BAUSCH + LOMB

A Safety and Effectiveness Study of a Contact Lens Cleaning and Disinfecting Solution

CLINICAL STUDY PROTOCOL

STUDY # 914

Sponsor: Bausch & Lomb Incorporated

This clinical investigation is being conducted in accordance with 21 CFR Parts 11, 50, 54, 56 and 812; 42 CFR Part 11 – Clinical Trials Registration and Results Information Submission; EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good clinical practice*; Medical Device Regulation (MDR) 2017/745; International Council for Harmonization (ICH) Good Clinical Practice; the Declaration of Helsinki and applicable local regulations. Additional information on the investigational test article(s) is presented in the BL-3100-NBR03 Multi-Purpose Solution Investigator's Brochure[1].

Revision Chronology:

(Original) 19 JAN 2023

Key design elements of this protocol will be registered on www.clinicaltrials.gov as required by current regulations and, if applicable, other public databases as required by local country regulations. In addition, results of this study will be made publicly available on www.clinicaltrials.gov regardless of outcome as required by current regulations and, if applicable, in other public databases as required by local country regulations. The identity of the subjects who participated in the study will be maintained confidential.

Sponsor Review and Approvals:

Name and Address of Manufacturer of Investigational Test Article(s):

Bausch & Lomb Incorporated
1400 North Goodman Street
Rochester, NY 14609 USA

Attestation from Manufacturer Representative:

I attest that the investigational test article(s) for this study are manufactured and verified under a controlled process according to the applicable regulations. With regard to those aspects, every precaution has been taken to protect the health and safety of study participants.

INVESTIGATOR STATEMENT OF APPROVAL

A Safety and Effectiveness Study of a Contact Lens Cleaning and Disinfecting Solution

STUDY # 914

I have read this clinical study protocol and 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 21 CFR Parts 11, 50, 54, 56 and 812; 42 CFR Part 11 – Clinical Trials Registration and Results Information Submission; EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good clinical practice*; Medical Device Regulation (MDR) 2017/745; International Council for Harmonization (ICH) Good Clinical Practice; the Declaration of Helsinki and applicable local regulations.

I will not initiate the study until I have obtained written approval by the appropriate IRB/EC and have complied with all financial and administrative requirements of the governing body of the clinical institution and the Sponsor. I agree to obtain written informed consent from each study subject prior to performing any study specific procedures.

I understand my obligation as the Principal Investigator to supervise all testing of the investigational products used in this study involving human subjects and to ensure that the investigational product is dispensed as per protocol.

I understand my obligation as the Principal Investigator to ensure that all study personnel assisting in the conduct of the study are qualified and are properly trained to conduct their assigned tasks and obligations during the entire course of the trial. I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.

I testify that I have never been disqualified as an Investigator by any Regulatory Authority, and have never been involved in a study or other research that was terminated due to misconduct or fraudulent activity.

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 signature on electronic case report forms 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 IRB/ECs, direct access to my medical records for study subjects.

_____

Principal Investigator, Printed Name

_____ _____

Principal Investigator, Signature Date

Address of Principal Investigator

_____

_____

PERSONNEL RESPONSIBLE FOR CONDUCTING THE STUDY

Function	Organization
Study Sponsor: protocol, investigational product supply and distribution, safety monitoring and reporting to FDA, study oversight, regulatory, and auditing	Bausch & Lomb Incorporated 1400 North Goodman Street Rochester, NY 14609 USA Main telephone number: 585-338-5306
Manufacturer of Investigational Test Article(s)	Bausch & Lomb Incorporated 1400 North Goodman Street Rochester, NY 14609 USA Main telephone number: 585-338-5306
Statistical Analysis	EMB Statistical Solutions, LLC 55 Corporate Woods 9300 West 110th Street, Suite 550 Overland, KS 66210 USA Main telephone number: 913-322-6555
Medical Writing	[redacted]
Medical Monitor	[redacted]
Electronic Data Capture (EDC), Randomization and Trial Supply Management (RTSM) System	Oracle Corporation 77 Fourth Avenue Waltham, MA 02457 Main telephone number: 781-890-7878
Clinical Study Management, Monitoring, Data management, and Safety Monitoring	MedTrials, Incorporated 2626 Cole Ave Dallas, Texas 75204 USA Main phone number: 214-630-0288
Investigative Clinical Sites	An up-to-date Protocol 914 Investigator Contact List[2] of Investigators, investigative sites, involved with this clinical investigation will be maintained by the Sponsor in a separate document.

SYNOPSIS

Name of Sponsor/ Company:
Bausch & Lomb Incorporated

Study #914

Name of Investigational Product:
- **Test:** BL-3100-NBR03 multi-purpose solution
- **Control:** renu® Advanced Formula multi-purpose solution

Title of Study:
A Safety and Effectiveness Study of a Contact Lens Cleaning and Disinfecting Solution

Number of Clinical Centers:
Approximately 22 investigative sites, United States

Objective:
The objective of this study is to evaluate the safety and effectiveness of BL-3100-NBR03 multi-purpose solution (Test) compared to renu® Advanced Formula multi-purpose solution (Control) when used by habitual contact lens wearers to clean and disinfect their contact lenses for approximately three months.

