TITLE PAGE

A Safety and Effectiveness Study of a New Preservative Free Rewetting Drop

PROTOCOL

STUDY #952

Sponsor:

Bausch & Lomb Incorporated

This clinical investigation is being conducted in accordance with 21 Code of Federal Regulations (CFR) Parts 11, 50, 54, 56, and 812. The protocol was developed with consideration of the provisions in: International Organization for Standardization (ISO) 14155-1:2011 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2011 Part 2: Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Optics – Contact lenses and contact lens care products – Guidance for clinical investigations; International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) – Declaration of Helsinki and applicable local regulations. The Sponsor intends to register this clinical trial with the public database https://ClinicalTrials.gov.

Revision Chronology:

Amendment 2	-	09Dec2019

SPONSOR APPROVAL PAGE

A Safety and Effectiveness Study of a New Preservative Free Rewetting Drop

PROTOCOL
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The final document associated with this signature approval is maintained in Rochester, New York. Bausch & Lomb Incorporated, 1400 North Goodman Street, 14609.

INVESTIGATOR STATEMENT OF APPROVAL

A Safety and Effectiveness Study of a New Preservative Free Rewetting Drop

PROTOCOL

STUDY #952

I have read the attached document, concur that it contains all information necessary to conduct the study, and agree to abide by all provisions set forth therein.

I agree to conduct this study in accordance with 21CFR Parts 11, 50, 54, 56, 812, and 42 USC 282(j); and with consideration of the provision in: ISO 14155-1:2011 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2011 Part 2: Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Optics – Contact Lenses and contact lens care products – Guidance for clinical investigations; ICH, GCPs, Declaration of Helsinki and applicable local regulations. I will not initiate the study until I have obtained written approval by the appropriate IRB and have complied with all financial and administrative requirements of the governing body of the clinical institution and the Sponsor. I will obtain written informed consent from each study subject prior to performing any study specific procedures.

I understand that my signature on this document indicates my agreement to this clinical Investigational Plan/Protocol and to review and, if appropriate, sign the clinical study report.

I understand that my e-signature on an electronic case report form indicates that the data therein has been reviewed and accepted by me.

I understand that this document and related information is subject to confidentiality terms found in my signed Confidentiality or Clinical Services Agreement. I agree to protect the confidentiality of my patients when allowing the Sponsor of this clinical investigation, and/or relevant regulatory authorities and IRBs, direct access to my medical records for study subjects.

_____

Principal Investigator, Printed Name

_____ _____

Principal Investigator, Signature Date

Upon signing, provide a copy of this page to Bausch & Lomb Incorporated and retain a copy for your files.

SYNOPSIS

Name of Sponsor/Company: Bausch & Lomb Incorporated
Name of Investigational Product: BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops
Name of Active Ingredient: Sodium Hyaluronate and Glycerol
Title of Study: A Safety and Effectiveness Study of a New Preservative Free Rewetting Drop
Primary Objective: The objective of this study is to evaluate the safety and effectiveness of lubricating and rewetting drop (Test) compared to OPTI-FREE® Replenish® Rewetting Drops (Control) when used by habitual contact lens wearers to bilaterally lubricate and rewet soft (hydrophilic) contact lenses including silicone hydrogel contact lenses and gas permeable (silicone acrylate and fluoro silicone acrylate) contact lenses. **Secondary:** None
Methodology: This is a multicenter, randomized, masked, parallel, bilateral clinical trial.
Number of patients planned: Approximately 368 subjects (736 eyes; 184 subjects per treatment arm) will be enrolled.
Diagnosis and main criteria for inclusion: • Subjects must be of legal age (at least 18) on the date the Informed Consent Form (ICF) is signed and have the capacity to provide voluntary informed consent • Subjects must be habitual wearers of included contact lenses. • Subjects must be adapted lens wearers and wear a lens in each eye and each lens must be of the same manufacture and brand. • Subjects must agree to wear their lenses on a daily wear basis for approximately 1 month.
Key exclusion criteria: • Subjects participating in any drug or device clinical investigation within two weeks prior to entry into this study and/or during the period of study participation.
Investigational product, dosage and mode of administration: BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops for use during contact lens wear.
Duration of treatment: 1 month
Reference therapy, dosage and mode of administration: OPTI-FREE Replenish Rewetting Drops
Criteria for evaluation: The primary endpoints are as follows. **Effectiveness:** 1. Overall comfort averaged over all follow-up visits 2. Dryness averaged over all follow-up visits **Safety:** 1. Slit lamp findings greater than grade 2 at any follow-up visit
Statistical methods: Continuous variables will be summarized using the sample size, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized using frequencies and percentages. Each primary endpoint will be evaluated statistically using a one-sided non-inferiority test with a one-sided alpha risk of 0.05. For overall comfort and dryness, each non-inferiority hypothesis will be tested using an analysis of variance model including the fixed factor of treatment and the fixed blocking factor of site with a non-inferiority margin magnitude of five points. For slit lamp findings, the non-inferiority hypothesis will be tested using a one-sided Newcombe-Wilson 95% upper confidence limit with a non-inferiority margin magnitude of 5%.
Sample size calculations: In a previous study (Bausch + Lomb study 872), the following outcomes were observed. These outcomes

serve as expected results for the current study.

1. Overall comfort averaged over all follow-up visits: standard deviation = 13.9 points
2. Dryness averaged over all follow-up visits: standard deviation = 13.9 points
3. Slit lamp findings greater than grade 2 at any follow-up visit were observed in 0.5% of eyes

When the sample size is 160 subjects per treatment group, the overall power of the trial will be 97%. To allow for losses of up to 13%, approximately 184 subjects will be enrolled per treatment group for a total of 368 subjects.

PERSONNEL AND FACILITIES

NOTE: ***The information on this page is subject to change. All changes will be provided under separate cover.***

Sponsor	
[redacted]	[redacted]

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APPENDICES

LIST OF ABBREVIATIONS

Abbreviation	Term
ADE	adverse device effect
AE	adverse event
BSCVA	best spectacle-corrected visual acuity
CFR	Code of Federal Regulations
eCRF	electronic Case Report Form
D	diopter
EDC	Electronic Data Capture System
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	identification
IDE	Investigational Device Exemption
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	intent-to-treat
logMAR	logarithm of the minimum angle of resolution
MCMC	Markov chain Monte Carlo
OD	Doctor of Optometry
ORS	Oracle Randomization and Supplies Management
PP	per-protocol
PAL	Product Accountability Log
QID	4 times per day
ROPI	Report of Prior Investigations
SAE	serious adverse event
UADE	unanticipated adverse device effect
US	United States
USAN	United States Adapted Name
VA	visual acuity

NOTE: The first occurrence of some abbreviations is not spelled out in the document (eg, units of measure).

1.0 INTRODUCTION

Bausch + Lomb is evaluating the investigational BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops for use with soft (hydrophilic) contact lenses including silicone hydrogel contact lenses and gas permeable (silicone acrylate and fluoro silicone acrylate) contact lenses.

The aim of this study is to evaluate the clinical performance of the investigational lubricating and rewetting drops when compared to currently marketed OPTI-FREE® Replenish® Rewetting Drops. All subjects will care for their lenses with specified cleaning and disinfecting solutions, and lens cases.

2.0 OBJECTIVE

The objective of this study is to evaluate the safety and effectiveness of BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops (Test) compared to OPTI-FREE Replenish Rewetting Drops (Control) when used by habitual contact lens wearers to bilaterally lubricate and rewet soft (hydrophilic) contact lenses including silicone hydrogel lenses and gas permeable (silicone acrylate and fluoro silicone acrylate) lenses.

3.0 STUDY DESIGN

This is a multicenter, randomized, masked, parallel, bilateral clinical trial.

3.1 Description of Study Design

Approximately 368 subjects (736 eyes) will be enrolled in this multicenter, randomized, masked, parallel, bilateral study at approximately 12-16 investigative sites in the United States (US). Approximately one-half of the eligible subjects will be randomized to receive Bausch + Lomb investigational BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops, and approximately one-half of the subjects will be randomized to receive OPTI-FREE Replenish Rewetting Drops. In addition, all subjects will be dispensed two new pairs (1 to wear, 1 back-up) of their habitual lenses at the beginning of the study for daily wear. A third pair will be kept at the site for each subject.

All subjects will be seen for a Screening/Dispensing Visit, at which informed consent will be obtained and eligibility will be assessed. If eligible, subjects will be dispensed two new pairs of their habitual contact lenses and a Study Kit containing a supply of either the test or control rewetting drops, according to the subject's randomly assigned treatment. The subject will also be dispensed lens care products (Biotrue multi-purpose solution or Boston SIMPLUS® Multi-Action Solution and lens cases) sufficient for the entire study. Subjects must NOT use ANY other cleaning and disinfecting solution or rewetting drops during the study.

Subjects will be required to wear their study lenses for a minimum of 8 hours on a daily wear basis for 1 month and during wear, place 1-2 study rewetting drops in each eye at least 4 times per day. Subjects are to use the specified lens care products after removing the lenses each day. Subjects will return their full, partially full and empty rewetting drop bottles/single-use dispensers and worn and unworn lenses to the unmasked designee at the 1-month follow up/exit visit (or early discontinuation visit) for return to the Sponsor. It is not necessary to return any bottles of Biotrue multi-purpose solution or Boston SIMPLUS Multi-Action Solution or unused lens cases.

Eligible subjects will be enrolled into one of eight lens groups based on their habitual contact lenses. Subjects will be randomized on a 1:1 basis within each lens group per site to receive either the Test or Control rewetting drops. The eight lens groups will be comprised of habitual wearers of soft contact lenses or gas permeable contact lenses based on lens material as indicated in table below.

Table 1: Lens Groups

Lens Group	Lens Material	Trade	Manufacturer
4	Etafilcon A	Acuvue2	Vistakon
5-A	Balafilcon A	PureVision2	Bausch + Lomb
5-B	Efrofilcon A, Fanfilcon A, Somofilcon A	N/A	N/A
5-C	Samfilcon A	Ultra	Bausch + Lomb
5-Cm	Lotrafilcon B	Optix Aqua	Alcon
5-Cr	Senofilcon C	Vita	Vistakon
Gas Permeable SA, Group II	To include, but not limited: Dimefocon A, Itafocon A and B, Synergicon A, Kolfocon A and B, Pasifocon A and C	N/A	N/A
Gas Permeable FSA, Group III	To include, but not limited: Paflufocon A,B,C and D, Unifocon A, Oxyflufocon A, Enflufocon A and B, Flusilfocon A, B and C, Hexafocon A and B, Hofocon A, Hybufocon A, Itafluorofocon A, Lotifocon B and C, Onsifocon A, Oprifocon A, Pemufocon A, Roflufocon A, C, D and E, Wilofocon A	N/A	N/A

3.2 Selection of Study Population

Written informed consent, enrollment in the study, or dispensing of study products cannot begin until the Investigator has received Institutional Review Board (IRB) approval to conduct the study. The Sponsor and IRB must approve any advertising used to recruit subjects prior to use of that advertising.

All consented subjects must be accounted for, whether they participate in the study or not. Bausch + Lomb will provide a Screening Log on which to enter information for each subject who signs an Informed Consent Form (ICF). All screened subjects must be entered onto the Screening Log, to include the subject identification (ID) number assigned by the randomization system. Once a potential subject is consented and their initials are entered onto the Screening Log, the Investigator should proceed with Screening procedures.

Potential subjects are deemed either “Screen Pass” or “Screen Fail.” “Screen Fail” subjects are subjects who have not met the study eligibility criteria and cannot be randomized into the study. Each subject will be assigned a subject identification (ID) number by the randomization system regardless of whether they are a “Screen Pass” or “Screen Fail”.

Only “Screen Pass” subjects can be randomized by the randomization system to receive the study drops.

Once a subject is randomized, a subject is considered active and must be accounted for at every visit until exited (completed or discontinued) from the study, even if they are not dispensed study materials. Refer to Section 3.2.4 for subjects determined to be lost to follow-up.

3.2.1 Eligibility

3.2.1.1 Inclusion Criteria

The subject is eligible for entry into the study if the subject meets all of the following criteria:

1. Is of legal age (at least 18) on the date the Informed Consent Form (ICF) is signed and has the capacity to provide voluntary informed consent.
2. Is able to read, understand, and provide written informed consent on the Institutional Review Board (IRB) approved ICF and provide authorization as appropriate for local privacy regulations.
3. Is a habitual wearer (at least 3 months) of one of the lens types included in Table 1: Lens Groups (page 13).
4. Is correctable through spherocylindrical refraction to 32 letters (0.3 logMAR) or better (distance, high contrast) in each eye.
5. Has clear central corneas and is free of any anterior segment disorders.
6. Is a habitual user of a lens care product for cleaning, disinfecting, and storage of lenses.
7. Wears a lens in each eye and each lens must be of the same manufacture and brand.
8. Wears their habitual lenses (or be willing to wear lenses) a minimum of 8 hours per day, at least 5 days a week.
9. Is willing to place 1 to 2 study rewetting drops in each eye at least 4 times per day when lenses are worn.
10. Is willing and able to comply with all treatment and follow-up/study procedures.

3.2.1.2 Exclusion Criteria

The subject is ineligible for entry into the study if the subject meets any of the following criteria:

1. Subjects who currently use a hydrogen-peroxide cleaning and disinfecting solution.
2. Participating in any drug or device clinical investigation within 30 days prior to entry into this study and/or planning to do so during the period of study participation.
3. Females of childbearing potential (those who are not surgically sterilized or postmenopausal) if they meet any one of the following conditions:
   - they are currently pregnant
   - they plan to become pregnant during the study
   - they are breastfeeding

4. Current user of the control rewetting drops (OPTI-FREE Replenish Rewetting Drops).
5. Has worn polymethylmethacrylate (PMMA) lenses within the last three months.
6. Has any systemic disease currently affecting ocular health or which in the Investigator's opinion may have an effect on ocular health during the course of the study.
7. Has any ocular disease or is using any ocular medication.
8. Is using any systemic or topical medications that will, in the Investigator's opinion, affect ocular physiology or lens performance.
9. Currently wears monovision, multifocal, or toric contact lenses.
10. Subjects who are adapted soft lens wearers with ocular astigmatism of 1.00D or greater in either eye.
11. Has anisometropia (spherical equivalent) of greater than 2.00D.
12. Has any grade 2 or greater finding during the slit lamp examination (refer to APPENDIX B: Methods of Clinical Evaluation). Subjects with corneal infiltrates, of ANY GRADE, are not eligible.
13. Subjects with any "Present" finding during the slit lamp examination (refer to APPENDIX B: Methods of Clinical Evaluation) that, in the Investigator's judgment, interferes with contact lens wear.
14. Has any scar or neovascularization within the central 6 mm of the cornea. Note that subjects with minor peripheral corneal scarring (that does not extend into the central area), that, in the Investigator's judgment, does not interfere with contact lens wear, are eligible for this study.
15. Is aphakic.
16. Is amblyopic.
17. Has had any corneal surgery (e.g., refractive surgery).
18. Is allergic to any component in the study care products.
19. Subjects who meet any of the following criteria:
    - the subject is an employee of the investigative site
    - the subject, or a member of the subject's household, is an Ophthalmologist, an Optometrist, an Optician, or an Ophthalmic Assistant/Technician
    - the subject, or a member of the subject's household, is an employee of a manufacturer of contact lenses or contact lens care products (e.g., Alcon, Bausch + Lomb, Ciba Vision, CooperVision, Johnson & Johnson, etc.)
20. Subjects who are adapted GP wearers with an ocular astigmatism of 3.00D or greater in either eye.

