Cover page

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Lessdrops™ Prophylactic Treatment after Routine Phacoemulsification Compared to Standard Drops Regimen.

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Principal Investigator:	Kerry D. Solomon, MD
Investigator Agreement:	I have read the clinical study described herein, recognize its confidentiality and agree to conduct the described trial in compliance with Good Clinical Practices (GCP), the Declaration of Helsinki, this protocol and all applicable regulatory requirements. Additionally, I will comply with all procedures for obtaining informed consent, data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the sponsor.
Principal Investigator:	_____ Signature Date
Name of the Investigator:	_____
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Lessdrops™ Prophylactic Treatment after Routine Phacoemulsification Compared to Standard Drops Regimen.

INTRODUCTION

Cataract surgery is one of the most commonly performed surgeries in the world today. To improve the overall procedure outcome, prophylactic topical antibiotics and anti-inflammatories (steroidal and non-steroidal, NSAID) are frequently used to decrease the risk of postoperative infection (e.g., endophthalmitis) and intraocular inflammation (e.g., macular edema, CME).

Although the incidence of endophthalmitis has been reported to be less than 0.25% (range 0.02% to 0.25%);[1-9] its consequences can be devastating. To prevent endophthalmitis, the use of prophylactic antibiotics has become the standard of care.[10-12] The type of prevention used varies from surgeon to surgeon and from Country to Country. Some surgeons prefer to use topical drops, others intracameral antibiotics, and some others rather use subconjuctival injections. Factors that could influence the ophthalmologist's selection include antibiotic spectrum, efficacy, side effects, cost, and experience, among others. Chang et al[11] reported that 91 % of American Society of Cataract and Refractive Surgery members used prophylactic antibiotics starting prior to surgery and 98% used them postoperatively. The use of intracameral antibiotics alone or in conjunction with the topical one has shown to further reduce the incidence of endophthalmitis.[3, 9, 13]

The incidence of pseudophakic cystoid macular edema (CME) has been reported from 0.1% up to 4% and it depends on the method used to diagnose it. The incidence of angiographic CME is higher (up to 70%) than the incidence of clinically significant CME.[14, 15] There are different factors that affect its incidence: type of surgery,[15] presence of predisposing conditions such as intraocular inflammation (i.e. uveitis)[16, 17] and systemic diseases (i.e. diabetes).[18]

Several studies have shown the effectiveness of steroids and NSAIDs in the prevention of CME after cataract surgery not just in diabetic patients. Furthermore, some studies have shown a greater reduction in the incidence of CME when using NSAIDs compared to steroid alone.[19-21]

Even though, the large body of literature that supports the significance of prophylactic eye drops prior to surgery, patient compliance is a common problem. Different factors have been associated with patient's lack of compliance. It could be due to patient's inability to self-

administer the drops, lack of understanding of the importance of using the prophylactic treatment as well as understanding the instructions of how to administer the drops and its storage,[22] or just forgetfulness or the fact that they don't like to put the drops multiple times a day for 2-4 weeks, therefore they just avoid doing it. About 64% of patients adhere to the prescribed treatment.[23, 24]

There is a new alternative that combines the most commonly used antibiotic and anti-inflammatories into a single drop. The use of a single drop compounded ophthalmic solution may offer advantages such as increased compliance, patient comfort and reduced ocular toxicity. Three combinations are available today: Pred-Gati, Prednisolone acetate and gatifloxacin hydrochloride; Pred-Nepaf, Prednisolone acetate and nepafenac; and Pred-Gati-Nepaf, Prednisolone acetate, gatifloxacin hydrochloride, and nepafenac. Different studies have shown the safety and efficacy of topical antibiotic/steroid combination with comparable results to standard single component topical medication used prophylactically pre and post cataract surgery.[25-28] Additionally, in a recent study, Pred-Moxi-Ketor used three times a day for one week followed by Pred-Ketor twice a day for 2 – 4 weeks was compared to an intravitreal injection containing triamcinolone, moxifloxacin and vancomycin (Tri-Moxi-Vanc). Results showed similar outcomes with good control of postoperative inflammation and patient comfort without any unexpected adverse events. [29]

The purpose of this study is to evaluate the efficacy of Pred-Gati-Brom and compare it to the standard topical drops regimen used for routine cataract surgery.

