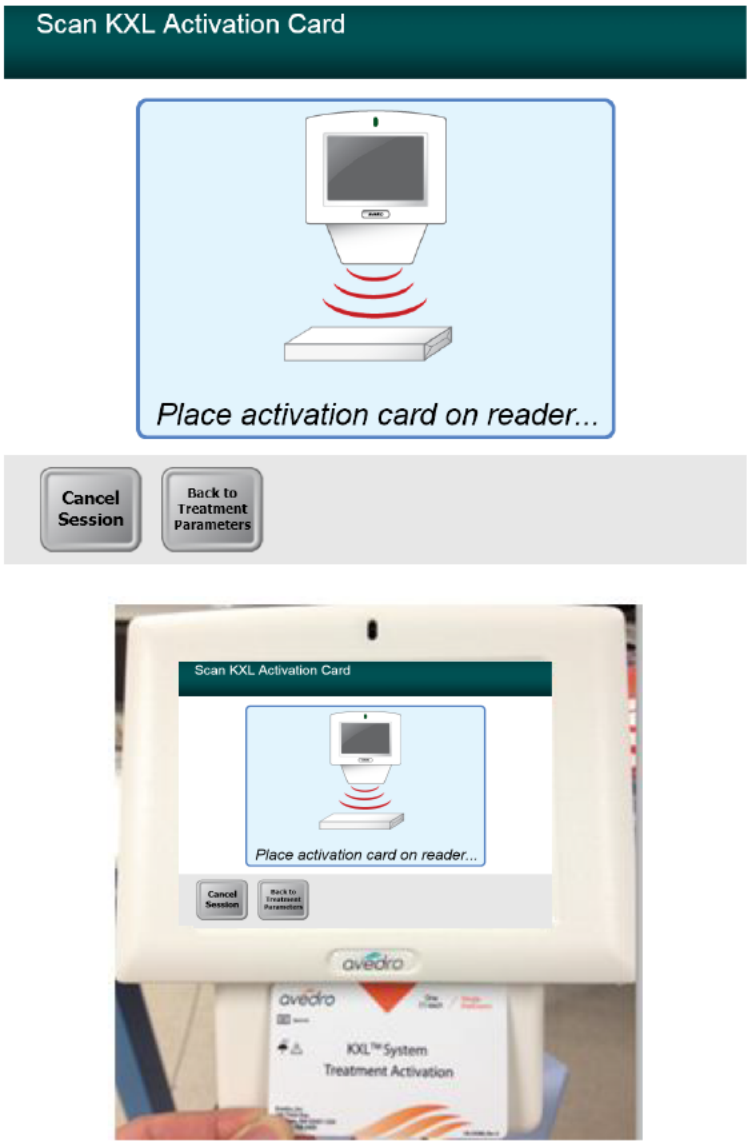


Figure 3-6. Reading Activation Card

WARNING: The Treatment Activation Card is pre-programmed with stated parameters of 3 mW/cm^2 and 5.4 J/cm^2.

3.9.1 Single-use disposables

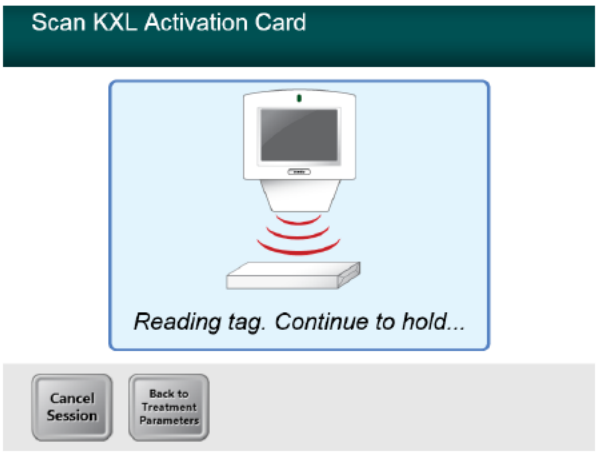
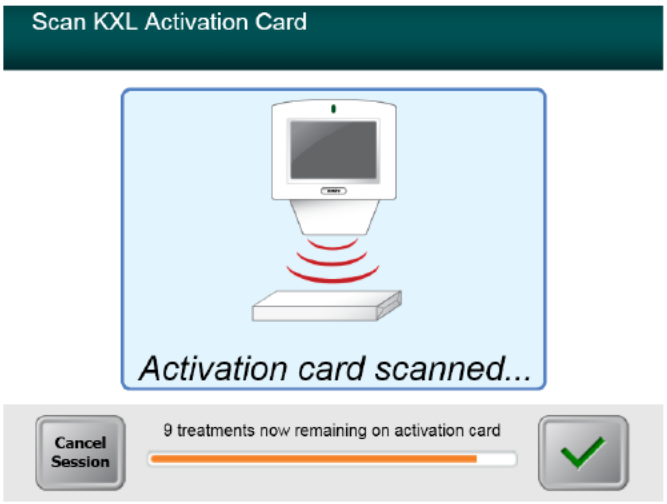


Figure 3-7. Reading Tag Screen

- Hold until read is complete and discard tag or activation card.

3.9.2 Multi-use disposables



- Once a multi-use activation card has been scanned, the display will show the number of treatments remaining on the card.