Intended Purpose:
BL-3100-NBR03 Multi-Purpose Solution is intended for use in cleaning, disinfecting, removing proteins, conditioning and storing all soft contact lenses, including silicone hydrogels.

Target Population:
BL-3100-NBR03 Multi-Purpose Solution is intended for users who wear soft (hydrophilic) contact lenses which require daily conditioning, cleaning, chemical (not heat) disinfection and storage of soft contact lenses, regardless of gender, age, or ethnicity, and who do not have contraindications for the device.

Methodology:
- Approximately 340 subjects (680 eyes) will be enrolled in this three-month, two-arm, 1:1 randomized, parallel-group, bilateral, double-masked study at approximately 22 investigative sites in the United States.
- Subjects will be required to wear dispensed study lenses on a daily wear basis for three months with scheduled in-office replacement of study lenses at the 1-Month and 2-Month Follow-Up Visits.

Number of Subjects Planned:
Approximately 340 subjects (680 eyes), with at least 300 subjects expected to complete the study

Diagnosis and Main Criteria for Inclusion:
- 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
- Is a habitual wearer (at least 3 months) of one of the following lens types:

Lens Group	Lens Material	Trade Name	Manufacturer
4	Etafilcon A	Acuvue2	Vistakon
5-A	Balafilcon A	PureVision2	Bausch + Lomb
5-C	Samfilcon A	Ultra	Bausch + Lomb
5-Cm	Lotrafilcon B	Air Optix Aqua	Alcon
5-Cr	Senofilcon A	Vita	Vistakon

- Has typically cleaned and disinfected their pre-study contact lenses daily
- Is a habitual user of lens care products for cleaning, disinfecting, and storage of lenses.
- Requires lens correction in both eyes
- Must have spectacle correctable distance visual acuity through spherocylindrical refraction to 40 letters [0.14 logarithm of the minimal angle of resolution (logMAR)] or better in each eye at 2 meters distance using a high contrast chart
- Wears the same brand of contact lenses in both eyes
- Agrees to wear study lenses on a daily wear basis for approximately three months

- Is willing and able to comply with all treatment and follow-up study procedures

Exclusion Criteria:

- Is currently using a hydrogen-peroxide cleaning and disinfecting solution
- Participated in any drug or device clinical investigation within 30 days prior to entry into this study
- Is a female 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
- Has worn gas permeable (GP) lenses within the last 30 days
- Has worn polymethylmethacrylate (PMMA) lenses within the last three months
- Has typically worn their pre-study contact lenses on an extended wear basis, sleeping in their lenses one night or more per week, during the last year
- 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
- Subjects with an active ocular disease or who are using any ocular medication
- Is using any medications that will, in the Investigator's opinion, affect ocular physiology or lens performance
- Currently wears monovision, multifocal, or toric contact lenses
- Has ocular astigmatism of 1.00 D or greater in either eye
- Has anisometropia (spherical equivalent) of greater than 2.00 D
- Has any grade 2 or greater finding during the slit-lamp examination (refer to Appendix B for Methods of Clinical Evaluation)
- Has corneal infiltrates of ANY GRADE
- Has any "Present" ungraded finding during the slit-lamp examination (refer to Appendix B for Methods of Clinical Evaluation) that, in the Investigator's judgment, interferes with contact lens wear
- Has any scar or neovascularization within the central 6 mm of the cornea, irregular cornea or a history of herpetic keratitis
  - ◊ *Note that subjects with minor peripheral corneal scarring (that does not extend into the 6 mm central area), that, in the Investigator's judgment, does not interfere with contact lens wear, are eligible for this study.*
- Is aphakic
- Is amblyopic
- Has had any corneal surgery (e.g., refractive surgery)
- Is allergic to any component in the study care products
- Is an employee of any of the study investigative sites or a family member of an employee of the investigative site, including family members living outside of the employee's household
- Is an Ophthalmologist, an Optometrist, an Optician, or an Ophthalmic Assistant/Technician, or currently resides with a person with any of these specialties

Is an employee of a manufacturer of contact lenses or contact lens care products (e.g., Alcon, Bausch + Lomb, Ciba Vision, CooperVision, Vistakon, Johnson & Johnson, etc.) or currently resides with a person employed by any of these manufacturers.

Investigational Product, Dosage and Mode of Administration:

- The Investigator or designee will instruct all subjects that they must comply with the instructions provided to them. Subject Instructions (Instructions for Use) will be included with each carton of study solution.
- In order to ensure that the Investigator and site staff remain masked to the study lens, an unmasked designee at each site will be responsible for all study materials accountability, including dispensation and collection of study supplies to subjects.
- Subjects are to be instructed not to discuss or show the dispensed study lenses to the Investigator or masked site staff during the study.
- Subjects will be instructed that other contact lenses (other than the assigned study lenses) and contact lens care products (other than any eye drops provided) are not allowed to be used during the study.