1. OBJECTIVE:

To assess the efficacy of a formulation containing prednisolone acetate, gatifloxacin hydrochloride, and bromfenac used as combination drop therapy before and after routine cataract surgery and intraocular (IOL) implantation compared to standard prophylactic treatment that includes the topical use of Gatifloxacin, Bromfenac, and Prednisolone acetate 1%.

2. STUDY DESIGN AND METHODS:

2.1. **Assessed article:** Formulation containing prednisolone acetate, gatifloxacin hydrochloride, and bromfenac.

2.2. Study Design: Prospective, randomized, single site, contralateral eye study.

2.3. Subjects:

2.3.1. Inclusion Criteria:

Subjects **MUST** fulfill the following conditions to qualify for enrollment into the trial

1. Subject is undergoing bilateral cataract extraction or refractive lens exchange with intraocular lens implantation.
2. Gender: both males and females.
3. Age: 50 years and older.
4. Willing and able to provide written informed consent for participation in the study.
5. Willing and able to comply with scheduled visits and other study procedures.
6. Willing and able to administer eye drops and record the times the drops were instilled.
7. Scheduled to undergo standard cataract surgery with topical anesthesia in both eyes within 6-15 days between surgeries.
8. Potential postoperative best-corrected visual acuity of 20/30 or better.

2.3.2. Exclusion Criteria:

Subjects with **ANY** of the following conditions on the eligibility exam may **NOT** be enrolled into the trial.

1. Severe preoperative ocular pathology: amblyopia, rubella cataract, proliferative diabetic retinopathy, shallow anterior chamber, macular edema, aniridia or iris atrophy, uveitis, history of iritis, iris neovascularization, medically uncontrolled glaucoma, microphthalmos or macrophthalmos, optic nerve atrophy, advanced macular degeneration, advanced glaucomatous damage, etc.
2. Uncontrolled diabetes.
3. Use of any systemic or topical drug known to interfere with visual performance.
4. Contact lens use during the active treatment portion of the trial.
5. Any concurrent infectious/noninfectious conjunctivitis, keratitis or uveitis.
6. History of chronic intraocular inflammation.
7. History of retinal detachment.
8. Pseudoexfoliation syndrome or any other condition that has the potential to weaken the zonules.
9. Any additional ocular surgical procedures at time of cataract extraction (i.e. iStent) except corneal incisions for the correction of astigmatism.
10. Anesthesia other than topical anesthesia (i.e. retrobulbar, general, etc).
11. Any clinically significant, serious or severe medical or psychiatric condition that may increase the risk associated with study participation or may interfere with the interpretation of study results.
12. Participation in (or current participation) any ophthalmic investigational drug or device trial within the previous 30 days prior to the start date of this trial.
13. Intraocular conventional surgery within the past three months or intraocular laser surgery within one month.

The principal investigator reserves the right to declare a patient ineligible or non-evaluable based on medical evidence that indicates the patient is unsuitable for the trial.

2.3.3. Exclusion Criteria during surgery

If any of the following exclusion criteria are applicable to the study eye, the subject should not continue in the study.

1. Significant vitreous loss.
2. Significant anterior chamber hyphema.
3. Uncontrollable intraocular pressure.
4. Zonular or capsular rupture.
5. Bag-sulcus, sulcus-sulcus or unknown placement of the haptics.
6. Suturing of incision required at time of surgery.
7. Significant sedation or retrobulbar block during surgery.
8. Other procedure, such as pupil stretch, expanders, iris hooks during surgery.