Figure 3-8. Treatments Remaining

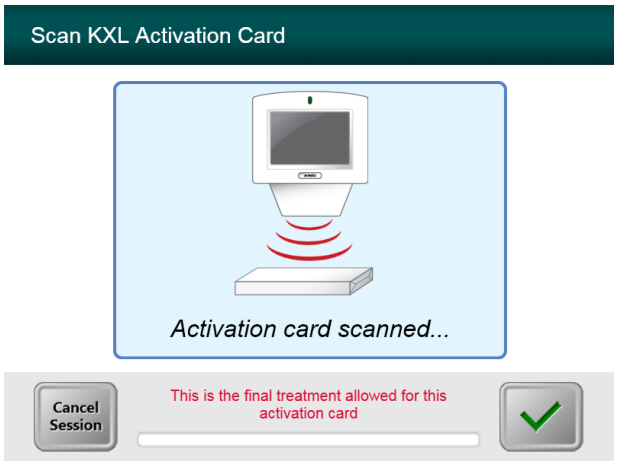


Figure 3-9. Final Treatment

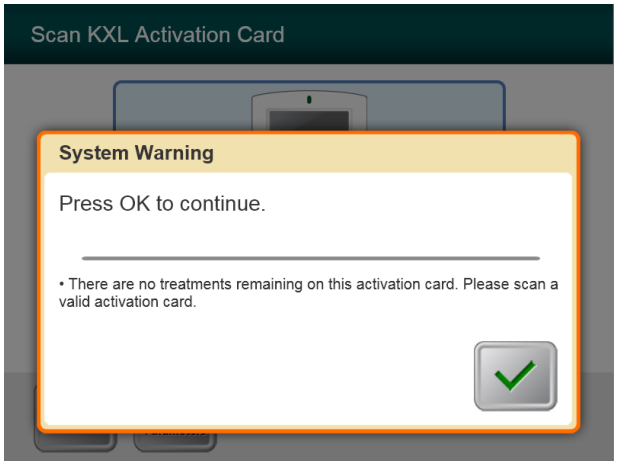


Figure 3-10. No Treatments Remaining

3.9.3 Sync Alignment Remote

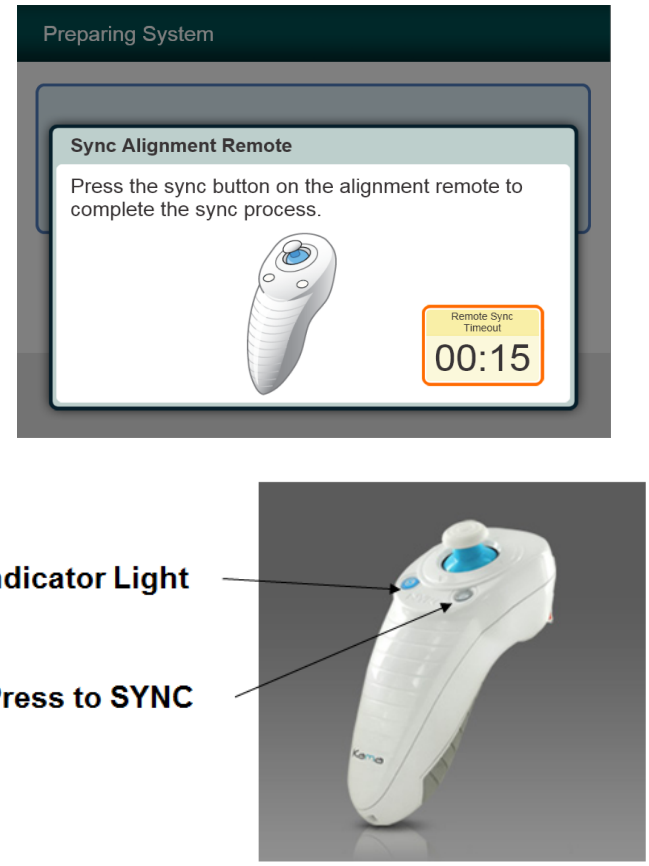


Figure 3-11. System Setup Status

- Press the "S" button on the remote to synchronize the remote within the 15 second window displayed on the screen. This is required for every procedure.

Indicator Light Status	Meaning
ON	Actively Synchronized with the device
Blinking once per second for 10 seconds	Disconnecting Sync (After procedure)
Blinking constantly, twice per second	Replace batteries immediately (2 AAA)

3.10 Preparing the Patient

- Ensure that the patient is lying flat or reclined on a patient table or chair. His or her head should rest in a head rest.
- Adjust the table or chair and head rest so that the patient can rest comfortably for the duration of the treatment without head movement.
- Apply a lid speculum and optional drapes using standard clinical technique.
- Apply riboflavin ophthalmic solution to the area of treatment in accordance with the Photrexa and Photrexa ZD package insert.

CAUTION: Photrexa and Photrexa ZD (riboflavin ophthalmic solution) is not a part of the KXL System described in this manual. For details of component use, please refer to the component's package insert.

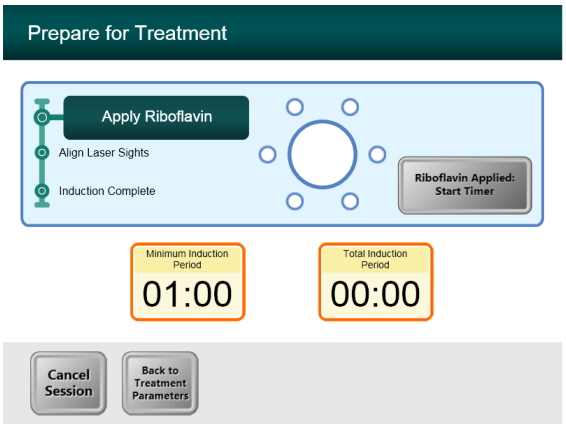


Figure 3-12. Prepare Patient Screen

NOTE: Once the riboflavin ophthalmic solution is applied to the eye, start the induction by pressing the "Riboflavin Applied: Start Timer" button.

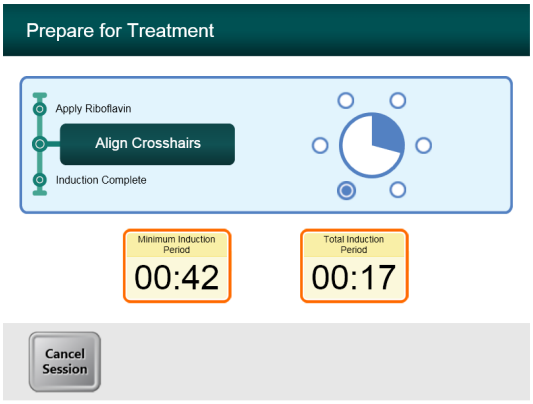


Figure 3-13. Align Crosshairs during induction

- KXL has two alignment lasers.
    - Red crosshair for X and Y axis positioning.
    - A second red crosshair for Z axis positioning.
- ***Note: For correct alignment when using the Remote, the Avedro logo on optics head should face the user***
- Manually move the Optics head back and forth and left and right until the red crosshairs are aligned to the center of the pupil.
- Manually move the Optics head up and down to align the Z axis or second red crosshair to the center of the first red crosshair.
- Fine tune the alignment as needed using the wireless remote.