If a subject meets all the inclusion criteria and does not exhibit any of the exclusion criteria, the subject is eligible for entry into the study. Ineligible subjects MUST NOT be

enrolled in this study and are considered a "Screen Fail". Any subject enrolled in the study who later is found to have not met the eligibility criteria at entry will be discontinued.

3.2.2 Subject Completion

The subject has completed the study when the 1-Month Visit is concluded. Subjects who require further follow-up will be followed according to the Adverse Event or Unscheduled Visit Section.

3.2.3 Subject Discontinuation

A subject MAY be discontinued (at the discretion of the Investigator, the Sponsor, and/or the IRB) prior to the final study visit for a variety of reasons, including, but not limited to:

- An adverse event (AE) occurring during the course of the study, which precludes continued treatment or follow-up
- Persistent Grade 3 or 4 slit lamp findings (must be reported to the Sponsor within 24 hours)
- Persistent study-related symptoms/complaints

A subject MUST be discontinued prior to the final study visit (1-Month Visit [Visit 3]) for any of the following reasons:

- Voluntary withdrawal
- Death
- Investigator decision that it is not in the best medical interest of the subject to continue participation in the investigation
- Ineligible at screening/dispensing – a subject who was enrolled but was later found to have not met the eligibility criteria
- Inability to maintain recommended wearing and rewetting drop schedule
- Continued failure to follow subject instructions
- Lack of motivation
- Lost to follow-up (refer to Section 3.2.4)
- Instillation of non-medically indicated solution not specified in the protocol
- Other eye is discontinued
- Becomes pregnant during the study

Prior to discontinuing a subject, every effort should be made to contact the subject, schedule an Exit Visit, obtain as much follow-up data as possible, and retrieve all study materials. Adverse events will be followed as described in Section 7.0. Subject discontinuations will be documented clearly on the source document and applicable electronic case report form (eCRF). The Investigator should indicate the PRIMARY (one) reason that the subject was discontinued for each eye. Subjects who are discontinued from the study following randomization will not be replaced.

Exit Visit assessments should be completed for discontinued subjects.

3.2.4 Lost to Follow-up

Subjects who do not return for scheduled follow-up visits, as defined by the visit window and cannot be contacted, are to be considered lost to follow-up. All attempts to contact the subject should be documented and kept with the subject's source documentation, and the applicable eCRFs will be completed. The exit date will be the date of the subject's last visit to the clinic as a study subject.

3.3 Investigators

The study will be conducted at approximately 12-16 investigative sites located in the US by Investigators who are determined by Bausch + Lomb to be suitably qualified by training and experience to conduct this study. The Principal Investigator will sign the Device Investigator Agreement form prior to the start of the study. This form contains a statement specifying that the investigator is not allowed to deviate from the study protocol, except under emergency circumstances where the deviation protects the rights, safety and well-being of human subjects.

Each Investigator will attempt to enroll approximately 23-31 subjects. In the event that selected sites do not meet full enrollment, the Sponsor may decide to increase enrollment as needed at other currently active sites and/or additional site(s) may be added to satisfy the enrollment requirements of the study.

3.4 Study Duration

Investigators will have four (4) weeks from the enrollment start date communicated by the Sponsor to conduct all Screening/Dispensing Visits.

Subjects will be followed for approximately one (1) month (unless discontinued, lost to follow-up, or requiring study follow-up) from the initial Screening/Dispensing Visit and must adhere to the following schedule:

SCHEDULED FOLLOW-UP VISITS		
Visit	**Target**	**Acceptable Visit Range**
2-Week Follow-up Visit	Day 15	Day 11-19
1-Month Follow-up Visit	Day 31	Day 27-35

The visit range is based on the date test articles are initially dispensed (Screening/Dispensing Visit). A visit scheduling table will be provided in the initial study shipment to aid the Investigator in scheduling follow-up visits.

3.5 Protocol Changes and Amendments

Changes to the protocol will be approved by the Sponsor. An amendment to the protocol will also require submission and approval from the IRB before implementation. The Sponsor (or designee) will distribute protocol amendments to the investigative sites. The Investigator is responsible for the ensuring that staff involved at his/her site have completed training on the changes before implementing with subjects.

3.6 Treatments

Eligible subjects will be randomized to use BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops (Test) or OPTI-FREE Replenish Rewetting Drops (Control). At the initial Screening/Dispensing Visit, each subject will be provided with a

Study Kit with a unique Study Kit number containing Test *or* Control Rewetting drops sufficient for the full study duration. Cleaning and disinfecting solutions, lens cases, and Subject Instructions will also be provided. Subjects will be required to wear lenses for a minimum of 8 hours on a daily wear basis for 1 month and during wear, place 1-2 study rewetting drops in each eye at least 4 times per day.

4.0 STUDY MATERIALS

Bausch + Lomb will provide all study solutions at no charge to the Investigator. All study lenses are to be purchased through the site's normal ordering process and will be reimbursed by the Sponsor. All other materials will be provided to the site prior to the start of the study. Refer to Product Replacement Section 4.8 for ordering replacement test or control product in case of loss or damage.

Use of other contact lenses, not listed in Table 1: Lens Groups, or lens care products is not allowed.

4.1 Description of Test Article(s)/Treatment(s)

PFM04 is a preservative-free, sterile isotonic aqueous solution containing glycerol (0.5%) and sodium hyaluronate (0.15%) drop manufactured by Bausch & Lomb Incorporated, Rochester, NY for lubricating and rewetting soft (hydrophilic) contact lenses including silicone hydrogel contact lenses and gas permeable contact lenses.

4.2 Description of Comparator [Product(s)/Treatment(s)]

OPTI-FREE Replenish Rewetting Drop is a sterile, buffered, isotonic, aqueous solution that contains a citrate/borate buffer and sodium chloride with edetate disodium 0.05% and POLYQUAD (polyquaternium-1) 0.001% as preservatives and RLM-100 (PEG-11 lauryl ether carboxylic acid) and TETRONIC®[1] 1304 manufactured by Alcon Laboratories, Inc., Fort Worth, TX for rewetting soft (hydrophilic) contact lenses, fluorosilicone acrylate and silicone acrylate gas permeable contact lenses, and silicone hydrogel contact lenses.

4.3 Instructions for Use and Administration

Based on the randomization assignment, each randomized subject will be assigned a unique Subject ID number. Each subject will be issued a Study Kit labeled with a unique Study Kit number. Subjects will be dispensed two pairs (one for back-up) of their habitual lenses at the Screening/Dispensing Visit. Subjects will be required to wear their study lenses for a minimum of 8 hours on a daily wear basis for 1 month and during wear, place 1-2 rewetting drops in each eye at least 4 times per day. The Investigator or designee will instruct all subjects to adhere to the Subject Instructions provided at the Screening/Dispensing visit.

In order to ensure that the Investigator and site staff remain masked to the study rewetting drops, an unmasked designee at the site will be responsible for all dispensation and collection of study supplies for the subjects.

Subjects are to be instructed not to discuss or show the dispensed study drops to the Investigator or site staff during the study.

4.3.1 Storage Requirements

All Test and Control articles provided by the Sponsor must be stored in a secure location accessible only by the unmasked designee and maintained at room temperature.

4.3.2 Subject Instructions

a. All subjects must be given Subject Instructions along with each Study Kit of study solution for the use with the study articles (refer to Subject instructions APPENDIX F: for Subject Instructions). Subjects must comply with the instructions provided to them.

b. The unmasked designee must review, with the subject, the Subject Instructions and the precautions and warnings for lens wear, lens care, handling, cleaning, and disinfecting, and return of study materials.

c. Any subject who does not follow instructions to a degree that, in the Sponsor or Investigator's opinion, jeopardizes the subject's well-being or the validity of the study, will be discontinued.

4.4 Packaging and Labeling

4.4.1 Lenses

The site is responsible for ordering all habitual contact lenses needed for the study and submitting an invoice for reimbursement. Three pairs of the subject's habitual contact lenses will be provided for each subject; two pairs will be dispensed to the subject at the Screening/Dispensing Visit (one to wear and one for back-up). The third pair will be retained in-office in the event that a non-scheduled replacement is required. Additional lenses should be ordered if the third pair is dispensed.

4.4.2 Study Kits

The Sponsor will provide Study Kits for each subject. All Study Kits will be assigned by the ORS randomization system and distributed to the subject by the unmasked designee. Each Study Kit will include the following materials:

- **Either 56 pouches containing 5 single-use dispensers of BL-300-PFM04 Preservative Free Lubricating and Rewetting Drops (Test) or six bottles of OPTI-FREE Replenish Rewetting Drops (Control).** The drops will be enclosed in a white carton. Each carton, bottle or pouch will be labeled with an investigational label including the Study Kit number (a unique 5-digit number). One randomized Study Kit will be provided to subjects at the Screening/Dispensing Visit. The subject number may be written on the outside carton ONLY. The rewetting drops should not be written on or labelled.

4.4.3 Other Study Supplies

The following will be stored at the sites to be provided to subjects:

- **One 10 FL. OZ. bottle of Bausch + Lomb Biotrue multi-purpose solution.**

-or-

- **Three 3.5 FL OZ bottles of Boston SIMPLUS Multi-Action Solution.**
- **Lens case.** Subjects are required to use the supplied lens cases. In the event of replacement lenses, use a lens case to store the lens(es).

- **Zippered Bag.** To hold empty multi-dose rewetting drop bottles or opened single-use dispensers.
- **Subject Instructions.** Will be provided at Screening/Dispensing visit.

4.5 Return of Study Materials

Each subject will have one opaque Subject ID sealable bag for return of all materials.

- **Study Kit Return Materials.** The unmasked designee will place all the subject's Test or Control articles (Study Kit with unopened multi-use bottles or single-use dispensers, partially full, and empty multi-use bottles or single-use dispensers) into an opaque Subject ID sealable bag along with worn/unworn lenses as described below. **Do not** seal the bag until full accountability at the study close out visit with the monitor is complete. It is not necessary to return the Biotrue multi-purpose solution or Boston SIMPLUS Multi-Action Solution bottles or unused lens cases.

- **Lens Return Materials**. The unmasked designee will place worn lenses in a lens case filled with Bausch + Lomb Sensitive Eyes Saline Solution. Complete a worn lens label provided for each lens case returned with identifying information such as study number, site identification number, subject number, subject initials, lens type, date dispensed, date removed, quantity of lenses returned (which should be one lens for each eye) and adhere the label to zippered bag. If replacement lenses were used, use a separate lens case and zippered bag with identifying information. Place the zippered bag(s) containing the lens case(s) into the opaque Subject ID sealable bag with any unworn lenses and all Study Kits as described above. **Do not** seal the bag until full accountability at the study close out visit with the monitor is complete.

  Use the supplied pre-printed FedEx labels for return of the study materials to the Sponsor after close out visit.

4.6 Accountability

The Unmasked Designee at each site will be responsible for keeping current and accurate records of the amount of single-use dispensers or bottles received and dispensed, and its disposition. The single-use dispensers or bottles must be stored under the appropriate conditions in a secure area and are to be dispensed only to subjects enrolled in the study, in accordance with the conditions specified in this protocol. During the course of the study, the Investigator must account for all lenses and rewetting drops received, dispensed, and returned. A Product Accountability Log (PAL) will be provided to the sites for rewetting drops and a Lens Accountability Log (LAL) will be provided for lenses.

The Unmasked Designee will instruct the subject to bring their Study Kit (i.e., white carton originally containing 56 pouches of 5 single-use dispensers or 6 multi-use bottles) to the 1-Month visit and will collect all study materials (Study Kit and lenses dispensed or provided to the subject) only at the final/exit study visit. Study materials will not be collected at any other visit than the final/exit visit.

At time points throughout the study and/or upon completion of the study, the Sponsor/Sponsor's representative will review and verify the Investigator's accountability records. Following verification, and as directed by the Sponsor, all Study Kits (Test and

Control) and lenses (worn and unworn) must be returned to the Sponsor at the address below using the study supplied pre-printed FedEx labels.

Bausch & Lomb Incorporated
Clinical Trial Materials Supply Chain, Area 56
1400 North Goodman Street
Rochester, New York 14609

4.7 Masking/Unmasking

This study is masked, therefore, the Investigator/site staff, subjects, and Bausch + Lomb personnel or designee(s) involved in the collection of study data will be masked to the study rewetting drops. Each site must have an unmasked designee that will be responsible for dispensing and accountability. This designee shall not participate in study assessments that may cause bias to the study data. Study Monitors should ensure that the unmasked designee is documenting accountability throughout the study, and should perform only accountability tasks during study that ensures they remain masked. (e.g. verify kit #, logs are present and being completed). Full accountability should be performed at study end.

The randomization schedule will be created by an unmasked statistician not otherwise involved in the study. Personnel involved with repackaging of clinical trial material will also be unmasked. Unmasked designees at the site will manage the dispensation and return of study rewetting drops and related supplies. All other study personnel will remain masked until database lock. Another research staff member may manage the dispensation of the habitual lenses.

Study rewetting drops will be provided in sealed opaque cartons with Study Kit numbers pre-printed on them. Although the Test and Control bottles/single-use dispensers will be visibly different, attempts will be made to mask the subjects by providing identical investigational labels and packaging identical kit cartons. Subjects will be instructed to place the drops in the eye and blink out of the sight of the Investigator or site staff. Subjects are not to show the study bottles/single-use dispensers to the Investigator or site staff unless instructed to do so.