Note: Any subject in which surgery has been aborted for either eye should immediately be discontinued from the study and an exit form completed for that subject. These subjects will be followed up as per the clinic standard of care, monitored for safety, and their data will be excluded from the study efficacy analysis (obtained from FDA Database Research Results Feb, 05, 2009). All adverse events will be appropriately documented and reported.

Additionally, participants who are considered to be a vulnerable subject population are not to be enrolled into the study without prior written authorization from both the Sponsor and the IRB to ensure that a description of additional safeguards are in place during the consenting and enrollment processes. Vulnerable populations include, but are not limited to, the following:

1. Prisoners
2. Nursing home residents /institutionalized individuals
3. Mentally disabled /cognitively impaired individuals
4. Sponsor employees and their family members
5. Site employees and their family members that are directly and indirectly involved with the study
6. Students of the university or the principal investigator participating in the study
7. Economically and/or educationally disadvantaged individuals
8. Comatose individuals / traumatized individuals
9. Adults who do not read and/or write
10. Hearing impaired individuals

11. Terminally ill individuals / individuals with life-threatening conditions

3. Study Procedures

3.1. Informed Consent / Subject enrollment

No subject will be enrolled into the study that does not meet the inclusion/exclusion criteria and does not sign the current approved informed consent document. Informed consent will be obtained prior to collecting any data for the study. The original signed documents will be maintained by the investigator as a permanent part of the subject's medical records. A signed copy will be provided to the subject.

3.2. Surgery Procedures:

Eyes of the study participants will be randomly assigned to one of two groups:

- Group A, test eye: Combination Drop Therapy (Pred-Gati-Brom)
  The combination drop therapy containing prednisolone acetate 1%, gatifloxacin 0.5%, and bromfenac 0.075% used three times a day (TID) starting 1 day prior to surgery and continuing after surgery for 2 weeks then twice a day for a week and once a day for another week.
- Group B, control eye:
  - Gatifoxacin 0.5%, 1 drop, QID for 3 days prior to surgery and will continue for 2 weeks after surgery and then discontinue.
  - Bromfenac 0.09%: 1 drop TID starting 3 days before surgery and TID for 2 weeks after surgery, tapered to BID for 2 weeks, and then discontinued.
  - Prednisolone acetate 1% will be started after surgery QID for 2 weeks, tapered to BID for 2 weeks, and then discontinued.

Additional Preoperative/Intraoperative Medications:

a. Routine medications including OVD, intracameral antibiotic (same to be used in both eyes), etc.

The use of antibiotics in the bottle is not allowed.

3.3. Study Visit Schedule and Assessments (Table 1).

3.3.1. Visit Schedule: Subjects will be examined at the following intervals:

1. Visit 1: Screening and enrollment: Preoperative evaluation completed not more than eight weeks before surgery

2. Visit 2: Day of Surgery
3. Visit 3: Day 1
3. Visit 4: Day 15 ±2 days postoperative after second eye surgery
4. Visit 5: Month 1: 30 ±5 days postoperative after second eye surgery

3.3.2. Measurements and evaluations

1. Visit 1: Informed consent process will be conducted at this visit. Assessments include uncorrected and best-corrected ETDRS visual acuity at 4 m (UCVA / BCVA), manifest refraction, intraocular pressure (IOP) using Goldman tonometer, and slit lamp examination including dilated fundus exam, cataract density and type, ultrasonic central corneal pachymetry (UCCP), and optical coherence tomography (OCT). Symptoms (foreign body sensation (FBS) and burning/stinging) and pain in each eye will be assessed and compared with that of the fellow eye. Any testing that is part of the site's standard of care preoperative cataract surgery evaluation may be performed prior to the informed consent being signed provided these tests are conducted within 90 days of the surgery and notation of the date performed is entered onto the source document.

   The first eye undergoing surgery will be randomized to either Group A (test) or Group B (control). Randomization will ensure that an equal number of first eyes are test and control.