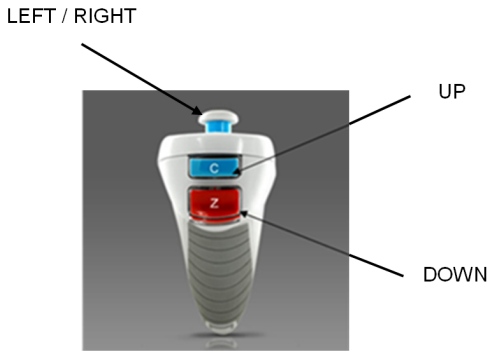


Figure 3-14. Remote Functions

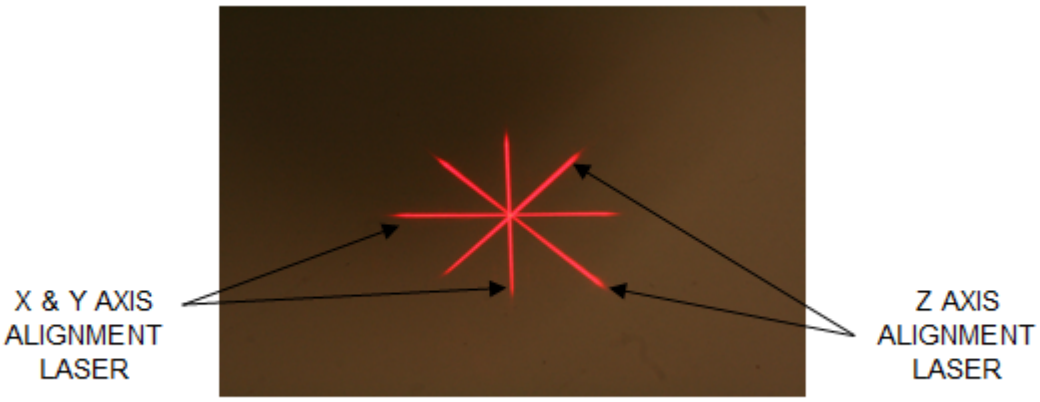


Figure 3-15. Red Crosshairs X & Y Axes, Red Crosshairs Z Axis Alignment

3.11 Initiating Treatment

- When the Induction Time is complete the "Begin UV Treatment" button will appear. Press the **"Begin UV Treatment"** button to initiate treatment.

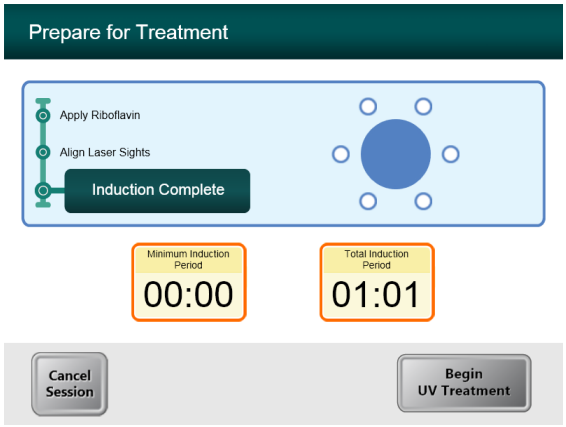


Figure 3-16. Induction Complete

WARNING: Start treatment only after the photosensitizer is applied.

CAUTION: UV light is emitted when the Avedro logo on the optical head changes state.

WARNING: Make sure that the KXL System and the patient's table or chair are secured and not moved after alignment and during treatment.

3.12 Monitoring Treatment

- Check continuously that the area of interest on the cornea is illuminated with the UVA light and adjust as necessary using the wireless remote.

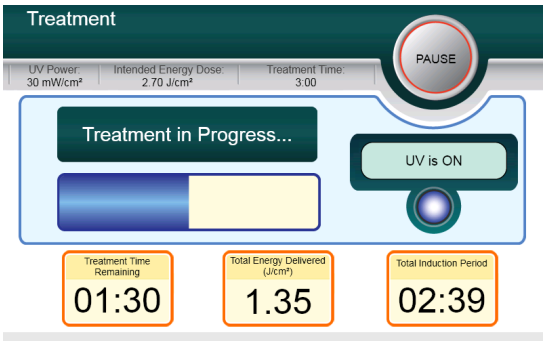


Figure 3-17. Treatment Screen

- The patient should fixate on the red X & Y alignment crosshair throughout the treatment.
- Patients should remain still during the treatment.

3.13 Stopping a Treatment

- The treatment stops automatically after the user-programmed timer expires.
- The user may decide to stop or interrupt the treatment. In such case, the UV light can be switched OFF by pushing the **Pause** button.

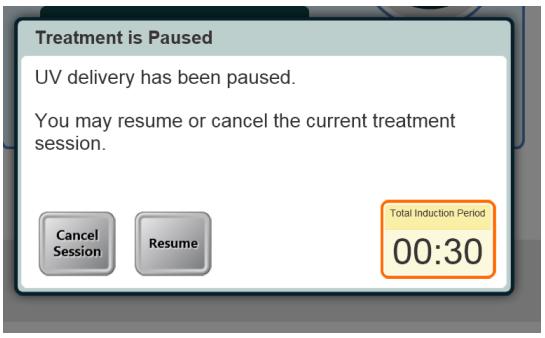


Figure 3-18. Treatment Paused Screen

- To cancel or resume treatment press appropriately. See section 3.15 if canceling a session.

3.14 Treatment Complete

- At the completion of a treatment the Total Treatment Parameters will be displayed and the screen will show Treatment complete. Press **Start New Treatment** to initiate next treatment.