If unmasking of a subject's randomly assigned treatment is required, the Investigator (or other designee) is required to attempt to contact the Medical Monitor to request permission to unmask. If this attempt is successful, then the Medical Monitor will contact the Sponsor designee (see Personnel and Facilities, Page 3) and obtain approval to grant permission to unmask. Upon receipt of authorization from the Sponsor designee, the Medical Monitor will advise the Investigator (or another qualified designee) to log into the randomization system and unmask the subject. If the Medical Monitor cannot be contacted, the Investigator (or other qualified designee) should attempt to contact the Sponsor designee who can authorize the unmasking of a subject. If the Medical Monitor or Sponsor designee cannot be contacted and the Investigator (or other qualified designee) deems the unmasking to be an emergency, the Investigator may log into ORS without authorization and unmask the subject. Whether unmasking occurs inadvertently or intentionally, the Investigator must notify the Medical Monitor or Sponsor designee as soon as possible after unmasking. In addition, the Investigator must record the date, time, and reason for unmasking the study treatment in the source documentation.

4.8 Product Replacement

Any additional/replacement (in the case of loss or damage) Test or Control rewetting drops must be ordered through the randomization system.

A back-up pair of lenses for each dispensed subject will be retained in-office in case a non-scheduled lens replacement is required, and the subject already used the two sets of lenses that were dispensed at the Screening/Dispensing Visit.

4.9 Risk Assessment

Information concerning potential risks associated with the investigational device (as well as possible interactions with concomitant medical treatments and risk-to-benefit ratio) can be found within the Investigator's Brochure (IB)/Report of Prior Investigations (ROPI) for the study. Risks are also summarized within the Informed Consent document. The assessments required for the study are routinely performed and are standard of care for contact lens wearers. The subjects will be informed of any potential study specific risks in the ICF or if new risks become apparent during the study.

5.0 SAFETY AND EFFECTIVENESS VARIABLES

Safety and effectiveness endpoints are also shown in Section 8.1.

5.1 Safety Variables

The safety of the rewetting drops will be determined by the following parameters:

- The primary safety endpoint will be slit lamp findings greater than grade 2.
- Adverse Events will also be evaluated. Information regarding any subject- or investigator- reported AEs will be obtained at each follow-up visit. The rate of adverse events is not a primary endpoint and is not associated with a predefined success criterion.

5.2 Primary Effectiveness Variables

Effectiveness of the rewetting drops will be determined by the following parameters:

- Overall comfort
- Dryness

5.3 Risk Assessment

The assessments required for the study are routinely performed and are standard of care for contact lens wearers. The subjects will be informed of any potential study-specific risks in the ICF or if new risks become apparent during the study. Upon review of the clinical and preclinical data, no additional risks were identified over the standard contact lens and care solution use.

6.0 STUDY METHODS

6.1 Study Visits

Refer to APPENDIX A: for a schedule of visits and parameters and APPENDIX B: for methods of clinical evaluation.

Prior to enrollment into the study, the Investigator (or designee) will explain the purpose of the study, procedures, risks/benefits, and subject responsibilities to the potential participant. The subject's willingness and ability to meet the follow-up requirements of the study will be determined. If the subject chooses to participate in the investigation, written informed consent, including Health Insurance Portability Accountability Act (HIPAA) authorization, will be obtained. The subject and the person obtaining written consent will sign and date the IRB-approved ICF. The Investigator should retain the signed original document in the subject's record and provide a copy to the subject. In addition, the applicable privacy regulation requirements must be met.

6.1.1 Screening/Dispensing Visit

After obtaining written informed consent, prospective subjects will be screened to determine whether they meet the entry criteria for the study.

A Screening and Enrollment Log will be provided by the Sponsor to track all consented subjects that the Investigator interviews regarding the study and completed study visits for enrolled subjects. Once the Screening and Enrollment Log is complete and all data is reviewed and confirmed by the field monitor, the Investigator will sign and date the form verifying the documented data is correct. The Investigator will retain a copy of the original document for their records and the field monitor will submit the original for Sponsor.

After obtaining written informed consent, prospective subjects will be screened to determine whether they meet the entry criteria for the study.

The Screening/Dispensing Visit will proceed as follows:

NOTE: All VA measurements MUST be made using a phoropter.

a. Enter the subject information on the next available line of the Screening Log.

b. Collect demographic and medical history (within 1 year of signing the ICF) and concomitant medications. Concomitant medications (as defined for this study) include any medications (systemic and ocular) for conditions taken within 30 days of signing the ICF.

c. Collect the following baseline lens/lens care history information and lens wear parameters from the subject:

   - Average number of days per week worn
   - Average daily wearing time, hours per day
   - Average hours of comfortable wear per day
   - Hours lenses worn on the day of this visit
   - Current lens brand, sphere power, base curve and diameter
   - Current lens care products

d. Perform the following baseline assessments (without lenses; remove the lenses if the subject wore lenses to the visit):

   - Spherocylindrical refraction
   - High contrast distance best spectacle-corrected visual acuity (BSCVA)
   - Keratometry

e. Perform a slit lamp examination (without lenses) and record:

- Any ungraded finding marked as "Present"
- Any corneal scars
- Any neovascularization within the central 6 mm of the cornea
- Any corneal staining
- Any corneal infiltrate (record details on the APPENDIX C: Corneal Infiltrates Evaluation Form)
- Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document.

f. Indicate on the Screening and Enrollment Log whether the subject is a "Screen Pass" or "Screen Fail." Only "Screen Pass" subjects should be randomized in the study. "Screen Fail" subjects are ineligible and cannot be randomized in the study. No eCRFs shall be completed for "Screen Fail" subjects.

- *If the subject is a "Screen Pass"*: Log into ORS to randomize the subject. Enter the subject number from ORS on the Screening and Enrollment Log.
- *If the subject is a "Screen Fail"*: Log into ORS and indicate the reason for screen failure. Enter the subject number from ORS on the Screening and Enrollment Log.

g. If the subject is a "Screen Pass" the Unmasked Designee should then dispense the randomized Study Kit (refer to Section 4.4.2) to the subject and record the required information in the subject's individual Product Accountability Log.

h. Dispense two pairs (one for back up only) of the subject's habitual contact lenses and record on the Lens Accountability Log.

i. Instruct subject to insert study lenses and collect the following Subjective Assessments for the insertion of study lenses using the 0-100 rating scales:

- Burning/Stinging Upon Insertion (Rating Scale #1)
- Comfort Upon Insertion (Rating Scale #2)
- Ease of Handling/Insertion (Rating Scale #5)

j. Unmasked designee will instruct, and view the subject placing 1-2 study rewetting drops in each eye and blinking. Within 1 minute, collect the following Subjective Assessments for the instillation of study drops using the 0-100 rating scales:

- Burning/Stinging Upon Drop Instillation (Rating Scale #16)
- Comfort Upon Drop Instillation (Rating Scale #17)
- Vision Upon Drop Instillation (Rating Scale #18)

k. Record the following into the subject's source documentation for entry in to EDC:

- Dispensed lens type (brand), sphere power, base curve and diameter
- High contrast distance lens VA
- Over-refraction and distance VA
- Lens wettability
- Lens centration
- Lens movement
- For each eye, compare the high contrast distance lens VA to the high contrast Distance Best Spectacle-Corrected VA obtained at this visit. If the VA has decreased by 5 letters (0.1 logMAR) or more, explain.

l. The Unmasked Designee will explain to the subject that:

- Study Kit cartons and its contents are NOT to be opened in front of any other site personnel.
- The subject should retain all study materials (bottles/single-use dispensers and lenses) during the course of the study.
- Prior to coming to the site for the 1-month, exit or early study termination visits, the subject should: (i) place zippered bag containing all used single-use dispensers or multi-dose bottles and unused single-use dispensers/bottles of study rewetting drops into their original white carton, (ii) place the carton and all lens cases into the opaque subject take-home white drawstring bag, (iii) close the bag, and (iv) return it to the unmasked designee.

m. The Unmasked Designee can dispense the Other Supplies, as needed by the patient (refer to Section 4.4.3).

n. If the Subject was randomized and needs to be exited during this visit, complete the Exit Visit as per Section 6.1.4.

o. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs, since consent was signed.

p. Complete the forms below and transcribe to the eCRFs:

- Screening/Dispensing Visit Form
- Exit Visit Form (to be used if the subject is discontinued after a subject ID has been assigned in ORS)

6.1.2 2-Week Follow-up Visit

The 2-Week Follow-up Visit will proceed as follows:

NOTE: All VA measurements MUST be made using a phoropter.

NOTE: Study lenses should not be dispensed at this visit unless replacement lenses are required. Lenses worn to this visit should be returned to the subject for use until the next scheduled visit.

NOTE: If the subject comes to a visit not wearing lenses due to requiring a replacement and is not experiencing any problems, it is preferred to do an Unscheduled Visit for Product Dispensing Only and reschedule the 2-Week visit within the visit window. Refer to Unscheduled Visit, Section 6.1.5

NOTE: If the subject comes to a visit not wearing lenses and does not require a replacement, reschedule the current visit within the visit window.

a. If a subject misses the scheduled follow-up visit and cannot be seen prior to the start of the visit window for the next scheduled follow-up visit, then the visit is considered missed.

b. Collect the following lens wear parameters from the subject, since last visit:

- Average number of days per week lenses were worn
- Average number of times rewetting drops used per day on days when lenses were worn
- Average daily wearing time
- Average hours of comfortable wear
- Hours lenses worn on the day of this visit

c. Collect the Symptoms/Complaints from the subject using the 0-4 rating scales.

d. Collect the Subjective Assessments from subject using the 0-100 rating scales.

e. Collect any relevant medical treatment information, including any adverse events, use of concomitant medications and/or culture that may have been taken since the last visit.

f. Evaluate the lenses (while on eye) and record the following assessments:

- Distance lens VA
- Over-refraction and distance VA
- Lens wettability
- Lens discoloration
- Lens deposits (type, percent and degree)
- Lens centration
- Lens movement
- For each eye, compare the high contrast distance lens VA to the high contrast distance lens VA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, explain.

e. Perform a slit lamp examination (remove and store the lenses in the appropriate disinfecting solution during the exam, either Biotrue multi-purpose solution or Boston SIMPLUS Multi-Action Solution) and record the following in subject source documents for entry in to EDC:

- Any ungraded finding marked as "Present"
- Any new corneal scars
- Any neovascularization within the central 6 mm of the cornea
- Any corneal staining
- Any corneal infiltrate (record details on the APPENDIX C: Corneal Infiltrates Evaluation Form)
- Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document.

g. Return the lenses to the subject to wear until the final study visit.

h. If the subject needs to exit the study at this visit, complete the Exit Visit as per Section 6.1.4.

i. Complete the forms below and transcribe to the eCRFs.

- 2-Week Follow-up Visit Form
- Exit Visit Form (to be used if the subject is discontinued or exited at this visit)

6.1.3 1-Month Follow-up

The 1-Month Follow-up will proceed as follows:

NOTE: All VA measurements MUST be made using a phoropter.

NOTE: If all scheduled visits are performed on time and the subject completes the 1-Month Visit, the Exit Visit will be done at the same time.

NOTE: If the subject comes to a visit not wearing lenses due to requiring a replacement and is not experiencing any problems, it is preferred to do an Unscheduled Visit for Product Dispensing

Only and reschedule the 1-Month visit within the visit window. Refer to Unscheduled Visit, Section 6.1.5.

NOTE: If the subject comes to a visit <u>not</u> wearing lenses and does not require a replacement, reschedule the current visit within the visit window.

a. Collect the following lens wear parameters from the subject, since last visit:

- Average number of days per week lenses were worn
- Average number of times rewetting drops used per day on days when lenses were worn
- Average daily wearing time
- Average hours of comfortable wear
- Hours lenses worn on the day of this visit

b. Collect the Symptoms/Complaints from the subject using the 0-4 rating scales.

c. Collect the Subjective Assessments from subject using the 0-100 rating scales.

d. Collect any relevant medical treatment information, including any adverse events, use of concomitant medications and/or culture that may have been taken since the last visit.

e. Evaluate the lenses (while on eye) and record:

- Distance lens VA
- Over-refraction and distance VA
- Lens wettability
- Lens discoloration
- Lens deposits (type, percent, and degree)
- Lens centration
- Lens movement
- For each eye, compare the high contrast distance lens VA to the high contrast distance lens VA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, explain.

f. Perform a slit lamp examination (remove and store the lenses in the appropriate disinfecting solution during the exam, either Biotrue multi-purpose solution or SIMPLUS Multi-Action Solution) and record the following:

- Any ungraded finding marked as "Present"
- Any new corneal scars
- Any neovascularization within the central 6 mm of the cornea
- Any corneal staining
- Any corneal infiltrate (record details on the APPENDIX C: Corneal Infiltrates Evaluation Form)
- Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document.

f. Complete the forms below and transcribe to the eCRFs.

- 1-Month Follow-up Visit Form

NOTE: Do not continue with the Exit Visit until/unless the subject is ready to exit the study. Subjects who require further follow-up at the conclusion of the 1-Month

Follow-Up Visit will be followed according to the AE and/or Unscheduled Visit Section until the AE is resolved or stabilized

6.1.4 Exit Visit

The Exit Visit will proceed as follows:

a. Indicate status of the subject on the Exit Visit Form. If the status is "Discontinued" (dispensed or non-dispensed), indicate the (one) PRIMARY exit reason for each eye on the Exit Visit Form.

b. Collect any relevant medical treatment information, including any adverse events, use of concomitant medications and/or culture that may have been taken since the last visit.

c. For all subjects, complete an exit ocular examination without lenses on the eyes. Collect the following assessments:

   - Spherocylindrical refraction
   - High contrast distance best spectacle-corrected visual acuity (BSCVA)
   - Keratometry

d. For each eye:

   - Compare the final visit high contrast distance BSCVA to the high contrast distance BSCVA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, explain.
   - Compare the final visit keratometry readings to the Screening/Dispensing Visit keratometry readings. If there is a change of 1.00 D or more, explain.

e. Indicate if there were any changes to pre-existing corneal scars.

f. Collect all dispensed lenses (worn and unworn) and Study Kit(s) from the subject and return all to the Sponsor or designee using the return materials provided (refer to Section 4.5). Worn lenses will be returned in lens cases filled with Bausch + Lomb Sensitive Eyes Saline Solution.

g. Complete the forms below and transcribe to the eCRFs.

   - Exit Visit Form

6.1.5 Unscheduled Visits

Additional visits may be scheduled, as necessary, to ensure the safety and well-being of subjects. All additional exams should be fully documented in the source documents and on Unscheduled Visit eCRFs, as appropriate. Visits intended to fulfill scheduled visit requirements, that fall outside the designated scheduled visit range, are not Unscheduled Visits. In these cases, the visit data will be collected and transcribed to the appropriate scheduled visit eCRF.