2. Visit 2: The surgeon may use his preferred cataract extraction technique (manual or laser). The lens will be implanted in the bag. The following information will be captured the day of surgery: phaco technique (manual or laser), phacoemulsification time, cumulative dissipated energy (CDE), estimated fluid used, and duration of surgery (from opening/creating the incision to hydration of the wound).

3. Visit 3: Slit lamp examination, UCVA, IOP, UCCP, patient satisfaction, symptoms and pain will be assessed.

4. Visit 4 and 5: Slit lamp examination, UCVA, BCVA, IOP, UCCP, OCT, patient satisfaction, symptoms and pain will be assessed as well as presence of rebound inflammation. Rebound inflammation will be diagnosed based on the following symptoms: ocular pain, blurry vision, light sensitivity and redness; and slit lamp examination showing anterior chamber cells and/or flare. Rebound inflammation will be treated with Prednisolone acetate 1% to QID for 2 days, continued BID for a week and QD for one additional week then discontinued.

All adverse events and complaints will be monitored and recorded at all study visits.

Appendix 1 summarizes the standard evaluation procedures.

Table 1. Visits and Study Assessments

Study Assessments	Visit 1 Preoperative	Visit 2 Operative	Visit 3 Day 1	Visit 4 Day 15 ±2	Visit 5 Day 30 ±5
Inclusion/Exclusion Criteria	x				
Consent Subject	x				
Patient demographics (age, gender, race, ethnicity)	x				
Manifest Refraction	x		x	x	x
UCDVA	x		x	x	x
BCDVA	x			x	x
Goldman Tonometry (IOP)	x		x	x	x
Complete slit lamp exam	x		x	x	x
Dilated fundus exam	x				†
Cataract density	x				
Ultrasonic central corneal pachymetry	x		x	x	x
Central macular thickness (OCT)	x			x	x
Use of femtosecond laser		x			
Phacoemulsification time		x			
CDE		x			
Estimated fluid used		x			
Duration of surgery		x			
Record Lens Model Implanted		x			
Patient satisfaction					x
Symptoms (FBS & burning/stinging)	x		x	x	x

Pain	x		x	x	x
Adverse events / device deficiency		x	x	x	x

x To be performed as scheduled
† To be performed as deem necessary by the investigator.

4. Study Completion Criteria

4.1. Patient Completion of Study: If a study patient has completed the final visit (Visit 5) of the study, he/she is considered to have completed the study.

4.2. Patient Discontinuation/Withdrawal: Each study patient may voluntarily discontinue the study at any time they choose. Study patients who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study. Study patients discontinued during the enrollment phase (prior to surgery) of the study will be replaced.

4.3. Patient Termination: A study patient will be terminated if the study patient develops any severe adverse event that may be related to the study. A study patient will receive appropriate treatment at the discretion of the investigator. Notification of termination will be clearly documented. These study patients are considered to have completed the study and will not be replaced.

4.4. Study Termination: The investigator with appropriate notification may terminate the study. If, after clinical observations, the investigator feels that it may be unwise to continue the study, he may stop the study.

4.5. Study Completion: The study will be complete when all enrolled patients have completed Visit 5 or have been terminated from the study.

5. STATISTICAL CONSIDERATIONS

5.1. Sample size

We estimate that the ability of the Cirrus OCT to measure changes in macular thickness has a standard deviation around 6 microns. For sample size calculation we set the statistical significance to alpha = 0.05 with a power (beta) of 0.9. Using a dependent model, detecting a 5 micron difference in the change in retinal thickness between eyes is estimated to require 30 subjects. To allow for 15% dropout, 35 subjects will be enrolled.

5.2. Statistical Analysis

All data will be collected by the site and entered into a database. Subjects will be assigned an ID number. Data analysis will be performed without patient identification. Statistical analysis will be performed using standard descriptive statistics and other tests as deemed appropriate based on the characteristics of the data to be analyzed. All statistical tests will be two-sided and interpreted at a 5% significance level. Comparisons between the groups will be made. Data analysis will be conducted by a third party consultant.