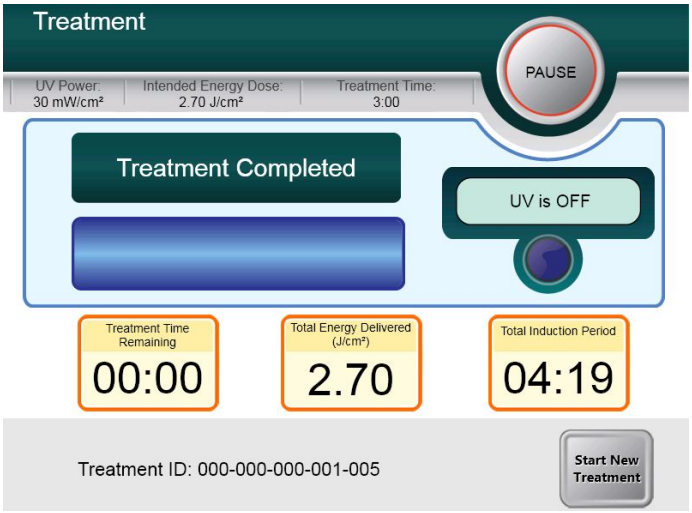


Figure 3-19. Treatment Complete Screen

- To exit treatment and / or start a new treatment press **Start New Treatment**.
- If treatments are complete Power OFF the system using the "Power Off" button on the Main Screen.
- Carefully remove the device from the patient area.
- Remove speculum.
- In order to prevent infections and manage pain, give post-op medication using a regimen similar to after photorefractive keratectomy (PRK): pain medication, steroids, antibiotics at the physician's discretion.

3.15 Pausing or Canceling a Treatment

If a session is **canceled** screen displays with **Confirm Cancel Session**.

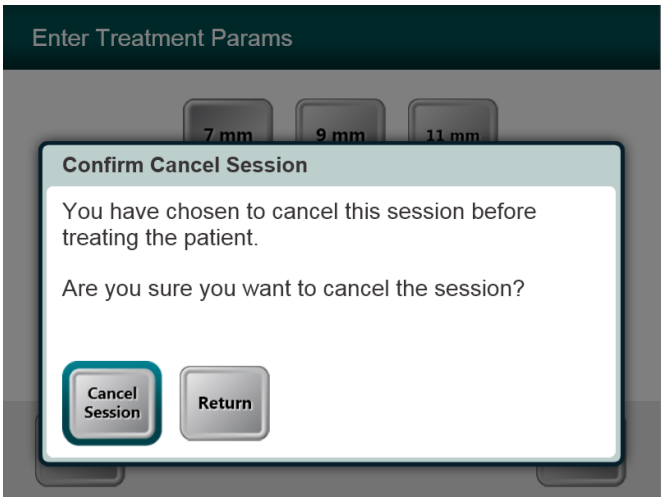


Figure 3-20. Initial Confirm Cancel Session Screen

- To cancel a session press **Cancel Session**.
- If the session is **Paused** the screen displays **Confirm Cancel Partial Treatment**.

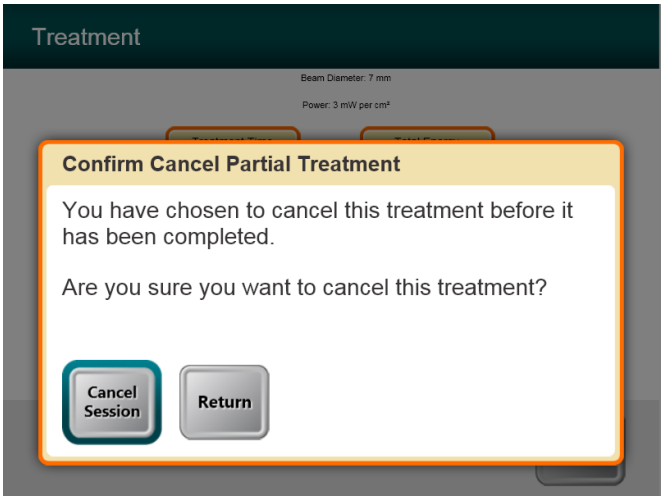


Figure 3-21. Confirm Cancel Partial Treatment

- To cancel the session press **Cancel Session**.

The screen displays **Partial Treatment Information**

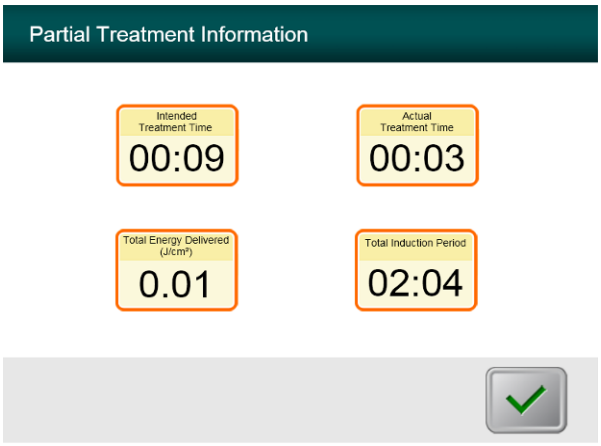


Figure 3-22. Partial Treatment Information

3.16 Powering Down the System

It is recommended that the KXL System be plugged into an electrical outlet when not in use or when stored.

Figure 3-23. Power Off

- Press the “Power Off” on the touch screen monitor.

Figure 3-24. Power Off Position

- Turn the system power switch to the "Off" position.

Figure 3-25. KXL System Plug

- Plug the KXL System in to an electrical outlet until next use.

3.17 Using the Device Settings Menu

- With the Initialization screen (New Patient Start) displayed, press and hold the KXL on the touch screen.

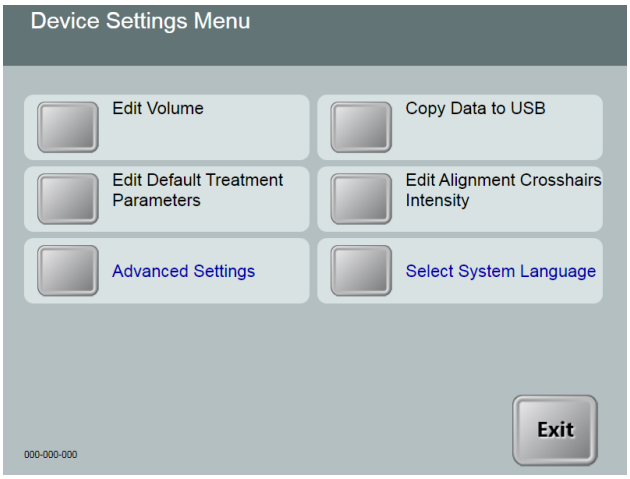


Figure 3-26. Device Settings Menu

3.17.1 Advanced Settings

- Advanced Settings are only available to Avedro and Service personnel with a KXL Advanced Settings access card. If selected the user will be prompted to scan an access card.