If a subject is seen for multiple visits during a given visit timeframe, the data from the visit that is intended to meet the protocol requirements for the scheduled visit should be captured on the visit eCRF. Where such a determination cannot be made, the first visit within the scheduled visit interval will be used for completion of the protocol required scheduled visit eCRF. Data from any additional visits within a scheduled visit interval will be captured on an Unscheduled Visit eCRF.

Subjects who require further follow-up on an AE/SAE upon discontinuation or at the conclusion of the 1-Month Follow-Up Visit will be followed according to the AE and/or Unscheduled Visit Section as necessary. At these follow-up visits, the subject should remove contact lenses s/he may be wearing. Assessments will be performed according to the investigator's judgement. The Investigator is required to follow the subject until the condition no longer warrants further follow-up for study purposes.

NOTE: All VA measurements MUST be made using a phoropter.

a. Determine the reason for the Unscheduled Visit.
   - If the visit is to dispense study materials only and the subject is not experiencing any problems, refer to Product Dispensing Only, Section 6.1.5.1.
   - If the subject is experiencing problems, proceed with the Unscheduled Visit assessments as needed, below.

b. Collect the following lens wear parameters from the subject, since last visit:
   - Average number of days per week lenses were worn
   - Average number of times rewetting drops used per day on days when lenses were worn
   - Average daily wearing time
   - Average hours of comfortable wear
   - Hours lenses worn on the day of this visit

c. Collect the Symptoms/Complaints from the subject using the 0-4 rating scales.

d. Collect the Subjective Assessments from the subject using the 0-100 rating scales.

e. Collect any relevant medical treatment information, including any adverse events, use of concomitant medications and/or culture that may have been taken since the last visit.

f. If the subject did not come to the visit wearing one or more study lenses, go to step g. Otherwise, evaluate the lenses (while on eye) and record the following assessments:
   - Distance lens VA
   - Over-refraction and distance VA
   - Lens wettability
   - Lens discoloration
   - Lens deposits (type, percent and degree)
   - Lens centration
   - Lens movement
   - For each eye, compare the high contrast distance lens VA to the high contrast distance lens VA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, explain.

g. Perform a slit lamp examination (remove and store the lenses in the appropriate disinfecting solution during the exam, either Biotrue multi-purpose solution, or SIMPLUS Multi-Action Solution) and record the following:
   - Any ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6 mm of the cornea

- Any corneal staining
- Any corneal infiltrate (record details on the APPENDIX C: Corneal Infiltrates Evaluation Form)
- Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document.

g. If additional study rewetting drops are required at this visit, log into ORS to dispense a new Study Kit (refer to Section 4.4.2) to the subject according to ORS and InForm and record in the Product Accountability Log.

h. If an unscheduled lens replacement is required at this visit in addition to performing assessments, dispense a new pair of subject's habitual lenses, record in Lens Accountability Log and collect the following information:

- Primary (one) reason for replacement
- Dispensed lens type (brand), sphere power, base curve, and diameter

i. If Study Lenses were replaced, collect the worn lenses from the subject and place in lens case with Sensitive Eye Saline Solution and place the lens case in zippered bag with worn lens labels provided. Record in Lens Accountability Log.

j. If the subject needs to exit the study at this visit, complete the Exit Visit as per Section 6.1.5.

k. Complete the form(s) listed below and transcribe to the eCRF as appropriate.

- Unscheduled Visit Form
- Exit Visit Form (to be used if the subject is discontinued or exited at this visit)

6.1.5.1 Product Dispensing Only (Part of the Unscheduled Visit - used only if lens and/or rewetting drop replacement is needed)

If a subject is only seen for an unscheduled lens or study drop replacement, a complete exam is not required as long as the subject is not experiencing any problems.

NOTE: For study drop replacement, an unmasked designee MUST dispense the study drops to the subject to ensure the Investigator remains masked.

a. If study lenses and/or drops are dispensed, collect the following information in the source document and transcribe to the Product Dispensing Only eCRF Form:

- Visit date
- Subject ID number
- Subject initials
- Primary reason for replacement

b. Record Study Kit dispensed on the Product Accountability Log. Record lenses dispensed on the Lens Accountability Log.

6.1.5.2 If any assessment is performed, then an Unscheduled Visit Form must be completed instead of a Product Dispensing Only Form.

6.1.6 Missed Visits

Missed Visits will be handled as follows:

If a subject misses the 2-Week visit and cannot be seen prior to the start of the visit range for the next scheduled follow-up visit, the visit is considered missed.

6.2 Study Completion

For purposes of the Investigator notifying the IRB, the study is complete when all subjects at the site have been exited. Sponsor approval is required prior to IRB notification.

6.2.1 Early Study Termination/Suspension

If during the study it becomes evident to the Sponsor that the study should be stopped prematurely or placed on hold, the study will be terminated, and appropriate notification will be given to the Investigator(s), IRBs, and FDA, as applicable. Bausch + Lomb will instruct the Investigators to stop/restart dispensing study materials and will arrange for study closeout, if applicable, at each site. Any subjects with ongoing Adverse Events at the time of premature study termination or hold will be followed by the Investigator, as outlined in the Safety Management Plan.

6.3 Concomitant Medications/Therapy

Other contact lens rewetting drops are not allowed to be used by subjects during the study.

Ocular medications or systemic or topical medications that, in the Investigator's opinion, could potentially affect ocular physiology or lens performance are also prohibited, unless medically necessary during the course of the study. Any medications that have been taken in the past 30 days before signing the ICF and any medications taken during the course of the study will be collected in the source and appropriate eCRF.

6.4 Treatment Compliance

The Investigator or other designee will review instructions and warnings for lens wear, lens care, handling, cleaning, disinfecting, and rewetting drop use with the subject. Any subject who does not follow instructions to a degree that, in the Sponsor or Investigator's opinion, jeopardizes the subject's well-being or the validity of the study must be discontinued.

6.5 Protocol Deviations

The date of and reason for deviations will be documented in all cases. Significant or major protocol deviations impacting the safety of the subject or the integrity of the study must be reported by the Investigator to the IRB immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB.

Subjects may continue to participate until the end of the study, unless the protocol deviations put the subject at risk or the subject's condition requires that they be discontinued from the study.

According to the Device Investigator Agreement, all investigators participating in this study agree to conduct the study in accordance with the relevant, current protocol and agree to only make changes in a protocol after being notified by the Sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

Site Corrective Action plans will be developed and completed as deemed necessary by the CRO for sites or investigators who deviate from this protocol in a way that adversely affects the rights, safety or well-being of the subject(s) and/or the quality or integrity of data. The Site Corrective Action Plan will outline the deviation and the site's corrective and/or remedial actions. Decisions regarding critical deviations that merit investigator disqualification and site closure will be made by the Sponsor and documented in the Trial Master File.

7.0 ADVERSE EVENTS

7.1 Adverse Event Definitions

For the purposes of this study, reportable adverse events (AEs) include ocular AEs and non-ocular serious adverse events (SAEs). All AEs will be classified first for seriousness and significance and then as to whether or not they are an adverse device effect (ADE), an anticipated serious adverse device effect (ASADEs) or an unanticipated serious adverse device effect (UADEs). AEs, ADEs, ASADEs, UADEs, SAEs, Significant Non-Serious AEs and Non-Significant Non-Serious AEs are defined as follows:

7.1.1 Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in a subject, user, or other persons, whether or not related to the investigational medical device. This definition includes events not related to the investigational medical device, comparator, or the procedures involved. For users or other persons, this definition is restricted to events not related to investigational medical devices.

Throughout the course of this study all efforts will be made to remain alert to reportable AEs. If an AE occurs the first concern will be the safety of the subject and appropriate medical intervention will be made.

AEs should be first assessed for seriousness and significance and then differentiated for device related and non-device related.

All reportable AEs occurring after signing of informed consent and through the subject's end of participation in the study must be reported. All reportable AEs must be followed until the event resolves or stabilizes.

Applicable AEs should be photo documented and communicated to the Medical Monitor in electronic form.

7.1.2 Adverse Device Effect (ADE)

An ADE is an AE that is assessed to be related to the use of an investigational medical device. This definition includes AEs resulting from insufficient or inadequate instructions for use; deployment, implantation, installation, or operation; or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.

7.1.2.1 Anticipated Serious Adverse Device Effect (ASADE)

An ASADE is an ADE that first meets the serious criteria (see Section 7.1.3) or significant non-serious criteria (see Section 7.1.4) and which, by its nature, incidence,

severity or outcome, has been previously identified in the investigational plan or application (including a supplementary plan or application) and/or in the risk analysis report. ASADEs include:

- Corneal Ulcer (infectious or non-infectious)
- Keratitis
- Sensitivity to light (photophobia)
- Excessive eye secretions including mucopurulent discharge
- Blurred vision, rainbows or halos around objects
- Poor visual acuity (reduced sharpness of vision)
- Moderate to severe eye pain not relieved by removing the lens

7.1.2.2 Unanticipated Serious Adverse Device Effect (UADE)

An UADE is an ADE that first meets the serious criteria (see Section 7.1.3) and has an effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.1.3 Serious Adverse Event (SAE)

An AE that:

- Led to death;
- Led to serious deterioration in the health of the subject, that resulted in:
  - A life-threatening illness or injury; or
  - A permanent impairment of a body structure or a body function (e.g., blindness); or
  - Inpatient or prolonged hospitalization; or
  - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
- Led to fetal distress, fetal death, or a congenital abnormality or birth defect.

Note: A planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered an SAE.

Serious adverse events are also those events that result in, or have potential to cause, either permanent impairment of an ocular function or damage to an ocular structure and may necessitate medical or surgical intervention.

Serious adverse events may include any hazardous, sight-threatening conditions occurring after exposure to the test article, including the following:

- A presumed infectious ulcer (defined as a progressive erosion of the corneal tissue). For the purposes of reporting, this includes:
  - Central or para-central location;
  - Penetration of Bowman's membrane;
  - Infiltrate ≥2 mm diameter;

- Associated with iritis;
- Associated with any increase in intraocular pressure;
- Culture positive for microorganisms;
- Increasing size or severity at subsequent visits;

NOTE: Signs of a presumed infectious corneal ulcer may include irregular focal infiltrates, active lesions with raised edges, significant diffuse infiltration, anterior corneal to mid-stromal involvement, erosion with overlying staining, conjunctival and lid edema, anterior chamber reaction (iritis), and severe bulbar and limbal redness. Symptoms associated with a presumed infectious ulcer (microbial keratitis) may include pain of rapid onset, severe redness, purulent or mucopurulent discharge, tearing, and photophobia.

- Any central or paracentral (within 6 mm of cornea) corneal event that results in permanent opacification (such as corneal scar or vascularization);
- Any serious adverse ophthalmic events including hypopyon and/or hyphema;
- Any neovascularization within the central 6 mm of the cornea;
- Permanent loss of ≥2 lines of BSCVA;
- All cases of iritis.

7.1.4 Significant Non-Serious Adverse Events

A significant non-serious adverse event is an AE that does not meet the serious criteria, is considered significant by the Sponsor, and requires expedited reporting. These events include:

- Peripheral non-progressive non-infectious corneal ulcers;
- All symptomatic corneal infiltrative events;
- All cases of corneal staining greater than or equal to Grade 3;
- A temporary loss of two or more lines of BSCVA (for greater than or equal to 2 weeks);
- Neovascularization cases Grade 2 or greater;
- Any ocular event that necessitates temporary lens discontinuation of greater than or equal to 2 weeks.

7.1.5 Non-Significant Non-Serious Adverse Events

A non-significant non-serious adverse event may include but are not limited to the following and does not require expedited reporting:

- Bacterial Conjunctivitis;
- Viral Conjunctivitis;
- Allergic Conjunctivitis;
- Corneal Edema;
- Contact Lens Related Papillary Conjunctivitis; and,
- Loss of Contrast Sensitivity

7.2 Adverse Event Treatment and Culturing

With any AE, treat the subject as appropriate to prevent further complications and to potentially resolve the event consistent with the standard of care.

For purposes of this study, the Sponsor requests that cultures should be obtained in cases of corneal ulcer or suspected ocular infection, unless medically contraindicated. Cultures should be taken from the cul-de-sac, lower eyelid margin, and the corneal lesion (if applicable). The required culturing techniques are outlined in APPENDIX D:.

When a culture is obtained, the contact lenses and contact lens cases which were being utilized by the subject at the time of the AE should be collected from the subject for culturing and processing by the local clinical laboratory designated by the site.

Microbial data generated from returned subject supplies (e.g. lenses, lens cases, and/or lens case solutions) are for information only. Because microbes may be introduced into subject supplies during use, recovery of microbes from returned subject supplies cannot be presumed to indicate etiology or direction of organism transmission.

The ocular cultures, along with the associated contact lenses and contact lens cases, will be sent to the local clinical laboratory designated by the site for analysis. The clinical laboratory will report the culture results to the Investigator who will record the results in the eCRF.

7.3 Evaluations

When evaluating for reportable AEs, the Investigator must first determine if the event is serious (refer to Section 7.1.3 for criteria) and/or significant (refer to Sections 7.1.4 and 7.1.5) and then assess the severity of symptoms and the relationship of the event to the study device using the following guidelines:

7.3.1 Severity

- **Mild:** Subject awareness of a sign or symptom that is easily tolerated, requires no treatment, and does not interfere with subject's daily activities.
- **Moderate:** Subject awareness of a sign or symptom which may be a low level of concern to the subject and may interfere with daily activities but can be relieved by simple therapeutic care.
- **Severe:** A sign or symptom that interrupts the subject's daily activity and requires systemic therapy or other treatment

7.3.2 Relationship to Study Device and/or Rewetting Drops

- **Related:** There is at least a reasonable possibility that the AE is related to the study device (study solution) and/or rewetting drops. Reasonable possibility means that there is evidence to suggest a causal relationship or association between the study device and/or rewetting drops and the AE. Also referred to as an ADE.
- **Not related:** There is little or no reasonable possibility that the AE is related to the study device (study solution) and/or rewetting drops. This assessment implies that the AE has no evidence to suggest either a causal relationship or association to the study device and/or rewetting drops and a more likely or certain alternative etiology exists.