Study Duration of Treatment:
Approximately 3 months

Criteria for Evaluation:
The primary endpoints are as follows:

- **Effectiveness:**
  - Overall comfort averaged over all scheduled follow-up visits
  - Vision averaged over all scheduled follow-up visits
  - The proportion of eyes with a maximum degree of front surface deposits grade of ≤ 2 over all scheduled follow-up visits
- **Safety:**
  - The proportion of eyes with any slit-lamp findings greater than Grade 2 over all follow-up visits

Statistical Methods:

- Continuous variables will be summarized using the sample size, mean, standard deviations, 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 0.025. For overall comfort and dryness, each non-inferiority hypothesis will be tested using an analysis of variance model including the fixed factors of treatment, site, and lens group with a non-inferiority margin of -5 points. For front surface deposits, the non-inferiority hypothesis will be tested using a one-sided Newcombe-Wilson 97.5% lower confidence limit with a non-inferiority margin of -10%. For slit-lamp findings, the non-inferiority hypothesis will be tested using a one-sided Newcombe-Wilson 97.5% upper confidence limit with a non-inferiority margin of 5%.

Sample Size Calculations:
Approximately 30 Test group subjects will be completed for each lens group in the table of lens types above. For each lens type, the probability of observing at least one subject-level event will be 0.95 when the probability of an event is 0.1. When the sample size is 150 subjects in each treatment group, the overall power of the trial will be 95%. To allow for losses of up to 10%, approximately 340 subjects (680 eyes) will be enrolled.

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APPENDICES

GLOSSARY OF TERMS

Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device. Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
Adverse Event (AE)	Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. Note 1: This definition includes events related to the investigational medical device. Note 2: This definition includes events related to the procedures involved. Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices.
Anticipated Serious Adverse Device Effect (ASADE)	Anticipated serious adverse device effect is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. Note 2: This definition includes device deficiencies related to the investigational medical device.
Investigational Medical Device	A medical device being assessed for clinical performance, effectiveness, or safety in a clinical investigation Note 1: This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes. Note 2: This includes medical devices already on the market that are being evaluated within their intended use in a post-market clinical investigation (interventional or non-interventional). Note 3: The terms “investigational medical device” and “investigational device” are used interchangeably.
Life-threatening Adverse Event	An adverse event is considered “life-threatening” if, in the view of either the Investigator or Sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Medical Device	An instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific purpose(s) of: • diagnosis, prevention, monitoring, treatment or alleviation of disease; • diagnosis, monitoring, treatment, alleviation of or compensation for an injury; • investigation, replacement, modification, or support of the anatomy or of a physiological process; • supporting or sustaining life; • control of conception; • disinfection of medical devices; • providing information by means of in vitro examination of specimens derived from the human body; and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.
Malfunction	Failure of a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Product Complaints	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Serious Adverse Event (SAE)	An adverse event that led to any of the following outcomes:
	• death
	• serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
	  ○ a life-threatening illness or injury, or
	  ○ a permanent impairment of a body structure or a body function including chronic diseases, or
	  ○ in-patient 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,
	• fetal distress, fetal death, a congenital abnormality, or birth

	defect including physical or mental impairment.
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. Note 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Treatment-Emergent Adverse Event (TEAE)	A treatment-emergent adverse event is defined as any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments.
Unanticipated Adverse Device Effect (UADE)	Unanticipated adverse device effect is an adverse event caused by or related to use a medical device not previously identified in nature, severity, or degree of incidence in the current risk assessment, or any other unanticipated problem associated with a device that relates to the rights, safety, or welfare of subjects.
Unanticipated Serious Adverse Device Effect (USADE)	Unanticipated adverse device effect is a serious adverse event caused by or related to use of a medical device not previously identified in nature, severity, or degree of incidence in the current risk assessment, or any unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
Use Error	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. Note 1: Use errors includes slips, lapses and mistakes. Use error includes the inability of the user to complete a task. Note 2: Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment. Note 3: Users might be aware or unaware that a use error has occurred. Note 4: An unexpected physiological response of the patient is not by itself considered a use error. Note 5: A malfunction of a medical device that causes an unexpected result is not considered a use error.

LIST OF ACRONYMS AND ABBREVIATIONS

Abbreviation /Acronym	Term
ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CIP	Clinical Investigation Plan
CRO	Contract Research Organization
D	Diopter
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	United States Food and Drug Administration
GCP	Good Clinical Practice
GP	Gas Permeable
H_0	Null Hypothesis
H_1	Alternative Hypothesis
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	The International Council for Harmonisation
IRB	Institutional Review Board
ISO	International Standards Organization
ITT	Intent-to-Treat
logMAR	Logarithm of the Minimum Angle of Resolution
MDR	Medical Device Regulation
MedDRA	Medical Dictionary for Regulatory Activities
mm	Millimeter
OD	Right Eye
RTSM	Randomization and Trial Supply Management
OS	Left Eye
PP	Per Protocol
PMMA	Polymethylmethacrylate
SAE	Serious Adverse Event
SD	Standard Deviation
TEAE	Treatment-Emergent Adverse Event
USADE	Unanticipated Serious Adverse Device Effect
US	United States
VA	Visual Acuity

1.0 INTRODUCTION

Bausch & Lomb Incorporated ("Bausch + Lomb") is evaluating an investigational cleaning and disinfecting solution, BL-3100-NBR03 multi-purpose solution, for use with soft contact lenses. The aim of this study is to evaluate the safety and effectiveness of the investigational BL-3100-NBR03 multi-purpose solution when compared to a currently marketed multi-purpose solution.