5.3. Study Endpoints:

Comparisons between the groups:

5.3.1. Primary Endpoints:

- Change from baseline (preoperative exam) in macular thickness at Days 15±2 and 30 ±5.

5.3.2. Secondary Endpoints:

- The change from baseline in corneal thickness at Day 1, Day15 ± 2, and Day 30 ± 3.
- Slit lamp (cornea exam) changes at all times points.
- The proportion of subjects reporting no eye pain/discomfort (“0” on the eye pain/discomfort) at all time points.
- The change from baseline in eye pain/discomfort score at all time points.
- The proportion of subjects reporting FBS (“0”) at all time points.
- The change from baseline in FBS at all time points.
- The proportion of subjects reporting burning/stinging (“0”) at all time points.
- The change from baseline in burning/stinging at all time points.
- The proportion of subjects with a corneal pachymetry change from baseline at all time points.
- The change from baseline in corneal pachymetry measurements at all time points.
- The proportion of subjects with patient satisfaction score of 3 or higher at Day 30 visit.

5.4. Safety Analyses

The type, severity, duration and frequency of reported ocular adverse events will be tabulated for each group. Adverse events will also be summarized for events that were

considered treatment-related. Comparison of treatment groups with respect to the proportion of study patients reporting adverse events will be made using Fisher's Exact Test.

6. DATA HANDLING AND RECORD KEEPING

6.1. Confidentiality

To ensure confidentiality in this study, records of the participants will be examined only by the principal investigator and research staff involved in the study. Study records will be kept on file at each site. Any statistical analysis and publication will not include any subject identifiers. Medical records will be made available only for review by the investigators, study Monitor or Auditor, Sponsor Company or Research Institution, the IRB, and other State or Federal Regulatory Agencies, if necessary. All information in these records will be kept confidential.

6.2. Records Retention

The PI is accountable for the integrity, retention and security of all study related data. The investigator must maintain accurate, complete and current records relating to the clinical study. The investigator must maintain the required records during the investigation and for a period of 1 year after the date on which the investigation is terminated or completed.

7. STUDY MONITORING, AUDITING, AND INSPECTING

7.1.1. The nature and location of all source documents will be identified to ensure that original data required to complete the case report forms (CRFs) exist and are accessible for verification by the monitor. If electronic source records are maintained, these records must be 21 CFR Part 11 compliant and will be printed and certified for verification by the monitor as needed.

7.1.2. Required examination must be recorded on the CRFs. CRFs can be used as source document. All data reported must have corresponding entries in the source documents. The principal investigator or sub-investigator must review the reported data and certify that the CRFs are accurate and complete. No subject identifiers should be recorded on the CRFs beyond subject number, subject initials and study specific identifiers.

7.1.3. Data from CRFs will be entered into a database. Database access is limited to study personnel and it is saved in the server.

7.1.4. Upon completion of the CRFs, the data will be reviewed and statistician for accuracy and completeness. If corrections and/or any additions to the data are deemed necessary, queries will be generated. Designated research staff expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data in the database are reflected in the subjects' source documentation. Any changes will need to be initialed and dated by the authorized personnel making such changes.

7.1.5. Data will not be sold to third parties nor will it be used for future research.

7.1.6. Electronic data will be stored and accessed on a portable device. However, the file is saved in the server that can be only accessed using a VPN private connection.

8. INVESTIGATIONAL PRODUCT

8.1. Description

The Symfony Toric IOL (ZXTx) is an extended depth of focus (EDOF) IOL design to improve the sharpness of vision at near, intermediate and far distances reducing the need of glasses after cataract surgery in patients with astigmatism. The EDOF IOL, similarly to a monofocal IOL, has one focal point, it is elongated in the EDOF, having less of a halo and glare problem compared to multifocal IOLs.