7.4 Procedures for Reporting SAEs and Significant Non-Serious Adverse Events

An AE classified as a SAE or a Significant Non-Serious AE requires expeditious handling and reporting to the Sponsor to comply with regulatory requirements, as follows:

- The event must be reported to the Medical Monitor (or designee) within 24 hours of the Investigator's awareness of the event via facsimile/email transmission on a paper SAE or Significant Non-Serious AE Report Form signed by the Investigator.

- The Medical Monitor (or designee) will email a copy of the form (within 24 hours) to

- Investigators should not wait to receive additional information to fully document the event before initially notifying the Medical Monitor of an SAE or a Significant Non-Serious AE. Additional relevant information such as hospital records and autopsy reports should be provided to the Medical Monitor as soon as they are available.
- The Investigator should take all appropriate measures to ensure the safety of the subjects: notably, he/she should follow a subject with an SAE or Significant Non-Serious AE until the event has resolved or the condition has stabilized. This may imply that follow-up will continue after the subject has left the study, and that additional evaluations may be requested by the Sponsor.
- Ensure that the subject's identity is protected and the subject's identifiers in the clinical trial are properly mentioned on the form.
- BEGIN TREATMENT OF THE AE IMMEDIATELY BY A SUITABLY LICENSED EYE CARE PROFESSIONAL.
- Continue to update the paper SAE or Significant Non-Serious AE Report Form, if applicable, each time the subject is seen during the management of the event and at resolution of the event. All updated report forms should be submitted to the Medical Monitor who will distribute the reports as stated above. Whenever possible, it is suggested that the Investigator take photographs of all applicable AEs and forward them to the Medical Monitor.
- Events requiring medical treatment will be evaluated by the Sponsor. Upon review of the medical treatment, Bausch + Lomb Clinical Operations representatives may contact the Investigator to request further information concerning the treatment.

- Report all UADEs to the reviewing IRB within 10 working days following awareness of the UADE or according to the established reporting procedures of the IRB, whichever is shorter.
- Submit all bills, prescription receipts, and culture reports/fees related to the AE to the Bausch + Lomb Clinical Operations. Expense incurred for study related medical treatment will be paid by Bausch +Lomb Clinical Operations.
- Full details of the process for reporting adverse events are outlined in the Safety Management Plan.

7.4.1 Off-Site Unanticipated Serious Adverse Device Effect Reporting

When participating in multicenter clinical investigations, Investigators may receive off-site UADE reports. These are Sponsor reports of UADEs which occurred at other clinical sites for the same trial, or in different trials using the same test article, that met the criteria for reporting to a regulatory agency. These should be reported to the reviewing IRB within 10 working days or per their established reporting procedures, whichever is shorter.

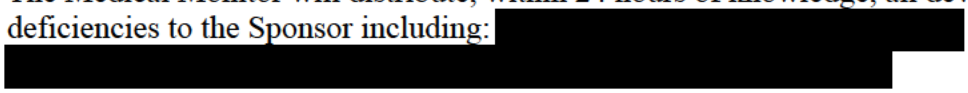
7.4.2 Reporting Device Deficiencies

A device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.

Investigators must evaluate, record, and report via applicable forms any complaints/ deficiencies or malfunctions experienced with the study solution during this trial to the Medical Monitor promptly. The Sponsor and Medical Monitor shall review all device deficiencies, and, upon the Sponsor's request, Investigators must supply any additional information related to the safety reporting of a particular event.

Report device deficiencies within 24 hours of knowledge to:

The Medical Monitor will distribute, within 24 hours of knowledge, all device deficiencies to the Sponsor including:



The Sponsor shall review all device deficiencies and determine and document in writing whether they could have led to an SAE. In the event of a disagreement between the Sponsor and the Investigator(s), the Sponsor shall communicate both opinions to the reviewing IRB per their established reporting procedures and the health authority.

7.4.3 Guidelines for Reporting Pregnancies

All female subjects of childbearing potential must use an effective method of birth control during the study, to include 2 weeks after last visit, in a manner such that risk of contraceptive failure is minimized. Abstinence is allowed as a birth control method.

During the study, all female subjects of childbearing potential should be instructed to contact the Investigator immediately if they suspect they might be pregnant (e.g. missed or late menstrual period). Female subjects who become pregnant during the study will be followed until completion of pregnancy. Every effort will be made to obtain the health status of the mother and infant or fetus (in cases of miscarriage or therapeutic abortion) at term. Pregnancy itself is not considered an AE.

All confirmed pregnancies must be reported on a paper Pregnancy Report Form and submitted to the Medical Monitor via facsimile or email transmission within 24 hours of the Investigator's awareness of the pregnancy. The Medical Monitor will distribute the completed form to the Sponsor as per the distribution list in Section 7.4.

All pregnancies will be followed until outcome even after study closure. The outcome of all pregnancies will be reported on a paper Pregnancy Outcome Report Form and submitted to the Medical Monitor via facsimile or email transmission once the outcome is learned. The Medical Monitor will distribute the completed form to the Sponsor as per the distribution list in Section 7.4.

Although pregnancy occurring in a clinical study is not considered to be an AE or SAE, any pregnancy complication, spontaneous abortion, or elective termination of a pregnancy, for medical reasons, will be recorded as an SAE. Any serious complication or event resulting from the pregnancy should be reported to the Medical Monitor within 24 hours on the SAE or Significant Non-Serious AE Report Form along with the Pregnancy Report Form.

The contact for reporting pregnancies and pregnancy outcomes is:

[redacted]

8.0 STATISTICAL METHODS

8.1 Study Endpoints

8.1.1 Primary Safety Endpoint

- Slit lamp findings greater than grade 2

8.1.2 Primary Effectiveness Endpoints

- Overall comfort at all scheduled follow-up visits
- Dryness at all scheduled follow-up visits

8.1.3 Secondary Effectiveness Endpoints

There are no secondary effectiveness endpoints.

8.2 Hypotheses

8.2.1 Slit Lamp Findings

The null hypothesis (H_0) is that the difference in the proportion of eyes with slit lamp findings greater than grade 2 (test group proportion [π_T] minus standard group proportion

$[\pi_S]$) is greater than or equal to 0.05 (5%). The alternative hypothesis (H_1) is that the difference is less than 0.05 (5%).

$$H_0: \pi_T - \pi_S \geq 0.05$$

$$H_1: \pi_T - \pi_S < 0.05$$

8.2.2 Overall Comfort

The null hypothesis (H_0) is that the difference in mean overall comfort (test group mean $[\mu_T]$ minus standard group mean $[\mu_S]$) is less than or equal to negative five points. The alternative hypothesis (H_1) is that the difference is greater than negative five points.

$$H_0: \mu_T - \mu_S \leq -5$$

$$H_1: \mu_T - \mu_S > -5$$

8.2.3 Dryness

The null hypothesis (H_0) is that the difference in mean dryness score (test group mean $[\mu_T]$ minus standard group mean $[\mu_S]$) is less than or equal to negative five points. The alternative hypothesis (H_1) is that the difference is greater than negative five points.

$$H_0: \mu_T - \mu_S \leq -5$$

$$H_1: \mu_T - \mu_S > -5$$

8.3 Sample Size

Estimates of standard deviations and proportions were obtained from Bausch + Lomb Study #872.[1]

The sample size calculations assume that the level of analysis will be the eye and that the outcomes from each subject's eyes will be independent. This is a standard assumption for contact lens care product trials.

The recommended minimum sample size is 20 Test group subjects per lens stratum. Therefore, with eight strata the targeted completed sample size will be (20 Test subjects/stratum + 20 Control subjects/stratum) x 8 strata = 320 subjects (assuming sufficient statistical power is provided by this sample size).

Sample size calculations were completed using nQuery Advisor® 7.0 software.

8.3.1 Slit Lamp Findings

In Study 872, the proportion of eyes with slit lamp finding greater than grade 2 at any follow up visits was 0.005. With 320 eyes (160 subjects) in each group, the upper limit of the observed one-sided 95% confidence interval will be expected to be less than 0.05 with 99% power when the Standard proportion, π_S, is 0.005 and the Test expected proportion, π_T, is 0.005. Results are based on 100,000 simulations using the Newcombe-Wilson score method to construct the confidence interval.[2]

8.3.2 Overall Comfort

In Study 872, the standard deviation of overall comfort ratings averaged over all visits was 13.9 units. When the sample size in each group is 320 eyes (160 subjects), a two group 0.05 one-sided t-test will have 99% power to reject the null hypothesis that the test

is not non-inferior to the control (the difference in means, μ_T - μ_S, is -5 or farther from zero in the same direction) in favor of the alternative hypothesis that the test is non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 13.9.

8.3.3 Dryness

In Study 872, the standard deviation of dryness ratings averaged over all visits was 13.9 units. When the sample size in each group is 320 eyes (160 subjects), a two group 0.05 one-sided t-test will have 99% power to reject the null hypothesis that the test is not non-inferior to the control (the difference in means, μ_T - μ_S, is -5 or farther from zero in the same direction) in favor of the alternative hypothesis that the test is non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 13.9.

8.3.4 Overall Power

If the primary endpoints are independent, the overall power of the study is 99% x 99% x 99% = 97%.

8.3.5 Enrollment Target

The desired completed sample size is 160 subjects per group. Allowing for up to 13% losses, the enrollment target in each treatment group will be approximately $\lceil 160 \div (1 - 0.13) \rceil = 184$ subjects. The total enrollment target will be approximately 2 x 184 = 368 subjects (736 eyes).

8.4 Randomization

Subjects will be randomized to one of two treatment arms in a 1:1 ratio, using Test drops or Control drops for the duration of the study. Randomization will be managed using ORS. The randomization will be stratified by lens group within investigational site. The lens group will be determined by the subjects' habitual lens material at Screening/Dispensing and will be one of the groups shown in Table 1: Lens Groups (page 13).

Efforts will be made to enroll subjects in at least four of the lens strata within each site to minimize confounding between site and lens strata. It should be noted that while the target enrollment for each lens strata is approximately 40 subjects (approximately 20 per treatment arm), some lens strata may be difficult to enroll.

An unmasked statistician who is not otherwise involved in the trial will create the randomization schedule.

8.5 Study Populations

8.5.1 Intent-to-Treat (ITT) Population

The ITT Population will consist of all randomized subjects and both of their eyes. Subjects will be included in ITT Population summaries according to the treatment group to which they were randomly assigned.

8.5.2 Per Protocol (PP) Population

The PP population will be the primary population used for analysis of the primary effectiveness endpoints. The PP Population will consist of all ITT Population subjects without important (major) protocol deviations for subject level summaries and, for eye level summaries, both of their eyes. Important protocol deviation categories are defined in Section 8.6.4. Subjects will be included in PP Population summaries according to the treatment group to which they were randomly assigned. Membership in the PP population will be determined prior to study unmasking.

8.5.3 Safety Population

The Safety Population will consist of all dispensed subjects and, for eye level summaries, both of their eyes. Subjects will be included in Safety summaries according to the treatment that they received. If a subject receives more than one treatment and one of those treatments is the Test solution, then the subject will be included in Safety Population summaries under the Test treatment group.

8.6 Statistical Analysis

8.6.1 Methods of Analysis

8.6.1.1 General Methods

Continuous data will be summarized using descriptive statistics: sample size, mean, standard deviation, median, minimum and maximum. Categorical data will be presented using the total counts for each category and corresponding percentages. The denominator for each percentage will be the number of subjects or eyes with non-missing data at the given visit for each respective study treatment, unless otherwise indicated.

As is customary for contact lens care product trials, eyes will be treated as independent sampling units in eye level analyses unless otherwise noted.

Further details will be provided in a separate statistical analysis plan which will be completed and approved prior to unmasking of the treatment assignments.

8.6.1.2 Graded Slit Lamp Findings

At each follow-up visit, graded slit lamp findings will be assessed for each eye using Grades 0 through 4. Using only the non-missing observations from all visits without imputation, each eye will be classified with respect to findings greater than grade 2 at any visit (Absent, Present). Missing data will not be imputed. Greater than grade 2 findings (Absent, Present) will be summarized at the eye level by treatment using categorical summary statistics for the Safety Set in a table. A one-sided upper 95% confidence limit around the difference in "Present" proportions between the test and control treatment groups will be constructed using the Newcombe-Wilson score method.[2] If the upper confidence limit is less than 5.0%, then the null hypothesis that the test solution is not non-inferior will be rejected, and the test solution will be statistically successful in this outcome.

8.6.1.3 Overall Comfort

At each follow-up visit, overall comfort will be assessed for each eye on a scale from 0 to 100, with 100 denoting the most favorable response. For each eye, mean overall comfort

over all follow-up visits will be computed as the average of the non-missing values over all scheduled follow-up visits. Missing data will not be imputed for the primary analysis. Mean overall comfort over all follow-up visits will be summarized at the eye level by treatment using continuous summary statistics for the Per Protocol Set in a table. A one-sided lower 95% confidence limit around the difference in means between the test and control treatment groups, computed using an analysis of variance model including the fixed factor of treatment and the fixed blocking factor of site, will be displayed. If the lower confidence limit is greater than -5, then the null hypothesis that the test solution is not non- inferior will be rejected, and the test solution will be statistically successful in this outcome.

As a sensitivity analysis, the ITT Population will be analyzed for this endpoint. Summaries by treatment and a confidence interval around the difference in means will be provided as described above using the available data. Twenty imputations of missing overall comfort data will be produced by treatment group using the Markov chain Monte Carlo (MCMC) method. The variables used to create the imputed datasets will be the overall comfort scores observed at each scheduled visit. The differences and standard errors estimated by imputation will be combined to create an estimated difference and confidence limit.

8.6.1.4 Dryness

At each follow-up visit, dryness will be assessed for each eye on a scale from 0 to 100, with 100 denoting the most favorable response. Dryness will be analyzed using the methods described above for overall comfort.

8.6.2 Subject Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized descriptively by treatment and overall for the ITT, PP, and Safety Populations. Demographics and baseline characteristics will also be listed.

8.6.3 Subject Discontinuation

The reasons for study discontinuation will be summarized by treatment and overall for the ITT Population. Details of discontinued eyes will be also listed by treatment.

8.6.4 Protocol Deviations

Important (major) protocol deviations will be summarized by category and treatment group for the ITT Population in a table.

Categories of important protocol deviations will include the following, which will be derived via data entered on the case report forms.

- Ineligibility
- Not dispensed study treatment
- Mis-randomization
- Dispensing of the incorrect study treatment
- Dispensing and use of lenses from the incorrect lens group
- Use of medications that could potentially affect any of the primary effectiveness endpoints

- Failure to comply with the procedures used to assess the primary effectiveness endpoints, such as missing the scheduled visit or failing to complete the procedure in accordance with instructions

Additional important protocol deviation categories may be added prior to unmasking.