The BL-3100-NBR03 multi-purpose solution contains known elements in the ophthalmic industry. The multi-purpose solution is preserved with [redacted] The solution is designed to clean, disinfect, remove proteins, condition, store and rinse soft contact lenses for a comfortable and favorable wear experience.

2.0 BACKGROUND, RATIONALE AND OBJECTIVES

2.1 Intended Purpose of Device

BL-3100-NBR03 Multi-Purpose Solution is intended for use in cleaning, disinfecting, removing proteins, conditioning and storing all soft contact lenses, including silicone hydrogels.

2.2 Target Population

BL-3100-NBR03 Multi-Purpose Solution is intended for users who wear soft (hydrophilic) contact lenses which require daily conditioning, cleaning, chemical (not heat) disinfection and storage of soft contact lenses, regardless of gender, age, or ethnicity, and who do not have contraindications for the device.

2.3 State of the Art

The BL-3100-NBR03 Multi-Purpose Solution is a sterile [redacted] The formulation does not incorporate tissues of human or animal origin and does not incorporate medicinal substances, dangerous, or radioactive materials. The multi-purpose solution contains known elements in the ophthalmic industry and is safe for use.

Table 1 contains the Multi-Purpose Solution ingredients and their functions.

Table 1: BL-3100-NBR03 Multi-Purpose Solution Ingredients

Ingredient	Function
[redacted]	Surfactant
[redacted]	Surfactant
[redacted]	Buffer
[redacted]	Buffer
[redacted]	Buffer

Ingredient	Function
[redacted]	Chelant
[redacted]	Tonicity Agent
[redacted]	Tonicity Agent
[redacted]	Tonicity Agent
[redacted]	Disinfectant
[redacted]	Disinfectant
[redacted]	Aqueous Base

2.4 Objective of Study

The primary objective of this study is to evaluate the safety and effectiveness of BL-3100-NBR03 multi-purpose solution (Test) compared to renu® Advanced Formula multi-purpose solution (Control) when used by habitual soft contact lens wearers to clean and disinfect their contact lenses for approximately three months.

2.5 Study Rationale

The study is designed to meet the defined objectives: an evaluation of the safety and effectiveness of BL3100-NBR03 multi-purpose solution for use with soft contact lenses. The investigational lens care regimen was developed based on laboratory and pre-clinical evidence and a preliminary clinical evaluation. The BL3100-NBR03 multi-purpose solution is intended for individuals requiring indications which include daily conditioning, cleaning, chemical (not heat) disinfection and storage of soft contact lenses, regardless of gender, age or ethnicity, and who do not have contraindications to the device.

The clinical investigational plan requires enrollment of a sufficient number of study subjects, wearing a variety of soft lens materials to adequately represent the targeted population. The design is based on statistical considerations and meets regulatory requirements. The study duration, lens replacement schedule, contact lens wearing schedule and daily use of the investigational test articles is sufficient to detect any potential lens performance and safety issues. The safety and effectiveness endpoints have been selected based on clinical evidence and the Sponsor's long history of developing similar products. Because patients are prescribed soft contact lenses for the correction of refractive ametropia (including myopia, hyperopia, and astigmatism) and presbyopia, it is important that study subjects have a stable refractive state over the course of the study. The patient eligibility criteria was designed to help detect unintended changes to subject ocular health, ocular function and contact lenses caused by the investigational lens care solution and are not intended as contraindications.

2.6 Minimization of Bias and Confounding Factors

The Sponsor will avoid improper influence on any parties participating in, or contributing to, the clinical investigation or the induction thereof. The selection and treatment of subjects and evaluation of clinical investigation data are potential sources of bias. Methods that are incorporated within the clinical investigation design to minimize potential bias include, but are not limited to, screening subjects to confirm eligibility with defined inclusion/exclusion criteria prior to enrollment; maintaining a log of all subjects screened and enrolled; collecting demographics and medical history at baseline to later assess possible characteristics that may influence endpoints; standardizing data collection

requirements and clinical investigation procedures; requiring a Financial Disclosure by Investigators; using standardized training materials for all trial personnel; and by scheduling regular monitoring visits will be conducted to verify adherence to the CIP and source data.

This clinical investigation is double-masked. The Investigator and site staff, with the exception of an unmasked designee, will be masked (blinded) to the subject's treatment group. An unmasked designee will be assigned at each site and will be responsible for all study materials accountability, including dispensation to and collection of study supplies from subjects. Subjects are to be instructed not to discuss or show the dispensed study materials to the Investigator or masked site staff during the study. The Investigator and all other study personnel will remain masked until database lock. The subjects will be randomized (1:1) to receive either the Test or Control solution using a Randomization and Trial Supply Management (RTSM) system.