3.17.2 Editing System Language

- The System Language option allows a user to select the language of the Graphical User Interface.
- Select the desired language from the dropdown menu.

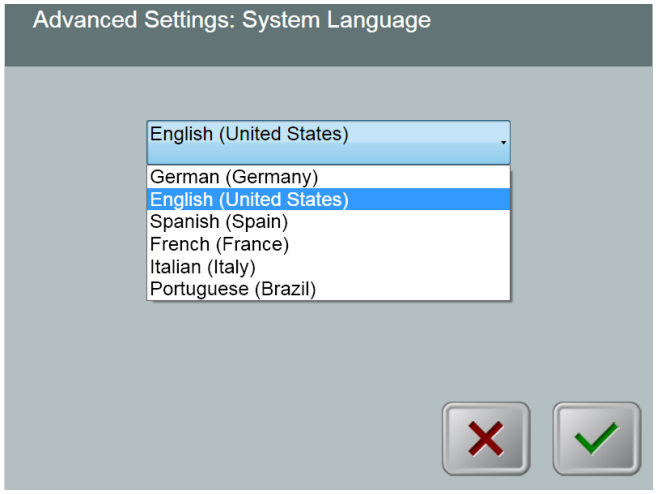


Figure 3-27. Edit System Language

3.17.3 Editing Alignment Crosshairs Intensity

- The Alignment Crosshairs Intensity option allows a user to edit the brightness of the alignment crosshairs.
- Select the **Edit Alignment Crosshairs Intensity** button on the Device Settings menu.

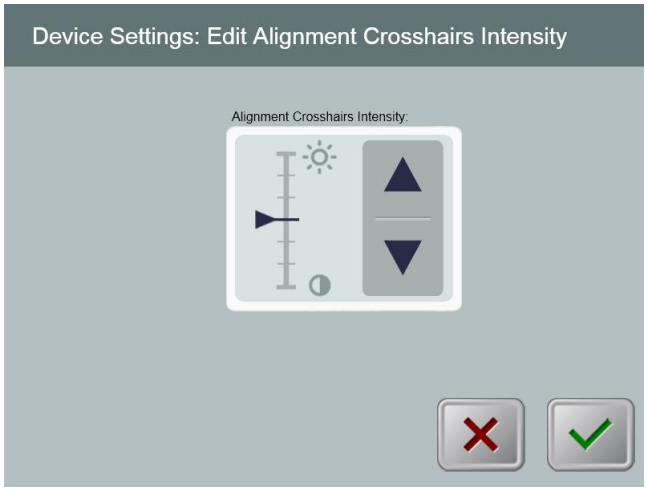


Figure 3-28. Edit Alignment Crosshairs Intensity

3.17.4 Editing System Volume

- The Edit Volume option allows a user with the appropriate security level to edit the system volume level.

- Select the **Edit Volume** button on the Device Settings menu.

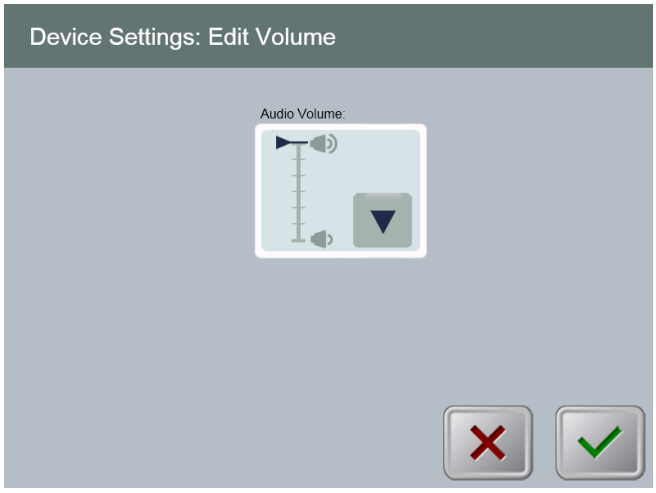


Figure 3-29. Edit Volume

3.17.5 Copying Treatment Data to USB

WARNING: The USB port can only be used when the system is not in treatment mode do not have items connected to the USB during treatment.

- Select the **Copy Treatment Data to USB** button on the Device Settings menu.

Figure 3-30. Device Settings Transfer to USB

- Insert a USB device to a USB port and then press the **Copy treatment data to USB** button. The system begins transferring the treatment data and shows a progress bar of the transfer process as shown in the screen below.

- Once complete press the **Return** button. The system will return you to the Device Settings menu.

3.17.6 Confirming Treatment Settings

- The Device Settings: Treatment Parameters option allows a user to confirm the treatment parameters that are displayed on that system.

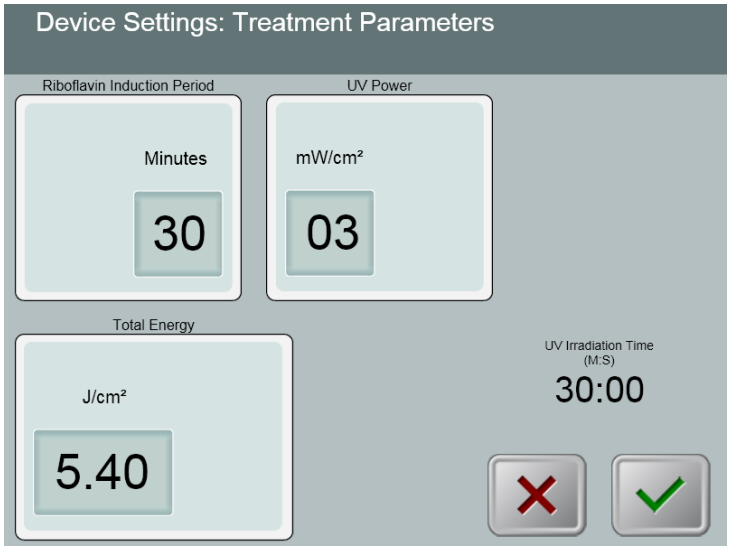


Figure 3-31. Edit Default Treatment Parameters

- When treatment parameters are confirmed, press the **Checkmark** button to exit these Settings.