Important (major) protocol deviations will also be displayed in a listing.

8.6.5 Treatment Compliance

As is customary for contact lens care product trials, treatment compliance will not be evaluated.

8.6.6 Treatment Exposure

As is customary for contact lens care product trials, treatment exposure will not be evaluated.

8.6.7 Missing Data

Imputation of missing data is not conservative in a non-inferiority analysis setting. Therefore, primary effectiveness analyses will be completed using the PP Set without imputation of missing data.

Sensitivity analyses of data from the ITT Set with missing data imputation are described in Section 8.6.1. Unless otherwise specified in the protocol or statistical analysis plan, missing data will not be imputed.

8.6.8 Multiple Comparisons

Statistical success depends on success for all primary endpoints. Therefore, adjustments for multiple comparisons are not necessary.

8.6.9 Interim Analyses

No interim analyses are planned.

9.0 DATA QUALITY ASSURANCE

9.1 Study Monitoring

Sponsor representatives must be allowed to visit all study site locations to assess the data, quality, and study integrity in a manner consistent with applicable health authority regulations and the procedures adopted by the Sponsor.

Prior to the start of the study, representatives of the Sponsor (or designees) will review the protocol, eCRF, regulatory obligations, and other material or equipment relevant to the conduct of the study with the Investigator/Sub-Investigator and relevant study site personnel.

Monitoring visits and telephone consultations will occur as necessary, or per the monitoring plan, during the course of the investigation to verify the following:

- The rights and well-being of subjects are protected.
- This clinical investigation is being conducted in accordance with 21 CFR Parts 11, 50, 54, 56, and 812. The protocol was developed with consideration of the

provisions in: ISO 14155-1:2011 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2011 Part 2: Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Optics – Contact lenses and contact lens care products – Guidance for clinical investigations; ICH GCP and applicable local regulations. The Sponsor intends to register this clinical trial with the public database https://ClinicalTrials.gov.

- The integrity of the data, including adequate study documentation.
- The facilities remain acceptable.
- The Investigator and site personnel remain qualified and able to conduct the study.
- Test article accountability

During the course of the study, if the Sponsor determines that an Investigator is not compliant with the protocol and/or applicable regulatory requirements, the Sponsor will take action to secure compliance. In addition, the Sponsor may terminate the Investigator's participation in the study if appropriate, or if the Investigator remains non-compliant despite the Sponsor's actions.

Full details for site monitoring procedures are covered in the study 952 Monitoring Plan.

9.2 Source Documentation

All medical information obtained at each study visit must be recorded in the subject's record (source documentation) in real time as it is collected. Source documentation consists of original subject documents, as well as data and records with information relevant to the subject and his/her participation in the study.

Examples of source documents include hospital records, clinical and office charts, laboratory notes, memoranda, signed ICF, evaluation checklists, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, and information initially recorded in an electronic format. Source documentation worksheets may be provided by the Sponsor to record pertinent information.

Subject-completed forms are also considered to be source data. Only subjects are to record information on subject-completed forms. In no instance should an Investigator or study site personnel record any data or make changes to subject-completed forms. The Investigator or designee should review subject-completed forms during study visits for completeness and accuracy. If an entry is found to be illegible or a mistake is found (eg, incorrect year was recorded), the subject should be instructed to edit the entry by drawing a single line through the original entry, entering the new information, and dating and initialing the change.

9.3 Case Report Forms and Data Verification

Subject data required by this protocol are to be transferred from the source to the eCRFs. The Investigator and his/her study site personnel will be responsible for completing the eCRFs. The Investigator is required to verify that all of the requested information is accurately recorded on the eCRFs by providing an electronic signature. All information requested on the eCRFs needs to be supplied, including subject identification and initials,

date(s), assessment values, etc., and any omission or discrepancy will require explanation. All information on eCRFs must be traceable to source documents.

The study monitor will be responsible for reviewing and verifying the data recorded on the eCRFs per the study Monitoring Plan, utilizing the original source documentation and will query discrepant findings. The Investigator and study site personnel will be responsible for answering all queries.

Details regarding procedures used for data review, database cleaning and issuing and resolving queries are provided in the study 952 Monitoring Plan and Data Management Plan. Procedures for verification, validation and securing of electronic clinical data systems are outlined in the Data Management Plan.

A copy of the eCRFs will be provided to the Investigator at the conclusion of the study, who must ensure that it is stored in a secure place.

9.4 Recording of Data and Retention of Documents

The subject will only be identified by the subject number and by their initials if also required. Confidentiality of subject records must be maintained to ensure adherence to applicable local privacy regulations.

The Investigator must retain essential documents indefinitely after the completion of the study, unless otherwise notified by the Sponsor. The Investigator agrees to adhere to the document retention procedures when signing the protocol Investigator Statement of Approval.

Essential documents include but are not limited to the following:

- IRB approvals for the study protocol, all amendments, ICF(s), and advertisements
- IRB annual study review
- IRB correspondence and reports (eg, AE reports, protocol deviations, and safety updates)
- Regulatory documents (eg, financial disclosure and delegation of authority forms)
- All source documents
- Archive of eCRFs
- Subject's signed ICF
- Device Investigator Agreement
- Accountability records for the test article
- Correspondence from and to the Sponsor
- Any other documents relevant to the conduct of the study

In the event that study records are transferred to another location, the Investigator will provide notice of such transfer in writing to Sponsor.

9.5 Auditing Procedures

Audits of clinical research activities to evaluate compliance with the principles of GCP may take place. A regulatory authority may also wish to conduct an inspection (during the study or after its completion). If an inspection is requested by a regulatory authority and/or IRB/EC, the Investigator must inform the Sponsor immediately that this request has been made.

9.6 Institutional Review Board/Ethics Committee Approval

The Investigator should ensure their participation in the study, in addition to the protocol, subject recruitment materials (written information or materials including web pages, radio advertisements, television spots, or written text developed to encourage subject enrollment) and the ICF to be used in this study are approved by their institution IRB, or if not using their institution's IRB, approved by the reviewing central IRB prior to entering any subjects in the study. Documentation of IRB approval of the study protocol and informed consent must be provided to the Sponsor prior to initiation of the study. In addition, the Investigator must ensure that the reviewing IRB has provided approval for any protocol amendments prior to implementation. If the amendment necessitates a revision to the ICF, the Investigator should ensure the revised form is also submitted to and approved by the Sponsor and the IRB and implemented as directed.

9.7 Publication of Results

All study data generated as a result of this study will be regarded as confidential, until appropriate analysis and review by the Sponsor or its designee and the Investigator(s) are completed. The results of the study may be published or presented by the Investigator(s) after the review by, and in consultation and agreement with the Sponsor, and such that confidential or proprietary information is not disclosed.

Prior to publication or presentation, a copy of the final text should be forwarded by the Investigator(s) to the Sponsor or its designee, for comment. Such comments shall aim to ensure the scientific integrity of the proposed publications and/or presentations and ensure that the data and material referring to Bausch & Lomb Incorporated products and activities receive fair, accurate, and reasonable presentation.

The Sponsor may also choose to submit the results of this study for publication.

9.8 Statements of Compliance

9.8.1 Ethics Review

The final protocol, including the final version of the Subject Instructions and Informed Consent Form, must be approved by an IRB before enrollment of any subject into the study. The Principal Investigator (or Sponsor/CRO on behalf of the Principal Investigator) is responsible for informing the IRB of any amendment to the protocol as per local requirements. Any additional requirements imposed by the IRB shall be followed.

9.8.2 Ethical Conduct of the Investigation

The study will be performed in accordance with the ethical principles that have their origin in the most recent version of the Declaration of Helsinki, and with applicable regulatory requirements. Patients who are close colleagues, associates or family members of, or in any way dependent on the Sponsor or the investigator, will not be included in this study.

9.8.3 Informed Consent Process

The Principal Investigator will ensure that each subject is given full and adequate oral and written information about the nature, purpose, possible risks and benefits of the study. Subjects must also be notified that they are free to discontinue participation in the

study at any time. The subject should be given the opportunity to ask questions and time for consideration.

The subject's signed informed consent must be obtained before conducting any study related procedures. The original must be filed by the investigative site. A copy of the signed Informed Consent Form should be given to the subject. If modifications are made to the Informed Consent Form, the new version must be approved by the IRB. The new version of revised Informed Consent Form(s) must be reviewed and signed by all active (if required by the IRB) and new subjects at the first opportunity after approval by the IRB.

10.0 REFERENCES

[1] Bausch & Lomb Incorporated Study 872 'A Safety and Effectiveness Study of a New Contact Lens Cleaning and Disinfecting Solution' Final Clinical Study Report, (Version 1, 14MAR2016)

[2] Newcombe RG (1988) Interval estimation for the difference between independent proportions: comparison of eleven methods. Statistics in Medicine 17:873-890.

APPENDIX A: SCHEDULE OF VISITS AND PARAMETERS

All study tasks should be performed by qualified study site personnel as indicated on the delegation of authority log under the supervision of the Principal Investigator.

[redacted]

[a] At screening, the study lenses/drops will be rated by an abbreviated list of Subjective Assessment scales (see section B-10, Appendix B).
[b] At screening, discoloration and deposits will not be collected
Note: All VA measurements MUST be made using a phoropter
Note: If this is an Exit Visit, also perform the procedures listed under the Exit Visit column.

APPENDIX B: METHODS OF CLINICAL EVALUATION

Maintenance and calibration of the equipment relevant to study assessments must be appropriately performed and documented by the investigative site, where applicable. Any changes to the procedures described in this appendix will be provided under separate cover.

1.0 Visual Acuity/Refraction

It is essential that a standard procedure be used to obtain VA measurements. The VA and refraction measurements should be obtained by a physician, optometrist, or trained technician. One standard logMAR chart, high 90% contrast, with Sloan letters will be used to obtain the VA measurements in this study. The following VA equipment from Precision Vision, Inc. will be used in this study: 90% High Contrast 6.5 feet (2.0 meters) testing distance Translucent Chart (CAT. NO. 2103-2), and the Precision Vision Small Illuminator Cabinet (CAT. NO. 914).

1.1 Illumination of the logMAR Chart and Room Illumination

The internal illumination of the logMAR chart should be turned on. This will provide the nominal contrast for each of the charts. **Room illumination should be turned off**, to ensure that the illumination is consistent for each measurement. Ambient sources of light in the room, such as computer monitors, should be turned off or covered. A small source of illumination may be used to allow recording of data and to ensure that it is not difficult or dangerous for staff or subjects to move around the testing area, but these light sources should not be placed so that they are directed toward the subject during testing. The room lighting and any ambient sources should be consistent in their use and placement at each subject visit throughout the course of this study.

1.2 Determination of High Contrast Visual Acuity

The subject should be seated so that the distance from the subject's eyes to the logMAR chart is 6.5 feet (2.0 meters). The chart should be at eye level for the subject. The logMAR charts have two alternative letter sequences from 28 letters (0.3 logMAR) to 62 letters (-0.3 logMAR). It is recommended that one letter sequence is used for the right eye, and the second letter sequence is used for the left eye, to minimize learning effects at each visit. Care should be taken to completely occlude the eye not being measured.

Since the test distance of the chart is not at optical infinity, refractive power compensation is required to simulate optical infinity. **The VA should be measured through the phoropter using the distance refractive correction with the addition of +0.50 D to compensate for the reduced test distance of 6.5 feet (2.0 meters).**

If all letters are correctly identified on any given line, then the subject is encouraged to read the next smaller line. When the subject says they cannot read a letter, they should be required to guess. A maximum effort should be made to identify each letter. A scoring sheet for each eye is provided to keep track of the letters correctly identified by writing an "X" over the incorrectly identified letter. The subject continues reading down the chart to the last letter of a given line, **until the subject has missed 3 letters on a line with 5 letters**. The incorrect letters can occur at the beginning, middle, or end of this line and do not have to be consecutive.

1.3 Recording and Scoring logMAR Values

Using the Sponsor supplied recording/scoring sheet, an example of which is shown below, the tester will record the actual VA measure.

The number of letters CORRECT will be recorded on the recording/scoring sheet in the far right box on the corresponding line. The lines will then be added up and the "TOTAL" number of letters correctly identified will be recorded on the recording/scoring sheet. The "TOTAL" is the number that will be entered onto the eCRF.

Example of Distance VA:

In the example below, all letters in lines 1 through 8 were read correctly. Line 9 had 4 correct responses, and line 10 had only 1 correct response. After line 10, the VA test would be considered complete. In this example, the total letters correctly identified is 42. This number is recorded in the space marked "TOTAL" and also recorded on the eCRF.

Distance Visual Acuity (High Contrast)				
Snellen	**logMAR**	**Chart**		**Letters Correct**
20/160	0.9	S Z N		3
20/125	0.8	R N C V		4
20/100	0.7	K C R H N		5
20/80	0.6	Z K D V C		5
20/63	0.5	H V O R K		5
20/50	0.4	R H S O N		5
20/40	0.3		K S V R H	5
20/32	0.2		H N K C D	5
20/25	0.1		N D V K O	4
20/20	0		~~D~~ ~~N~~ O ~~S~~ ~~V~~	1
20/16	-0.1		V R N D O	
20/12.5	-0.2		C Z H K S	
20/9.5	-0.3		O R Z S K	

TOTAL	42

2.0 Slit Lamp Examination

The following parameters will be assessed during the Slit Lamp Examination (without lenses):

Epithelial Edema

0 - None: No epithelial or sub-epithelial haziness. Normal transparency.

1 - Trace: Barely discernible localized epithelial or sub-epithelial haziness.

2 - Mild: Faint but definite localized or generalized epithelial haziness.

3 - Moderate: Significant localized or general epithelial haziness.

4 - Severe: Definite widespread, epithelial cloudiness giving dull glass appearance to cornea, or numerous coalescent buliae.

Epithelial Microcysts

0 - None: No microcysts seen using retroillumination.

1 - Trace: Fewer than 50 microcysts over central or para-central cornea. No overlying staining or surface anomaly.

2 - Mild: More than 50 microcysts over central or paracentral cornea. No overlying staining or surface anomaly.

3 - Moderate: More than 50 microcysts, tending to be coalescent and accompanied by overlying faint staining or dry spots.

4 - Severe: Numerous, dense, coalescent microcysts accompanied by overlying significant staining or erosion.

Corneal Staining

Corneal staining must be assessed after the instillation of fluorescein. If needed, a Wratten Gel Filter will be provided by the Sponsor for the evaluation of corneal staining. The Wratten Gel Filter must be used as a barrier filter in the observation pathway, in combination with the cobalt blue filter.