8.2. Treatment/Dosing Regimen

The Symfony Toric IOL (ZXTx) is intended for primary implantation for the visual correction of aphakia secondary to removal of a cataractous lens in adult patients. The IOL will be implanted at time of uncomplicated routine cataract surgery. Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the patient.

8.3. Method for Assigning Subjects to Treatment/Dosing Groups

The statistician will provide randomization envelopes. The envelopes will be sequentially numbered and they will be provided to each site.

8.4. Subject Compliance Monitoring

Since the IOL is implanted at time of cataract surgery, subject compliance will not be an issue in this particular study.

8.5. Packaging, Receiving, Storage, Dispensing and Return

An account will be set up with the manufacturer of the lens (Abbott Medical Optics - AMO) that will provide the lens at no cost to the participants. IOLs will be ordered once the subjects qualification for the study has been confirmed. IOLs will be shipped to the site or ambulatory surgery center and will be stored and dispensed following the routine standard of care for cataract surgery. Unused IOLs will be returned to AMO following their instructions.

9. ETHICAL CONSIDERATIONS

This clinical trial will be conducted in accordance with the principles of the Declaration of Helsinki, and Good clinical practice. The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that all personnel involved in the conduct of the clinical trial are qualified to perform their assigned duties through relevant education, training, and experience. Deviations from the clinical protocol must be documented in each subject's study records including the dates and reasons for each deviation. The PI must ensure that all aspects of the trial are in compliance with the applicable regulatory laws and conditions of approval imposed by the IRB.

10. IN CASE OF AN INJURY RELATED TO THIS RESEARCH STUDY

Every effort to prevent study-related injury will be taken by the study doctor and staff. In the event a patient is injured as a direct result of the study while following the study instructions and requirements, the patient will be instructed to immediately contact the principal investigator and/or study staff. Treatment will be provided as needed for those injuries caused directly by this research study. In the event of injury or illness caused by or occurring during the participation in this study, all charges for medical care provided will be billed to the patient's insurance company. The medical care costs for injuries or illnesses that are not caused directly by the research study will not be covered.

11. CONFIDENTIALITY/PUBLICATION OF THE STUDY

The existence of this Study is confidential and should not be discussed with persons outside of the Study. Results will be submitted for publication and presentation at national and/or international meetings. A manuscript will be submitted to peer-review journals for publication but there is no guarantee of acceptance.

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Appendix 1: Standard Evaluation Procedures.

1. Uncorrected and Best-corrected Visual Acuity: To be evaluated preoperatively, at days 1, 15 and 30.

Visual acuity will be measured before tonometry or any other test that would affect vision. Visual acuity is measured using the ETDRS chart 1 at 4 m. If the subject cannot read at least 4 letters on the 20/200 line then the chart or the patient need to be moved to 1 meter and visual acuity recorded.

a. ETDRS technique*:*
   i. Testing starts with right eye; therefore, left eye is occluded.
   ii. The patient is seated and his/her back should firmly touch the back of the chair. The examiner should ensure that the patient is sitting comfortably, that the head does not move forward or backward during testing, and that the patient's eyes remain at the same distance.
   iii. The patient should be told that the chart has letters only and no numbers. If the patient forgets the instructions and reads a number, he or she should be reminded that the chart does not have numbers and the examiner should request a letter instead of a number.
   iv. The patient should be asked to read slowly (at a rate not faster than about one letter per second) in order to achieve the best identification of each letter and to not proceed until the patient has given a definite response. If the patient loses his or her place in reading or the examiner loses his or her place, the examiner should ask the patient to go back to the line where the place was lost. Examiners should not point to the chart or to specific letters on the chart or read any of the letters during the test. When the patient says he/she cannot read a letter, he/she should be encouraged to guess. If the patient identifies a letter as one of two or more letters, he/she should be asked to choose one letter. When it becomes evident that no further meaningful readings can be made, the examiner should stop the test for that eye. Each letter is scored as right or wrong. Once a patient has identified a letter with a definite single-letter response and has read the next letter, a correction of the previous letter cannot be accepted. If the patient changes a response aloud (e.g. "That was a "C," not an "0") before he or she has read aloud the next letter, then the change should be accepted. If the patient

changes a response after beginning to read the next letter, the change is not accepted.