3.0 STUDY DESIGN

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

3.1 Description of Study Design

The study is designed to examine whether BL-3100-NBR03 multi-purpose solution cleaning and disinfecting solution is non-inferior to renu® Advanced Formula multi-purpose solution in several primary endpoints.

Approximately 340 subjects (680 eyes) will be enrolled in this three-month multicenter, randomized, double-masked, parallel-group, bilateral study at approximately 22 investigative sites in the United States (US). Approximately one-half (50%) of the eligible subjects will be randomized to receive Bausch + Lomb investigational BL-3100-NBR03 multi-purpose solution (Test), and approximately one-half (50%) of the eligible subjects will be randomized to receive renu® Advanced Formula multi-purpose solution (Control). In addition, all subjects will be dispensed three new pairs (including two back-up pairs) of their habitual lenses at the beginning of the study for daily wear, and scheduled replacement lenses at the 1-Month and 2-Month Follow-up Visits.

All subjects will be seen for a Screening/Dispensing Visit, at which the informed consent form (ICF), including the Health Insurance Portability Accountability Act (HIPAA), will be obtained and eligibility will be assessed. If eligible, subjects will be dispensed three new pairs of their habitual lenses and a Study Kit containing a cleaning and disinfecting solution according to the subject's randomly assigned treatment. Subjects may also be dispensed a supply of *Bausch + Lomb renu® Contact Lens Moisture Drops* to be used on an as needed basis. Subjects must NOT use ANY other cleaning and disinfecting solution or rewetting drops during the study.

Subjects are to wear their study lenses on a daily wear basis and are to use the Test or Control multi-purpose solution and care regimen after removing the lenses each day. Subjects will return their worn lenses to the unmasked designee at each monthly follow-up visit and will return their used and unused study solutions to the unmasked designee at the three-month follow-up visit (or early study termination/suspension visit) for return to the Sponsor.

Eligible subjects will be enrolled into one of five lens groups based on their habitual contact lenses. Subjects will be randomized to receive either the Test or Control multi-purpose

solution. The five lens groups will be comprised of habitual wearers of soft lenses based on lens material as indicated in the table below.

Table 2: Lens Groups

Lens Group	Lens Material	Trade Name	Manufacturer
4	Etafilcon A	Acuvue2	Vistakon
5-A	Balafilcon A	PureVision2	Bausch + Lomb
5-C	Samfilcon A	Ultra	Bausch + Lomb
5-Cm	Lotrafilcon B	Air Optix Aqua	Alcon
5-Cr	Senofilcon C	Vita	Vistakon

3.2 Informed Consent Process

Voluntary written informed consent must be obtained from every subject prior to the initiation of any study related activities. The Investigator must have a defined process for obtaining consent. Subjects must be given ample time to read, understand, and ask questions, in order to consider voluntary participation. The subject must indicate voluntary consent by providing a written signed and dated ICF. A copy of the signed and dated ICF must be provided to the subject, and the original document must be filed in the subject's study records.

The ICF must meet all applicable local laws and be written in language that the subject understands. Subjects must be informed that their participation in the study is voluntary and that their decision to withdraw from participation at any time during the study will not impact any aspect of their standard care. Subjects will be provided with contact information for the appropriate individuals should questions or concerns arise after signing the ICF during the clinical study.

Subjects must also be informed that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must ensure all procedures and practices are in place to protect the privacy and the best interest of the subject.

3.3 Selection of Study Population

Recruitment for the study may start at any point after the Investigator agrees, in writing, to participate in the study. Written ICF, including HIPAA, enrollment in the study, or dispensing of study products cannot begin until the Investigator has received Institutional Review Board (IRB) and Sponsor 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 or not they participate in the study. The Sponsor will record information for each potential study subject who signs an ICF. Once a potential subject is consented, their information will be recorded in the Randomization and Trial Supply Management (RTSM) system and the Investigator should proceed with screening procedures.

Potential subjects will be classified as eligible or "Screen Failures." A subject deemed a Screen Failure cannot participate in the study since he/she has not met the study inclusion criteria or has met the exclusion criteria. Electronic case report forms (eCRFs) must not be completed for subjects who are Screen Failures; however, the copy of their signed ICF and

any information collected as part of screening (e.g., source documents, etc.) must be kept in their medical records.

Once a subject is randomized to a treatment group, the individual 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 3.3.4 for subjects determined to be lost to follow-up.

3.3.1 Eligibility

3.3.1.1 Inclusion Criteria

To be considered for entry into the study, the candidate must meet *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 presented in Table 2
4. Has typically cleaned and disinfected their pre-study contact lenses daily
5. Must have spectacle correctable distance visual acuity through spherocylindrical refraction to 40 letters [0.14 logarithm of the minimal angle of resolution (logMAR)] or better in each eye at 2 meters distance using a high contrast chart
6. Has clear central corneas and is free of any anterior segment disorders
7. Is a habitual user of a lens care product for cleaning, disinfecting, and storage of lenses
8. Requires lens correction in both eyes
9. Wears the same brand of contact lens in both eyes
10. Agrees to wear study lenses on a daily wear basis for approximately three months
11. Is willing and able to comply with all treatment and follow-up study procedures.