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4 Maintenance / Service

By definition, “maintenance” refers to those non-technical procedures an everyday operator must perform to keep the system working properly. The word “service,” by contrast, refers to tasks that are intended to be performed only by a qualified service representative.

4.1 Installation Policy

- For each new KXL System customer, your Avedro-authorized distributor provides a full initial installation and start-up of the system. Following initial installation and once the system is operating properly, the Avedro representative may also provide basic training to a designated operator about the basic operation of the KXL System.

- Consequently, this manual does not include any specific instructions relating to installation or set-up of the system. Per your service agreement, any further hardware adjustment, other than what is specified for normal operation, should be performed by, or with the guidance of, an Avedro-authorized distributor.

4.2 Customer Maintenance

- In general, there is no customer maintenance required for The KXL System. All technical maintenance or service will be performed by a qualified service representative while under service contract. If you have trouble with your system, refer to the troubleshooting section below or call your local Avedro Representative.

4.3 Warranty Information

- A Warranty is supplied separately with the purchasing information.

4.4 Service Contract Information

- A service contract is available on all KXL Systems. The contract provides for regularly scheduled maintenance and field upgrades. It also provides for any non-scheduled service calls that may be necessary.

4.5 Per Patient Disposables

- Per Patient Disposables can be ordered from Avedro or your Avedro-authorized distributor. **Use only Avedro products or Avedro-approved products with your KXL System**. Avedro shall not be liable for damage to or malfunction of the system, which it deems, was caused by the use of unauthorized materials.

4.6 Trouble Shooting

- The KXL System checks its status at start-up automatically. If the status is incorrect, the software prevents the operator from initiating treatments when the system is in the normal operating state.

Wireless Remote

- The KXL System uses a remote control with replaceable batteries. If the batteries run low the system will lose its connection with the remote and notify the user of the need to re-synchronize and will not allow the user to initiate a procedure. If the remote synchronization is lost during a treatment the user will be prompted to determine if they want to continue the treatment without the remote.

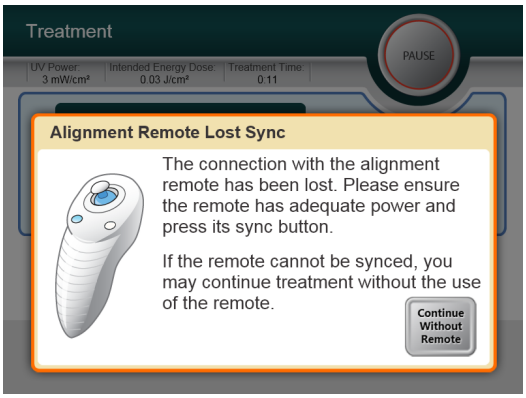


Figure 4-1. Remote Lost Sync

  - If light on the remote is flashing two times per second the remote's batteries need to be changed. If the light on the remote is flashing once per second then it is not synchronized.

  - If the remote does not re-synchronize by pressing the "Sync" button, replace the batteries.

  - If replacing the batteries does not allow the system to synchronize contact your local Avedro Service Representative.

Internal Rechargeable Battery

- The KXL system is supplied with a rechargeable battery, if the system does not appear to be turning on ensure that the battery is charged by plugging it into an outlet and checking the charging indicator on the column of the system. If the light is orange or yellow the system is charging, if it is green it is fully charged.

  - If the indicator is green or yellow and the system still does not turn on contact your local Avedro service representative.

- If the indicator is orange wait until it turns yellow or green and try turning the system on, if it still does not turn on or the indicator does go yellow or green within 8 hours contact your local Avedro service representative.

4.7 Directions for Sterilization or Disinfection

- No components of the KXL System are designed to be sterilized by the operator. External cleaning and disinfection ONLY is recommended. For disinfection purposes, use only isopropyl alcohol spray or preparations. Use small amounts of liquid and soft fiber-free wipes.

4.8 Cleaning the System

- Use a soft damp cloth to clean the system.
- The exterior of the KXL System can be cleaned using a lint-free cloth dampened with dilute bleach, soapy water, or isopropyl alcohol.
- A 70% alcohol or 10% chlorine bleach solution can also be used if necessary.
- DO NOT submerse the system in liquid or pour liquid onto the system.

CAUTION: Remove the power supply cord from the main outlet and turn off the power switch prior to any cleaning procedure.

CAUTION: Aggressive cleaning agents, especially those containing abrasives or aggressive solvents can damage component surfaces.

- The glass window of the beam aperture must not under any circumstances be in contact with any of the aforementioned substances.
- While cleaning the surfaces of the device, ensure that cleaning fluids do not seep inside the device, as this leakage can damage the device.

4.9 Cleaning the Aperture

- Check the beam aperture routinely prior to treatment.
- Use special camera lens wipes or compressed air to remove dust and particles from the glass surface of the aperture.

4.10 Articulating Arm Adjustment

If the articulating arm does not hold the Optical Head in a fix vertical position contact your local Avedro service representative.

4.11 Performing Periodic Maintenance

Interval	Specific Task
Annual	Calibration by Avedro trained personnel.

4.12 Moving the System

- The KXL is designed as a movable system within an office environment. If it ever proves necessary to transport or ship the KXL System, for any reason, contact your local Avedro representative. Packing and transporting the system should be performed only by Avedro trained and authorized personnel.

- Prior to moving the KXL System from one room to another, the monitor should be moved sideways and the optics head should be positioned close to the cart handle with the elbow protruding at the back. The system can then be easily pushed by the cart handle through the door frame.