v. Ask the patient to read the smallest line that he/she could comfortably read. If patient misses one letter, ask the patient to read the line before and continue from there until patient misses 3 or more letters in a single line.

vi. After the test of the right eye is completed, occlude the right eye. The test is repeated for the left eye following the same instructions.

b. ETDRS visual acuity scoring

i. The examiner records letters read incorrectly and letters for which the patient makes no guesses with an "x".

ii. The examiner underlines the last line on which the patient read any letter.

iii. Each letter read incorrectly is scored as one point. The total number of missed letters is multiply by 0.02 to this result, the last line that the patient read correctly added and the log MAR score calculated and recorded on the source document for that visit

2. Manifest Refraction: will be done with a plus cylinder phoropter or trial lenses and the ETDRS chart R using the "Push plus" refraction technique. If refracting at 1 m, add a +0.75 D sphere lens to compensate for the closer distance.

1. <u>Sphere</u>		
a. Plus	Clearer	Increase plus.
(lowest line read)	No Change	Increase plus
	Blurrier	STOP
b. Minus	Clearer	Increase minus if additional letter(s) read.
(lowest line read)	No Change	STOP
	Blurrier	STOP
c. Plus	Clearer	Increase plus.
(lowest line read)	No Change	Increase plus.
	Blurrier	STOP
2. <u>Cylinder</u>		
a. Axis (C or O above lowest line read)	Clearer at 1 or 2	Move axis toward preferred plus axis until position 1 and 2 are equal.
3. <u>Cylinder</u>		
a. Power	Clearer at 1 or 2	Increase or decrease plus power until

(C or O on or above lowest line read)		neither position 1 or 2 is better. If power changes by ≥0.50 adjust sphere.
(Not present)	JCC at 90/180 JCC at 45/135	Place 0.25 D cylinder at preferred axis. Then, check cylinder axis and power as above.

4. Refine sphere Refine with +/- spheres as in step #1 until no improvement in vision.

3. **Corneal Edema:** Postoperatively at day 1, 15 and 30, corneal edema evaluation will be divided in stromal edema/folds and epithelial edema and it will be measured before tonometry or any other test that would affect examination. Both will be graded by the examiner using the following scale:

0 - no edema
1 - trace (0% - 5%)
2 - mild (5% - 25%)
3 - moderate (26% - 50%)
4 - severe (>50%)

4. **Anterior Chamber Cells and Flare:** Postoperatively at day 1, 15 and 30, anterior chamber cells and flare wi ll be evaluated before tonometry or any other test that would affect examination. Both wi ll be graded by the examiner using the following scale:

Number of Cells	**Flare**
0- none	0- none
1 - 1-5 cells	1 - Tyndall effect barely discernible
2 - 6-15	2 - mild Tyndall effect
3 - 16-30	3 - stronq Tyndall effect
4- > 30	4 - intense Tyndall effect - aqueous has milky white appearance

5. **Macular thickness** (preop, days 15 and 30): It will be measured before tonometry or any other test that would affect OCT measurements. Macular thickness will be performed using SD-OCT (Cirrus [Zeiss]) following the manufacturer's recommendations. One 512 x 128 Macular Cube scan will be acquired per eye.

6. **Central corneal ultrasound pachymetry:** To be measured preop, and at day 1, 15 and 30. Three measurements will be taken and recorded as well as the average of the 3 measurements taken.

7. **Intraocular pressure measurements:** IOP measurements will be measured at the Screening visit and at day 1, 15 and 30 postoperatively using Goldmann tonometry.