3.3.1.2 Exclusion Criteria

The candidate is ineligible for entry into the study if they meet *any* of the following criteria:

1. Is currently using a hydrogen-peroxide cleaning and disinfecting solution
2. Participated in any drug or device clinical investigation within 30 days prior to entry into this study

3. Is a female 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. Has worn gas permeable (GP) lenses within the last 30 days
5. Has worn polymethylmethacrylate (PMMA) lenses within the last three months
6. Has typically worn their pre-study contact lenses on an extended wear basis, sleeping in their lenses one night or more per week, during the last year
7. 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
8. Subjects with an active ocular disease or who are using any ocular medication
9. Is using any medications that will, in the Investigator's opinion, affect ocular physiology or lens performance
10. Currently wears monovision, multifocal, or toric contact lenses
11. Has ocular astigmatism of 1.00 D or greater in either eye
12. Has anisometropia (spherical equivalent) of greater than 2.00 D
13. Has any grade 2 or greater finding during the slit-lamp examination (refer to Appendix B for Methods of Clinical Evaluation)
14. Has corneal infiltrates of ANY GRADE
15. Has any "Present" ungraded finding during the slit-lamp examination (refer to Appendix B for Methods of Clinical Evaluation) that, in the Investigator's judgment, interferes with contact lens wear
16. Has any scar or neovascularization within the central 6 mm of the cornea, irregular cornea or a history of herpetic keratitis
    - ◊ *Note that subjects with minor peripheral corneal scarring (that does not extend into the 6 mm central area), that, in the Investigator's judgment, does not interfere with contact lens wear, are eligible for this study.*
17. Is aphakic
18. Is amblyopic
19. Has had any corneal surgery (e.g., refractive surgery)
20. Is allergic to any component in the study care products
21. Is an employee of any of the study investigative sites or a family member of an employee of the investigative site, including family members living outside of the employee's household

22. Is an Ophthalmologist, an Optometrist, an Optician, or an Ophthalmic Assistant/Technician, or currently resides with a person with any of these specialties
23. Is an employee of a manufacturer of contact lenses or contact lens care products (e.g., Alcon, Bausch + Lomb, Ciba Vision, CooperVision, Vistakon, Johnson & Johnson, etc.) or currently resides with a person employed by any of these manufacturers.

If a subject meets all the inclusion criteria and does not meet any of the exclusion criteria, the subject is eligible for entry into the study. Ineligible subjects MUST NOT be enrolled in this study. Any subject enrolled in the study who later is found to have not met the eligibility criteria at entry will be discontinued.

3.3.2 Subject Completion

A subject has completed the study when the individual has completed the Exit Visit procedures at the 3-Month Follow-up Visit. Subjects who require further follow-up for an adverse event (AE) will be followed according to Sections 3.3.3. and 7.0.

3.3.3 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 AE occurring during the course of the study, which precludes continued treatment or follow-up
- Persistent grade 3 or 4 slit-lamp findings
- Persistent study related symptoms/complaints
- Unacceptable distance lens visual acuity (VA)
- Unacceptable lens centration
- Unacceptable lens movement
- Failure to follow study procedures

A subject MUST be discontinued prior to the final study visit 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
- Lost to follow-up (refer to Section 3.3.4)
- Either eye is discontinued
- Becomes pregnant during the study

Prior to discontinuing a subject, every effort should be made to contact the subject, schedule a final study visit, obtain as much follow-up data as possible, and to retrieve all study materials. Adverse events will be followed as described in Section 7.0.

Subject discontinuations must be documented clearly on the source document and applicable eCRF. The Investigator should indicate the PRIMARY (one) reason that the subject was discontinued for each eye. Subjects who voluntarily withdraw from the study are not required to provide a reason for their decision but should be encouraged to share

this information. Subjects that are discontinued from the study following randomization will not be replaced.

Exit Visit assessments should be completed for early discontinued subjects, if possible.

At the final study visit, all study subjects who are discontinuing should be examined to ensure that their ocular health is consistent with pre-study, baseline conditions. Any adverse effects determined to have been reasonably caused by participation in the study will be followed per the standard of care. Participation in the study will not impact post-study choices of study subjects for correcting their vision using marketed products (e.g., contact lenses and contact lens care solutions).

Whether a subject completes or is discontinued from the study, they will be directed by the Investigator to resume their habitual lens care regimen.

3.3.4 Lost to Follow-up

Subjects who did not return for scheduled follow-up visits, as defined by the visit window, and could not be contacted via two telephone calls and one letter with delivery confirmation, 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. If the Investigator determines that a subject has been lost to follow-up, the "study exit date" should be recorded as the last successful contact or the date a certified letter was sent. Just prior to database lock, the database will be reviewed for all lost to follow-up entries to confirm, once again, that contact with the subject was never made. A study participant may withdraw from the study at any time for any reason.