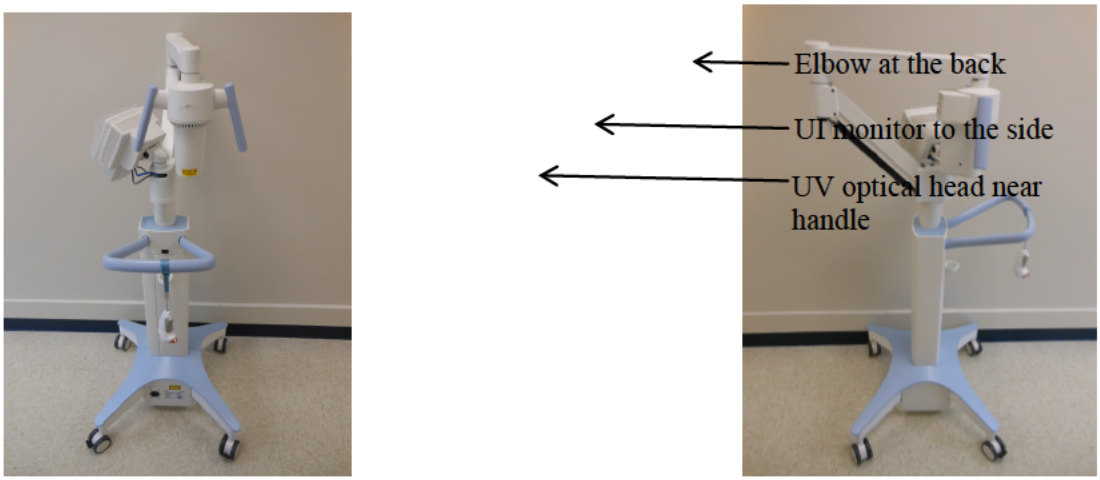


Figure 4-2 Moving System Configuration

4.13 Storing the System

- Follow all the storage temperature and humidity range specifications as listed in the Specifications chapter 7.0.

- Close all panels on the system to prevent dust and moisture from entering; this is mandatory.

- Turn OFF all the components and the main power supply as well. Disconnect the power cord physically from its electrical outlet.

- Remove the batteries from the wireless remote.

- Cover the touch screen LCD display and keyboard with its original cover or packaging to prevent any damage.

- Do not disassemble any part of the system as this could cause misalignment or damage.

4.14 Software

- Should the software become corrupted and fail to work correctly at some point, call your local Avedro service representative. Software updates will only be carried out by Avedro service representatives.

4.15 Identifying Risks Associated with Disposing of Waste Products

- When disposing of waste products, follow all applicable local regulations.

4.16 Performing a Visible Check

- Check all components of the device routinely for damage or malfunction prior to each treatment.

- Do not use a damaged or malfunctioning device. Use of such devices may harm the user and/or patient.

5 Equipment Classification

5.1 Essential Performance

The KXL system delivers to the cornea UV-A radiation of nominally 365 nm wavelength at an irradiance of 3 mW/cm^2 over an exposure period of up to 30 minutes to deliver a total energy density of up to 5.4 J/cm^2.

5.2 Equipment Classification

According to IEC60601-1 Medical Device Electrical Standard

- Protection against electrical shock
  - Class 1 (external electrical power source)
  - Internally powered equipment (internal battery operation)
- Degree of protection against electric shock
  - Not classified, equipment not provided with applied part
  - Ingress protection: IP20
- Method of sterilization or disinfection
  - Disinfect-able device
- Degree of protection for use in the presence of a flammable aesthetic mixture
  - No protection
- Use conditions
  - Continuous service

According to FCC Part 15, IEC55011 and IEC60601-1-2

- Class B

According to IEC60825-1 Safety of laser productions

- Alignment lasers are Class 1 Laser Product

According to IEC62471 Photobiological safety of lamps and lamp systems

- UVA LED is Risk Group 1

According to Annex II.3 of Directive 93/42/EEC

- Class IIa

5.3 EMC Guidance

Guidance and manufacturer's declaration - electromagnetic emissions		
The KXL UV Illumination System is intended for use in the electromagnetic environment specified below. The customer or the user of the KXL UV Illumination System should assure that it is used in such an environment.		
Emissions test	**Compliance**	**Electromagnetic environment — guidance**
RF emissions CISPR 11	Group 1	The KXL UV Illumination System uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The KXL UV Illumination System is suitable for use in all establishments other than domestic, and may be used in domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes, provided the following warning is heeded: **Warning:** This equipment/system is intended for use by healthcare professionals only. This equipment/system may cause radio interference or may disrupt the operation of nearby equipment. It may be necessary to take mitigation measures, such as re-orienting or relocating the KXL UV Illumination System or shielding the location.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Complies	

Table 5-1

Guidance and manufacturer's declaration — electromagnetic immunity			
The KXL UV Illumination System is intended for use in the electromagnetic environment specified below. The customer or the user of the KXL UV Illumination System should assure that it is used in such an environment.			
Immunity test	**IEC 60601 test level**	**Compliance level**	**Electromagnetic environment - guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	±6 kV contact ±8 kV air	±6 kV contact ±8 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.

Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines ±1 kV for input/output lines	±2 kV for power supply lines Not Applicable Input /Output Lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	±1 kV line(s) to line(s) ±2 kV line(s) to earth	±1 kV line(s) to line(s) ±2 kV line(s) to earth	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	<5 % U_T (>95 % dip in U_T) for 0,5 cycle 40% U_T (60% dip in U_T) for 5 cycles 70% U_T (30% dip in U_T) for 25 cycles <5% U_T (>95 % dip in U_T) for 5 sec	0% for 0.5 cycles 40%V for 5 cycles 70%V for 25/30 cycles 0%V for 250/300 cycles	Mains power quality should be that of a typical commercial or hospital environment, If the user of the KXL UV Illumination System requires continued operation during power mains interruptions, it is recommended that the KXL UV Illumination System be powered from an uninterruptible power supply or a battery.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
NOTE U_T is the a.c. mains voltage prior to application of the test level.			

Table 5-2

Guidance and manufacturer's declaration – electromagnetic immunity
The KXL UV Illumination System is intended for use in the electromagnetic environment specified below. The customer or the user of

the KXL UV Illumination System should assure that it is used in such an environment.

Immunity test	IEC 60601 test level	Compliance level	Electromagnetic environment — guidance
			Portable and mobile RF communications equipment should be used no closer to any part of the KXL UV Illumination System, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. **Recommended separation distance**
Conducted RF IEC61000-4-6	3 Vrms 150 kHz to 80 MHz	$[V_1]$ 3Vrms	$d = [\frac{3,5}{V_1}]\sqrt{P}$
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2,5 GHz	$[E_1]$ 3 V/m	$d = [\frac{3,5}{E_1}]\sqrt{P}$ **80 MHz to 800 MHz** $d = [\frac{7}{E_1}]\sqrt{P}$ **80 MHz to 2,5 GHz** where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in metres (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,[a] should be less than the compliance level in each frequency range.[b] Interference may occur in the vicinity of equipment marked with the following symbol: 

NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

a Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the KXL UV Illumination System is used exceeds the applicable RF compliance level above, the KXL UV Illumination System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the [ME EQUIPMENT or ME SYSTEM].

b Over the frequency range 150 kHz to 80 MHz, field strengths should be less than [V1] 3 V/m.