8. **Questionnaires:** Examiner will read aloud the questions to the subject and will record the response given by the subject in the source document. For the Visual Analog Scale (VAS), the examiner will ask the patient to place a vertical mark on the line for each question then use ruler (cm) to calculate the score with 1 mm equal to 0.1 cm. A decimal value should be recorded (i.e., 2.1, 4.0). Questions 4 to 6 will be asked only at the Day 30 visit.

9. **Dilated fundus examination:** To be performed preoperatively and at Day 30 (if deemed necessary by the investigator) using the investigator's preferred technique.

Appendix 1: Symptoms and Pain Questionnaire

1. Have you experienced foreign body sensation?

☐ Yes ☐ No If yes, ☐ OD ☐ OS ☐ OU

If yes, did it start immediately after drop instillation?

OD: ☐ Yes ☐ No ☐ Don't remember

OS: ☐ Yes ☐ No ☐ Don't remember

How long did it last?

OD: ☐ 1 min or less ☐ 2 to 5 min ☐ 6-10 min ☐ > 10 min

OS: ☐ 1 min or less ☐ 2 to 5 min ☐ 6-10 min ☐ > 10 min

How severe was it?

OD: ☐ Mild ☐ Moderate ☐ Severe

OS: ☐ Mild ☐ Moderate ☐ Severe

Place a vertical mark on the line below to indicate the severity.

OD

No pain |_____| Very Severe Pain ☐

OS

No pain |_____| Very Severe Pain ☐

2. Have you experienced stinging/burning?

☐ Yes ☐ No If yes, ☐ OD ☐ OS ☐ OU

If yes, did it start immediately after drop instillation?

OD: ☐ Yes ☐ No ☐ Don't remember

OS: ☐ Yes ☐ No ☐ Don't remember

How long did it last?

OD: ☐ 1 min or less ☐ 2 to 5 min ☐ 6-10 min ☐ > 10 min

OS: ☐ 1 min or less ☐ 2 to 5 min ☐ 6-10 min ☐ > 10 min

How severe was it?

OD: ☐ Mild ☐ Moderate ☐ Severe

OS: ☐ Mild ☐ Moderate ☐ Severe

Place a vertical mark on the line below to indicate the severity.

OD

No pain |_____| Very Severe Pain ☐

OS

No pain |_____| Very Severe Pain ☐

3. Have you experienced any pain/discomfort?

☐ Yes ☐ No If yes, ☐ OD ☐ OS ☐ OU

If yes, did it start immediately after drop instillation?

OD: ☐ Yes ☐ No ☐ Don't remember

OS: ☐ Yes ☐ No ☐ Don't remember

How long did it last?

OD: ☐ 1 min or less ☐ 2 to 5 min ☐ 6-10 min ☐ > 10 min

OS: ☐ 1 min or less ☐ 2 to 5 min ☐ 6-10 min ☐ > 10 min

How severe was it?

OD: ☐ Mild ☐ Moderate ☐ Severe

OS: ☐ Mild ☐ Moderate ☐ Severe

Place a vertical mark on the line below to indicate the severity.

OD

No pain |_____| Very Severe Pain ☐

OS

No pain |_____| Very Severe Pain ☐

4. Overall, how satisfied have you been with the results of your cataract surgery in your …?

OD	**OS**
☐ Very dissatisfied	☐ Very dissatisfied
☐ Dissatisfied	☐ Dissatisfied
☐ Neither satisfied nor dissatisfied	☐ Neither satisfied nor dissatisfied
☐ Satisfied	☐ Satisfied
☐ Very satisfied	☐ Very satisfied

5. Given your postoperative vision/outcome, if you had to do it all over again, would you select:

☐ LessDrops

☐ 3-Drops

6. Given your postoperative experience, if you had to do it all over again, would you select:

☐ LessDrops

☐ 3-Drops