3.4 Investigators

The study will be conducted at approximately 22 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. This will include appropriate current state licensing and study-specific training. Principal Investigators will sign the Device Investigator Agreement form prior to the start of the study. Investigators will be compensated for their services with appropriate standard professional rates. Compensation will not be dependent on the study outcomes.

Each Investigator should enroll approximately 15 subjects, 30 eyes. 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.

3.5 Finances

The study will be financed through Bausch & Lomb Corporate Research & Development. A Clinical Trial Agreement[3] will be executed between Bausch + Lomb and each Investigator prior to their participation in the clinical trial. The agreement will include the responsibilities of each party, payment and reimbursement procedures and requirements, intellectual property and publication terms, insurance and indemnification, coverage for subject injury. Investigator and subject compensation are outlined in the Investigator's Clinical Trial Agreement. Each Investigator will be required to maintain General Liability and Professional/Medical Malpractice Insurance during the duration of the study. Bausch + Lomb agrees to indemnify investigative sites per conditions outlined in the Clinical Trial

Agreement. Bausch + Lomb will be responsible for payment of actual and reasonable medical expenses, incurred as a direct result of the treatment of a study subject's injuries.

3.6 Study Duration

Investigators should 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 three (3) months (unless discontinued or lost to follow-up) from the initial Screening/Dispensing Visit and must adhere to the following schedule:

SCHEDULED FOLLOW-UP VISITS		
Visit	**Target**	**Acceptable Visit Range (from Screening/Dispensing Visit)**
2-Week Follow-up Visit	14 Days	11 – 19 Days
1-Month Follow-up Visit	30 Days	27 – 35 Days
2- Month Follow-up Visit	60 Days	54 – 68 Days
3-Month Follow-up Visit	90 Days	84 – 98 Days

The visit range is based on the date Study Kits 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.

3.7 Treatments

Eligible subjects will be randomly assigned to use BL-3100-NBR03 multi-purpose solution (Test) or renu® Advanced Formula multi-purpose solution (Control). At the initial Screening/Dispensing Visit, each eligible subject will be provided with study lenses, Study Kit (containing Test or Control solution, a lens case, and Subject Instructions), and with other study supplies as needed (e.g., *renu® Contact Lens Moisture Drops* and product return materials). Subjects will be required to wear dispensed study lenses on a daily wear basis for three months with scheduled in-office replacement of study lenses at the 1-Month and 2-Month Follow-Up Visits.

4.0 STUDY MATERIALS

Bausch + Lomb will provide all study solutions and Bausch + Lomb lenses at no charge to the Investigator. All other 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 Section 4.7 (Product Replacement) for ordering replacement Test or Control product in case of loss or damage.

Use of other contact lenses or care products is not allowed.

Conformity to general safety and performance requirements to protect the health and safety of the subjects for the investigational test article are addressed in the design verification design review process referenced in BL SOP 20-D022-3.[4]

4.1 Description of Investigational Test Article (Test)

The BL-3100-NBR03 Multi-Purpose Solution is a [redacted]

[redacted]. The Investigational Test Article will be provided to subjects with masked labeling (Section 4.4.2).

4.2 Description of Control Product (Comparator)

renu® Advanced Formula multi-purpose solution is a marketed product indicated for the care of soft contact lenses. It is a sterile, isotonic, aqueous solution that contains poloxamine, poloxamer 181, diglycine, sodium citrate, boric acid, sodium borate, edetate disodium and sodium chloride and preserved with polyaminopropyl biguanide 0.00005%, polyquaternium 0.00015%, and alexidine 0.0002%. The Control solution will be provided to subjects with masked labeling

4.3 Instructions for Use and Administration

Each subject will be issued a Study Kit labeled with a unique Study Kit number. Subject Instructions for use of the assigned study solution (Test Article or Control) will be provided by the unmasked designee. Subjects will be dispensed three pairs (two for back-up) of their habitual lenses at the Screening/Dispensing Visit with additional pairs of lenses being dispensed at each of the monthly follow-up visits except for Month 3. Subjects will wear their assigned lenses on a daily wear basis for the duration of the study.

The Investigator or designee will instruct all subjects to adhere to the Subject Instructions provided for the daily care of their contact lenses.

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

4.3.1 Storage Requirements

All Test and Control study solutions 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. Subjects must comply with the instructions provided to them (refer to Appendix C).

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.

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 for non-Bausch + Lomb lenses. Six pairs of the subject's habitual contact lenses will be provided for each subject; three pairs will be dispensed to the subject at the Screening/Dispensing Visit (two for back-up) and a new pair will be dispensed at each of the 1-Month and 2-Month Follow-up Visits. The sixth pair will be retained in-office in the event a non-scheduled replacement is required. Additional lenses can be ordered and dispensed, if needed.

4.4.2 Study Kits

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

- **1 bottle of study solution (Test or Control).** Each labeled bottle will be enclosed in a labeled white carton. Each carton and bottle will be labeled with an investigational label including a unique 5-digit Study Kit number. The subject number may be written on the outside carton ONLY. The bottles should not be written on or labelled.
- **Study Lens Cases.** A new lens case will be included with each carton of study solution for the subject to use for the month. Subjects are required to use the supplied lens case.
- **Subject Instructions.** Instructions will be provided by unmasked designee at study visit.