Table 5-3

Recommended separation distances between portable and mobile RF communications equipment and the KXL UV Illumination System			
The KXL UV Illumination System is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the KXL UV Illumination System can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the KXL UV Illumination System as recommended below, according to the maximum output power of the communications equipment.			
Rated maximum output power of transmitter W	**5.3.1 Separation distance according to frequency of transmitter m**		
	150 kHz to 80 MHz $d = [\frac{3,5}{V_1}]\sqrt{P}$	**80 MHz to 800 MHz** $d = [\frac{3,5}{E_1}]\sqrt{P}$	**800 MHz to 2,5 GHz** $d = [\frac{7}{E_1}]\sqrt{P}$
0,01	0,12	0,12	0.84
0,1	0,37	0,37	3.0
1	1.2	1.2	8.4
10	3.7	3.7	26
100	12	12	84
For transmitters rated at a maximum output power not listed above, the recommended separation distance *d* in metres (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer. NOTE 1 At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies. NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

Table 5-4

5.4 RF Transmitters

5.4.1 RFID reader:

- 13.56MHz Reader/Writer
- Integral Antenna: Maximum 4" Read Range
- US/FCC number SX90RFID1
- Max output power is 200mW
- Meets: ISO18000-3, ISO15693

Fundamental	Frequency (MHz)	Level (dB µV/m) at 30 m	Limit (dB µV/m) at 30 m	Limit (µV/m) at 30 m	Margin (dB)
Paragraph 15.225(a)	13.56 (peak)	29.8	84	15,848	-54.2

Other	Frequency (MHz)	Level (dB µV/m)	Limit (dB µV/m)	Margin (dB)
Harmonics	27.12 (peak)	-5.2	29.5	-34.7
Spurious	200.6 (peak)	34.5	40.0	-5.5
Conducted	0.199 (avg)	38.8	54.6	-15.8

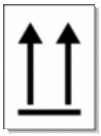
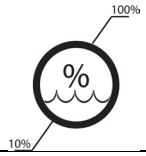
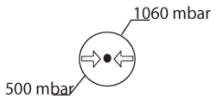
Table 5-5

5.4.2 Wireless remote control:

- FCC ID SXJ87027-T
- Frequency Range 2402MHz to 2476MHz
- Max Effective power: 0.501mW

6 Symbol Library

Text Symbol	Symbol Illustration	Definition
1. No AP symbol in presence of flammable anesthetics		Danger, Risk of Explosion. Not for use
2. AC symbol		Alternating current
3. "I" in a book		Attention: Consult ACCOMPANYING DOCUMENTS
4. Ground symbol in circle		Protected earth (ground)
5. Power Switch		ON
6. Power Switch		OFF
7. Fuse symbol		Fuse
8. Manufacturer		Name and address of the manufacturer
9. ! in a Triangle		Caution specific warning in operators manual
10. Net Weight (kgs) Gross Weight (kgs)	NW GW	Weight
11. Umbrella with raindrops		Keep Dry: Store protected from moisture (symbol is with or without rain drops)
12. Wine glass with crack on it	 or	Contents are fragile, handle with care

Text Symbol	Symbol Illustration	Definition
13. Two up arrows		Keep arrows on carton pointing up
14. Water drop in a box		Humidity limits (percentages below symbol are the acceptable range for humidity)
15. Temperature limits		Temperature shipment limits
16. MR crossed in a circle		MR Unsafe – Keep away from magnetic resonance imaging (MRI) equipment
17. Signal emitted		RF transmitted through device
18. Pressure limits		Atmospheric pressure limits (storage / operating)

Appendix H – Post-Approval Study Proposal

Avedro provided the following proposal for a post-approval study:

Title	A Phase IV, Prospective, Observational Study of the Long-term Safety and Efficacy of the KXL System with Photrexa (Riboflavin Ophthalmic Solution) for Corneal Collagen Cross-Linking in Eyes with Progressive Keratoconus or Corneal Ectasia
Purpose	To evaluate long-term safety and efficacy of corneal collagen cross-linking performed with Photrexa (riboflavin ophthalmic solution) and the KXL System in eyes with progressive keratoconus or corneal ectasia
Population	Male or female patients with progressive keratoconus or corneal ectasia, ages 12 and above Female patients of childbearing potential must not be pregnant or nursing and must agree to use a medically acceptable method of birth control from 1 week before treatment until 1 month after the treatment; Corneal ectasia post refractive surgery or topographic evidence and diagnosis of mild, moderate, or severe keratoconus; Maximum corneal curvature (Kmax) $\geq$ 47 D; Best spectacle-corrected visual acuity (BSCVA) of $\geq$ 1 letter and $\leq$ 80 letters on ETDRS chart; Corneal pachymetry $\geq$ 375 microns at the thinnest point prior to epithelial debridement
Number of Study Eyes	Approximately 500 study eyes will be enrolled in the study to have at least 250 evaluable eyes at 36 months
Study Treatments	This is a non-randomized study. The corneal epithelium will be removed. All study eyes will receive 0.12% riboflavin ophthalmic solution 1 drop every two minutes for 30 minutes followed by 30 minutes of 3mW/cm^2 UVA irradiation from the KXL system per dosing instructions on the prescribing information
Study Follow-up duration	Study eyes will be followed for up to 3 years post cross-linking procedure, with study visits at 1 day, 1 week, and 1, 3, 6, 12, 24, and 36 months
Study Endpoints	Primary efficacy criteria will be the change from baseline in maximum keratometry (K_{max}) at 12, 24, and 36 months Key safety criteria will include adverse events, slit lamp biomicroscopy, visual acuity (BSCVA), pachymetry, tonometry, endothelial cell counts (if available)

Source: Amendment 9/29/14. Module 1.11.4, Table 48