0 - None: No fluorescein staining.

1 - Trace: Minimal superficial staining or stippling, and non-coalescing. Includes superficial foreign body staining.

2 - Mild: Lightly coalescent or diffuse punctate staining, with no stain diffusion into stroma.

3 - Moderate: Significant or densely coalescent punctate staining, including slight diffusion of stain into stroma.

4 - Severe: Severe abrasion or erosion with loss of epithelial substance. Marked and rapid diffusion of stain into stroma.

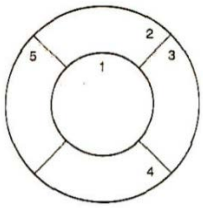
New corneal scar or pre-existing corneal scar (Record for both OD and OS)

Absent or Present

Location: Check all that apply

- ☐Central (central 6 mm, 3 mm from corneal center)
- ☐Nasal
- ☐Inferior
- ☐Temporal
- ☐Superior

Size: X.X (mm) Draw:



Limbal Injection

0 - None: No hyperemia present. Normal appearance of limbal vessels including prominent limbal vascular arcades.

1 - Trace: Very slight hyperemia of limbal vessels in one quadrant.

2 - Mild: Mild hyperemia of limbal vessels in more than one quadrant.

3 - Moderate: Marked hyperemia of limbal vessels in any quadrant.

4 - Severe: Marked hyperemia of limbal vessels in all quadrants.

Bulbar Injection

0 - None: No hyperemia present. Normal appearance of conjunctival vessels.

1 - Trace: Slight hyperemia of conjunctival vessels in one quadrant.

2 - Mild: Mild hyperemia of conjunctival vessels in more than one quadrant.

3 - Moderate: Marked hyperemia of conjunctival vessels in any quadrant.

4 - Severe: Marked hyperemia of conjunctival vessels in all quadrants.

Upper lid tarsal conjunctival abnormalities

0 - None: Normal, velvet tarsal conjunctival appearance. No hyperemia or enlarged papillae.

1 - Trace: Slight tarsal conjunctival hyperemia with slight loss of smoothness.

2 - Mild: Slight tarsal conjunctival hyperemia with slight loss of smoothness. Noticeable enlargement of papillae, but <1.0 mm in diameter.

3 - Moderate: Definite loss of smoothness with enlarged papillae, but <1.0 mm in diameter with marked tarsal conjunctival hyperemia.

4 - Severe: Localized or generalized giant papillae, >1.0 mm in diameter and/or severe tarsal conjunctival hyperemia.

Corneal neovascularization

0 - None: Normal appearing limbus, including prominent limbal vascular arcades.
1 - Trace: Vascularization <1.5 mm of advancement into cornea in one quadrant.
2 - Mild: Vascularization <1.5 mm of advancement into cornea in more than one quadrant.
3 - Moderate: Vascularization 1.5 mm to <2.5 mm of advancement into cornea in any quadrant.
4 - Severe: Vascularization >2.5 mm of advancement into cornea in any quadrant.

Corneal Infiltrates

0 - No infiltrates.
1 - Single infiltrate; (focal and peripheral), asymptomatic.
2 - Single or multiple infiltrate(s); with injection and/or associated symptoms.
3 - Single or multiple infiltrate(s); injection with overlying corneal defect(s).
4 - Single or multiple infiltrate(s); injection with diffusion of stain into stroma.

Absent or Present

New Corneal Scar
Corneal Striae
Conjunctivitis
Other Anterior Segment Abnormalities
External Adnexa Abnormalities

3.0 Method for the Examination, Description and Classification of Lens Deposits

The following procedure has been developed to assist in the examination, description, and classification of deposits found on contact lenses at all follow-up visits in the Investigator's office.

Materials needed: Slit Lamp

Procedure: Each lens should be examined on the eye using the slit lamp employing a 7X to 15X magnification.

Classify the deposit and record findings at each visit as follows:

I. Type of Deposit

Indicate the type of the most prominent lens surface deposit found using the following classifications:

- none
- crystalline deposits
- crust-like deposits
- film
- spots

II. Estimated Percentage of Lens Surface Covered By Deposits

Estimate the percentage of the lens surface that is covered by deposits using the following classifications:

- none
- 1 - 25%
- 26 - 50%
- 51 - 75%
- 76 - 100%

III. Degree of Deposit

Indicate the degree of the deposit on the lens surface using the following classifications:

- none
- light
- medium
- heavy

IV. Wettability

Grade 0 - 100% of anterior lens surface is wettable
Grade 1 - Presence of small (<0.1 mm), individual discrete non-wetting areas
Grade 2 - Presence of single area of non-wetting between 0.1 mm and 0.5 mm in size
Grade 3 - Presence of several areas of non-wetting between 0.1 mm and 0.5 mm in size
Grade 4 - Presence of one or more non-wetting areas greater than 0.5 mm in size

V. Discoloration

If while on-eye, any discoloration is observed, remove lens and confirm discoloration using the following classifications:

0 - None
1 - Faded
2 - Yellow
3 - Brown
4 - Pink

4.0 Method for the Examination, Description and Classification of Lens Fit

The following procedure has been developed to assist in the examination, description, and classification of contact lenses fit at all visits in the Investigator's office.

Materials needed: Slit Lamp

Procedure: Each lens should be examined on the eye using the slit lamp employing a 7X to 15X magnification.

Lens fit will be assessed utilizing the scales below:

I. Lens Centration (Enter Rating 0-3)

Qualitative Lens Centration

- Compare lens edge overlap of limbus in all visible sectors.
- The centration diagram is pictured as lateral decentration toward 9:00 on the clock dial. Centration assessment applies to all clock hours.
    - If the limbus is an ill-defined band, assess from the center of the band.
    - If the contact lens edge translates with blinking, assess to the average lens edge position.
    - Centration assessment applies to primary gaze.
    - If the inferior edge of the contact lens is not visible, gently pull the lower eyelid away.
- Rate and record lens centration on a scale of 0 to 3 based on the following lens diagrams and descriptors:

    0) Equal Overlap 360 degrees
    1) Maximum overlap ≤ 2/3 in any sector
    2) Maximum overlap > 2/3 in any sector
    3) Any Corneal Exposure

II. Lens Movement

- As the subject blinks normally, observe lens movement, with particular attention to the inferior portion of the lens.
    - All movement depicted in the diagram below is from the absolute centered position.
    - All movement descriptions apply from the various decentered positions.
    - Corneal exposure in any sector is an unacceptable fit.
    - If the inferior edge of the contact lens is not visible, gently pull the lower eyelid away.
- Rate and record lens movement on a scale of -2 to +2 based on the following lens diagrams and descriptors:

-2	No observable movement (perform Josephson push-up test, see below)
-1	Minimal; Just observable movement, lens returns to origin.
0	Optimal/Free movement, lens returns to origin.
+1	Substantial movement; but lens does not immediately return to origin.
+2	Excessive movement; lens does not return to origin, may result in corneal exposure.

Josephson Push Up Test

- Use Josephson Push-up test when specified or indicated (-2 = No observable lens movement, see lens movement ratings above).
    - Apply gentle upward digital pressure to the lower lid such that the lower lid margin pushes on the inferior aspect of the contact lens edge.
- Determine if this action causes the contact lens to move and rate as follows:
  1 - Lens is mobile
  2 - Lens is immobile

BAUSCH + LOMB™

PRIMARY GAZE
LENS CENTRATION

PRIMARY GAZE
LENS MOVEMENT

5.0 Symptoms and Complaints

1. The question asked by the technician or ECP, "Are you experiencing any symptoms or problems with these lenses?"
2. If no is checked, all symptoms are registered as 0.
3. If the subject says yes, the technician or ECP asks "What specifically are you noticing?" The subject is not shown the list of options/descriptions. From the subject's response, the technician or ECP selects the most appropriate symptom and asks the subject to rate it on the following scale:
    a. 0 – No Symptoms
    b. 1 – Slight symptom; just feel or notice symptom occasionally
    c. 2 – Mild symptom; noticeable but not irritating or limiting use
    d. 3 – Moderate symptom; is irritating or annoying, use of device being limited by <25% (short wear time, etc.)
    e. 4 – Severe; very irritating or annoying, lens cannot be tolerated

Data Table:

"Are you experiencing any symptom or problems with these lenses?"

OD: Y N OS: Y N

OD	Symptom	OS
0-4	Discomfort	0-4
0-4	Excessive tearing	0-4
0-4	Photophobia	0-4
0-4	Halos	0-4
0-4	Itching/Burning	0-4
0-4	Spectacle blur	0-4
0-4	Variable vision	0-4
0-4	Blurred vision	0-4
0-4	Lens needs cleaning	0-4
0-4	Handling	0-4

6.0 Subjective Assessment Scales

Subjects should be provided the Rating Scales (separate document) to refer to while responding to the assessments being collected. Enter rating from 0-100 (eg, 90).

At Screening/Dispensing only, the following abbreviated assessments are to be collected for Study Lenses/Study Drops:

For all Follow-up visits, the following assessments are to be collected for Study Lenses/Study Drops:

APPENDIX C: CORNEAL INFILTRATES EVALUATION FORM

Infiltrate Size (Largest): OD: _____(X.X mm) OS: _____(X.X mm)

Infiltrate Depth (Deepest):

OD: _____ OS: _____

1. Epithelial
2. Anterior Stroma
3. Full thickness

Infiltrate Density:

OD: _____ OS: _____

Grade	Description
0	None
1	Faint
2	Moderate (iris/lens details clear)
3	Marked (iris/lens details hazy)
4	Intense (iris/lens details obscured)

Infiltrate Type:

OD: _____ OS: _____

Grades

0 None
1 Micropunctate
2 Macropunctate
3 Coalesced Macropunctate
4 Patch

Ocular Discharge:

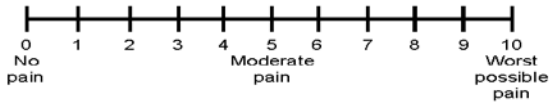
OD: _____ OS: _____

1. None
2. Mucopurulent (green or yellow in color)
3. Whitish
4. Watery

Degree of Pain:

OD: _____ OS: _____

0–10 Numeric Pain Rating Scale



Size of any overlying defect:

OD: _____(X.X mm) OS: _____(X.X mm)

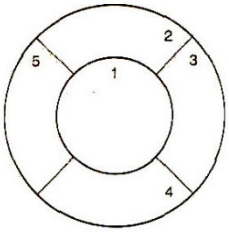
Location:

Check all that apply

OD:

- ☐ Central (central 6 mm, 3 mm from corneal center)
- ☐ Nasal
- ☐ Inferior
- ☐ Temporal
- ☐ Superior

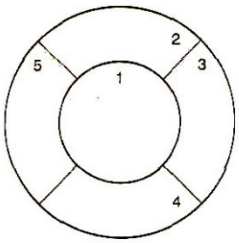
Draw:



OS:

- ☐ Central (central 6 mm, 3 mm from corneal center)
- ☐ Nasal
- ☐ Inferior
- ☐ Temporal
- ☐ Superior

Draw:



APPENDIX D: CULTURE PROCEDURE

NOTE: The site must use their standard of care culture kit and ship specimens to their local laboratory for testing per the local lab's required procedures. Hard copy results must be filed in the subject record and entered into the eCRF.

PROCEDURES FOR THE INVESTIGATOR

A. In the case of corneal ulcer or suspected ocular infection, the cul-de-sac, lower lid margin, and the corneal lesion (if applicable) of the affected eye must be cultured.

1. **Cul-de-sac Culture**
   a. The swab from a culture collection kit is moistened in sterile, physiological saline solution, with no preservatives.
   b. The ocular specimen is obtained by holding the lids open and asking the subject to gaze upward. The moistened swab should be drawn across the cul-de-sac while rotating the swab 360 degrees around the axis of the stick. Care should be taken to avoid contact of the swab with the lashes and the lid margins.
   c. Place the swab in the transport tube media according to manufacturer's directions.
   d. Repeat steps a through c using a separate swab and a separate tube of transport media for the other eye if both eyes require culturing.
2. **Eyelid Culture**
   a. The swab from a culture collection kit is moistened in sterile, physiological saline solution, with no preservatives.
   b. The specimen is obtained from the margin of the lower lid by drawing the swab along the margin of the lid.
   c. Place the swab in the transport tube media according to manufacturer's directions.
   d. Repeat steps a through c using a separate swab and a separate tube of transport media for the other eye if both eyes require culturing.
3. **Corneal Culture**
   a. The swab from a culture collection kit is moistened in sterile, physiological saline solution, with no preservatives.
   b. The specimen is obtained from the corneal lesion by rotating the swab on the lesion for 10 seconds.
   c. Place the swab in the transport tube media according to manufacturer's directions.
   d. Repeat steps a through c using a separate swab and a separate tube of transport media for the other eye if both eyes require culturing.

B. Labeling and Transportation of Cultures to the Clinical Laboratory:

1. Complete the report form supplied by the central laboratory included with the culture collection kit. Affix labels supplied in the culture collection kit to the ocular specimens as well as to the container used to transport the contact lens case (which contains the contact lens[es] and contact lens case solution) if available.
2. The specimens, contact lens(es), lens case(s), lens case solution(s) and report form are then sent to the central laboratory under refrigerated conditions using the supplies provided by the central laboratory.

APPENDIX E: SUBJECT INSTRUCTIONS – SOFT CONTACT LENSES

Rewetting Drop Subject Instructions

PLEASE READ INSTRUCTIONS CAREFULLY AND KEEP FOR FUTURE USE

You will be participating in a study evaluating the safety and effectiveness of an Investigational Lubricating and Rewetting Drop compared to a marketed rewetting drop. Please keep all appointments and **follow these instructions thoroughly**. If you have any questions or problems, consult your study doctor.

NOTE**:** *It is important to wear your study lenses to each of your follow-up visits and place 1 to 2 drops of rewetting solution in each eye about 30 to 60 minutes before each scheduled study visit.*

STUDY PRODUCT INFORMATION:

For this study, you will be using the following products:

- **Study Rewetting Drops**
  - You will receive 1 carton that will contain either 6 multi-dose bottles or 56 pouches of 5 single-use dispensers.
- **Study Contact Lenses**
  - You will be provided with 2 new pairs of your current contact lenses at the start of the study. One pair will be used as back-up, only if needed.
- **Other Study Supplies.** The following supplies will be provided to you as needed:
  - **One 10 FL OZ bottle of Biotrue multi-purpose solution.**
  - **Study Lens Cases.** You are required to use only the lens cases provided during the study. You will be provided three lens cases, one to store your lenses for disinfection after wear and two for lens replacements if needed.
  - **Zippered Bag.** To hold empty multi-dose rewetting drop bottles or opened single-use dispensers.
  - **Subject Instructions.** A copy of this sheet to be included.
- **Carton/Bottle/Single-Use Dispenser Return Materials.** Opaque, drawstring bag to place all study materials into, including Study Kit (carton) with unused study rewetting drops, zippered bag for returning partially full, and empty multi-dose drop bottles or opened single-use dispensers along with all worn and unworn lenses.

SUBJECT INSTRUCTIONS (continued, page 2 of 4)

IMPORTANT SUBJECT INSTRUCTIONS:

This is a "masked" clinical study in which the Investigators and Coordinators cannot see the Study Drops that are dispensed to you. There will be a special study employee – the "unmasked designee" – at the site who will dispense all study materials to you in a white drawstring bag and who will handle any questions you have related to the study materials.

It is very important that you keep your study drops in the opaque white bag when coming to the study visits.

GENERAL INFORMATION:

- Do NOT use any products other than those listed above or dispensed to you by your study doctor for use in this study.
- Do NOT use any other care products other than those listed above.
- Do not use any topical ocular medications (eye drops) during this study.
- Do NOT discuss or show the dispensed study products or these Subject Instructions to the study doctor or site staff other than the "unmasked designee" during the study.
- Save **ALL** study materials (drops and lenses) during the course of the study in the subject opaque drawstring take-home bag. Bring all opened and unopened study materials (drops and lenses) to the 1-month follow-up/exit visit. Place the multi-dose bottles or single-use dispensers, lens cases, and worn and unworn lenses into the white drawstring bag provided.
- Always wash and rinse your hands before you handle your lenses.
- Always handle the same lens (right or left) first, to avoid mix-ups.
- Always keep the products tightly closed when not in use.
- Lenses must be thoroughly cleaned, rinsed, and soaked using **Biotrue multi-purpose solution** each time they are removed to achieve disinfection. **See the Package Insert printed on the inside of the Biotrue multipurpose solution carton for important safety information.**
- Rinse each case well with the **Biotrue multi-purpose solution** before and after each use.

PRECAUTIONS:

- Lens care procedures recommended by your study doctor must be followed.
- Failure to follow these procedures may result in the development of serious eye infections.
- Discard the **Biotrue multi-purpose solution** from the lens case after each use.
- Store **Study Drops and Biotrue multi-purpose solution** at room temperature.

SUBJECT INSTRUCTIONS (continued, page 3 of 4)

- Use **Biotrue multi-purpose solution** before the expiration date marked on the bottle label and carton.
- Do not use any eye medication in conjunction with the **Study Drops** and **Biotrue multi-purpose solution** unless under medical supervision.
- Do not touch the tip of the **Study Drops** or **Biotrue multi-purpose solution** to any surface or to your eye since this may contaminate the study solutions.
- Keep the **Study Drops** and **Biotrue multi-purpose solution** cap closed when not in use to avoid contamination or evaporation.
- Do not use **Biotrue multi-purpose solution** with a heat disinfection method.
- Keep **Study Drops** and **Biotrue multi-purpose solution** out of reach of children.
- Consult with your study doctor if you have any allergies that may affect your ability to use the **Study Drops** or **Biotrue multi-purpose solution**.

IMPORTANT:

- If irritation or excessive tearing occurs, persists or increases, or if vision is impaired, discontinue use and promptly consult your study doctor.

REWETTING DROP USAGE:

Place study rewetting drops in each eye at least 4 times every day that lenses are worn during the one month you are in this study:

- During wear, place 1 to 2 study rewetting drops in the eye and blink. To avoid contamination, do not touch tip of container to any surface.
- As required by this study, always place drops in the eye 30 to 60 minutes before removing the lenses each day.
- If you have multi-dose bottles, replace the cap on the bottle after each treatment. Begin with "Bottle 1". When "Bottle 1" is empty place in zippered bag to return at exit visit. Open "Bottle 2" and continue to use until empty and place in zippered bag to return at exit visit. Continue to open the next sequential bottle when the last bottle opened becomes empty. Always keep products tightly closed when not in use. All bottles, used and unused will need to be returned at your exit visit.
- If you have single-use dispenser, to open, completely twist off tab and use one dispenser to treat both lenses at each treatment interval. Do not use the dispenser again after treatment even though there may be remaining drops in the dispenser. Place the used dispenser in the zipper bag to return at end of study. All single-use dispensers, used and unused will need to be returned at your exit visit.

Remember: It's important to wear your study lenses to each of your follow-up visits and place 1 to 2 drops of rewetting solution in each eye about 30-60 minutes before each scheduled study visit.

SUBJECT INSTRUCTIONS (Page 4 of 4)

LENS CLEANING INSTRUCTIONS:

See the Package Insert printed on the inside of the Biotrue multipurpose solution carton for important safety information.

When used as directed, **Biotrue multi-purpose solution**: Conditions, Cleans, Removes Protein, Disinfects, Rinses and Stores.

Directions: To condition, clean, remove protein and disinfect lenses, complete these simple steps. This daily regimen is recommended by Bausch + Lomb for a healthy and comfortable contact lens wearing experience:

STEP 1: Place at least 3 drops of **Biotrue multi-purpose solution** on each side of lens surface and gently rub for 20 seconds.

STEP 2: Thoroughly rinse each side of the lens for 5 seconds with **Biotrue multi-purpose solution**.

STEP 3: Place cleaned contact lenses in the lens case and fill with fresh **Biotrue multi-purpose solution**. Soak at least 4 hours. Remember to always use fresh solution – discard solution from lens case after each use.

Your lenses are now ready to wear. If any debris remains on contact lenses, rinse with **Biotrue multi-purpose solution** prior to insertion.

Always follow your study doctor's instructions.

If not wearing contact lenses immediately, store them in a closed lens case. Do not store your lenses in simple saline in place of **Biotrue multi-purpose solution**. **Saline solution and study rewetting drops will not disinfect.**

CARE OF THE STUDY LENS STORAGE CASE:

Clean, rinse and air-dry your lens case each time you remove your lenses. In order to permit excess solution to drain, you can flip over your lens case while air drying.

- For visits to the office other than the 1-month follow-up/exit visit, you do not need to bring the lens case to the office.
- If there is a reason to bring any material provided to you for this study to the office, PLACE THEM IN THE WHITE OPAQUE BAG FOR TRANSFER TO THE OFFICE.

APPENDIX F: SUBJECT INSTRUCTIONS – RIGID CONTACT LENSES

Rewetting Drop Subject Instructions

PLEASE READ INSTRUCTIONS CAREFULLY AND KEEP FOR FUTURE USE

You will be participating in a study evaluating the safety and effectiveness of an Investigational Lubricating and Rewetting Drop compared to a marketed rewetting drop. Please keep all appointments and **follow these instructions thoroughly**. If you have any questions or problems, consult your study doctor.

NOTE**:** *It is important to wear your study lenses to each of your follow-up visits and place 1 to 2 drops of rewetting solution in each eye about 30 to 60 minutes before each scheduled study visit.*

STUDY PRODUCT INFORMATION:

For this study, you will be using the following products:

- **Study Rewetting Drops**
  - You will receive 1 carton that will contain either 6 multi-dose bottles or 56 pouches of 5 single-use dispensers.
- **Study Contact Lenses**
  - You will be provided with 2 new pairs of your current contact lenses at the start of the study. One pair will be used as back-up, only if needed.
- **Other Study Supplies.** The following supplies will be provided to you as needed:
  - **Three 3.5 FL OZ bottles of Boston SIMPLUS Multi-Action Solution.**
  - **Study Lens Cases.** You are required to use only the lens cases provided during this study. You will be provided 3 lens cases, one to store your lenses for disinfection after wear and two for lens replacements if needed.
  - **Zippered Bag.** To hold empty multi-dose rewetting drop bottles or opened single-use dispensers.
  - **Subject Instructions.** A copy of this sheet to be included.

- **Carton/Bottle/Single-Use Dispenser Return Materials.** Opaque, drawstring bag to place all study materials into, including Study Kit (carton) with unused study rewetting drops, zippered bag that contains partially full, and empty study rewetting drop bottles or opened single-use dispensers along with all worn and unworn lenses.

SUBJECT INSTRUCTIONS (continued, page 2 of 4)

IMPORTANT SUBJECT INSTRUCTIONS:

This is a "masked" clinical study in which the Investigators and Coordinators cannot see the Study Drops that are dispensed to you. There will be a special study employee – the "unmasked designee" – at the site who will dispense all study materials to you in a white drawstring bag and who will handle any questions you have related to the study materials.

It is very important that you keep your study drops in the white bag when coming to the study visits.

GENERAL INFORMATION:

- Do NOT use any products other than those listed above or dispensed to you by your study doctor for use in this study.
- Do NOT use any other care products other than those listed above.
- Do not use any topical ocular medications (eye drops) during this study.
- Do NOT discuss or show the dispensed study products or these Subject Instructions to the Study doctor or site staff other than the "unmasked designee" during the study.
- Save **ALL** study materials (drops and lenses) during the course of the study in the subject opaque drawstring take-home bag. Bring all opened and unopened study materials (drops and lenses) to the 1-month follow-up/exit visit. Place the multi-dose bottles or single-use dispensers, lens cases, and unworn lenses into the opaque drawstring bag provided.
- Always wash and rinse your hands before you handle your lenses.
- Always handle the same lens (right or left) first, to avoid mix-ups.
- Always keep the products tightly closed when not in use.
- Lenses must be thoroughly soaked, cleaned, and rinsed using **Boston SIMPLUS Multi-Action Solution** each time they are removed to achieve disinfection. **See the Package Insert printed on the inside of the Boston SIMPLUS Multi-Action Solution carton for important safety information.**
- Before first and after each use, always empty and rinse the lens case with the **Boston SIMPLUS Multi-Action Solution** and allow to air dry.

PRECAUTIONS:

- Lens care procedures recommended by your study doctor must be followed.
- Failure to follow these procedures may result in the development of serious eye infections.
- Discard the **Boston SIMPLUS** M**ulti-Action Solution** from the lens case after each use.
- Store **Study Drops** and **Boston SIMPLUS Multi-Action Solution** at room temperature.
- Use **Boston SIMPLUS** M**ulti-Action Solution** before the expiration date marked on the bottle label and carton.
- Do not use any eye medication in conjunction with the **Study Drops** and **Boston SIMPLUS Multi-Action Solution** unless under medical supervision.

SUBJECT INSTRUCTIONS (continued, page 3 of 4)

- Do not touch the tip of the **Study Drops** or **Boston SIMPLUS Multi-Action Solution** to any surface or to your eye since this may contaminate the study solutions.
- Keep the **Study Drops** and **Boston SIMPLUS Multi-Action Solution** cap closed when not in use to avoid contamination or evaporation.
- Keep **Study Drops** and **Boston SIMPLUS Multi-Action Solution** out of reach of children.
- Consult with your study doctor if you have any allergies that may affect your ability to use the **Study Drops** or **Boston SIMPLUS Multi-Action Solution**.

IMPORTANT:

- If irritation or excessive tearing occurs, persists or increases, or if vision is impaired, discontinue use and promptly consult your study doctor.

REWETTING DROP USAGE:

Place study rewetting drops in each eye at least 4 times every day that lenses are worn during the one month you are in this study:

- During wear, place 1 to 2 study rewetting drops in the eye and blink. To avoid contamination, do not touch tip of container to any surface.
- As required by this study, always place drops in the eye 30 to 60 minutes before removing the lenses each day.
- If you have multi-dose bottles, replace the cap on the bottle. Always keep products tightly closed when not in use.
- If you have single-use dispenser, to open, completely twist off tab and use one dispenser at each treatment interval to treat both lenses. Do not use the dispenser again after treatment even though there may be remaining drops in the dispenser. Place the used dispenser in the zippered bag to return at end of study. All single-use dispensers, used and unused will need to be returned at your exit visit.

Remember: It's important to wear your study lenses to each of your follow-up visits and place 1 to 2 drops of rewetting solution in each eye about 30-60 minutes before each scheduled study visit.

SUBJECT INSTRUCTIONS (Page 4 of 4)

LENS CLEANING INSTRUCTIONS:

See the Package Insert printed on the inside of the Boston SIMPLUS Multi-Action Solution carton for important safety information.

To ensure proper disinfecting, all steps listed below must be followed:

1. Wash your hands with mild soap. (Caution - pump soaps may contain oil-based suspension agents.)
2. Place lenses in empty lens case and fill with fresh **Boston SIMPLUS Multi-Action Solution**. **Soak lenses for at least 4 hours (or overnight) before wearing.**
3. Wash hands with mild soap before cleaning (rubbing) lenses. After soaking, remove lenses from lens case and rub both sides of the lenses carefully with 4 drops of **Boston SIMPLUS Multi-Action Solution** in the palm of your hand for 20 seconds. **NO SEPARATE DAILY CLEANER IS REQUIRED.**
4. Rinse for approximately 5 seconds with a steady stream of **Boston SIMPLUS Multi-Action Solution** to eliminate loosened surface deposits and insert lenses.
5. Discard solution from lens case after each use.

Always follow your study doctor's instructions.

If not wearing contact lenses immediately, store them in a closed lens case. Do not store your lenses in simple saline in place of **Boston SIMPLUS Multi-Action Solution**. **Never use water, saline solution or study rewetting drops to disinfect your lenses. These solutions will not disinfect your lenses.**

You should not expose or store your lenses in or rinse your lens case with any water, such as tap, distilled, or with any non-sterile solution.

CARE OF THE STUDY LENS STORAGE CASE:

Clean contact lens cases with digital rubbing with fresh Boston SIMPLUS Multi-Action Solution. Never use water. Cleaning should be followed by rinsing with fresh Boston SIMPLUS Multi-Action Solution (never use water) and wiping the lens cases with a fresh, clean tissue is recommended. Air-drying or recapping the lens case lids after use without any additional cleaning methods should be avoided. If air drying, be sure that no residual solution remains in the case before allowing it to air dry.

- For visits to the office other than the 1-month follow up/exit visit, you do not need to bring the lens case to the office.
- If there is a reason to bring the lens case to the office, PLACE THE LENS CASE IN THE WHITE OPAQUE BAG FOR TRANSFER TO THE OFFICE.

NOTE: *For care of lens storage case please follow the above instructions for care of your lens storage case instead of the instructions printed on the Boston SIMPLUS Multi-Action Solution bottle and carton.*