4.4.3 Other Study Supplies

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

- **Carton/Bottle Return Materials.** Comprised of opaque bags and pre-printed labels for return of Test and Control solutions (full, partially full, and empty bottles along with their cartons) to the Sponsor.
- **Contact Lenses**: New contact lenses will be dispensed at the Screening/Dispensing, 1-Month and 2-Month Follow-up Visits.
- **Rewetting Drops***: Bausch + Lomb renu® Contact Lens Moisture Drops.*

The following will be stored at the sites to return study materials to the Sponsor:

- **Solution for Returning Lenses:** *Bausch + Lomb Sensitive Eyes® Saline Solution*
- **Lens Return Materials**. Comprised of zippered plastic bags and pre-printed labels for return of worn lenses in a lens case filled with *Bausch + Lomb Sensitive Eyes*® Saline Solution to the Sponsor. The unmasked designee will prepare the lenses for return.

4.5 Accountability and Traceability

The unmasked designee will be responsible to keep current and accurate records of study materials during the study. The records will include receipt and acknowledgement of all study lenses, Study Kits, and other supplies as identified in Sections 4.4.2 and 4.4.3. The disposition of study solutions and habitual contact lenses dispensed and returned by the subjects will be recorded on study product accountability logs. The study solutions are to be dispensed only to subjects enrolled in the study, in accordance with the conditions specified in this protocol.

Upon completion of the study, a Clinical Monitor will review and verify the Investigator's accountability logs.

Following verification, and as directed by the Sponsor, all used and unused study supplies (study solutions, unused contact lenses, and worn lens in cases filled with *Bausch + Lomb Sensitive Eyes® Saline Solution* must be returned to the Sponsor at the address below:

Bausch & Lomb Incorporated
Clinical Trial Materials Supply Chain
[redacted]
1400 North Goodman Street
Rochester, NY 14609

The study will use a randomization trial supply management (RTSM) system. All clinical supply kit orders, shipments, receipts, and subject dispensation will be tracked in the RTSM system. The clinical supply label includes a unique kit number and a labeling and packaging batch number for material lot number traceability.

4.6 Masking/Unmasking

Study solutions will be provided in sealed opaque white boxes with Study Kit numbers preprinted on them.

This is a double-masked study. The Investigator and Sponsor or their representatives involved in the conduct of the study will be masked to the study cleaning and disinfecting solutions. These procedures are intended to reduce or eliminate bias that might impact study outcomes and their interpretation.

The randomization schedule will be created by an unmasked statistician not otherwise involved in the study and uploaded into the RTSM system. Personnel involved with any repackaging/ relabeling of clinical trial material will also be unmasked. A Clinical Monitor will become unmasked during product reconciliation, at the conclusion of each site's participation in the study and prior to locking the database. Unmasked designees at the site will manage dispensing and return of study solutions, study contact lenses and related supplies.

Study solutions will be provided in sealed opaque white boxes with Study Kit numbers preprinted on them. Subjects are not to show or discuss the study the study solution appearance with the Investigator or site staff unless instructed to do so. Subjects may discuss any questions they have with the unmasked designee at the site.

In the event that unmasking of a subject's randomly assigned treatment is required, the Investigator (or other designee) is required to contact the Medical Monitor to request permission to unmask. The Medical Monitor will contact the Sponsor designee and obtain approval to grant permission to unmask. Upon receipt of authorization from the Sponsor designee, the Medical Monitor will advise the Investigator (or other qualified designee) to log into the RTSM system and unmask the subject. If the Medical Monitor cannot be contacted, the Investigator (or other qualified designee) should then contact the Sponsor designee who can authorize the unmasking of a subject. In the event that the Medical Monitor or Sponsor designee cannot be contacted, and the Investigator (or other qualified designee) deems the unmasking emergent, the Investigator may log into the RTSM system 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.

4.7 Product Replacement

Any additional/replacement (in the case of loss or damage) Test or Control study solutions must be ordered through the RTSM system.

5.0 SAFETY AND EFFECTIVENESS VARIABLES

Key safety variables and the primary effectiveness variables are presented below. A full list and description of all safety and efficacy variables and study procedures are provided in Appendix A (Schedule of Visits and Parameters) and Appendix B (Methods of Clinical Evaluation). A summary of the planned statistical analyses is presented in Section 8.0. Product risks are also described in the Investigator's Brochure.

5.1 Key Safety Variables

The safety of the Test and Control solutions will be determined by the following parameters:

- The primary safety endpoint will be the proportion of eyes with any slit-lamp findings greater than grade 2 over all follow-up visits.
- 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

The effectiveness of the Test and Control solutions will be determined by the following parameters:

- Overall comfort averaged over all scheduled follow-up visits
- Vision averaged over all scheduled follow-up visits
- The proportion of eyes with a maximum degree of front surface deposits grade of ≤ 2 over all scheduled follow-up visits.

5.3 Risk Assessment and Mitigation

Laboratory, pre-clinical studies and a preliminary clinical study have evaluated BL3100-NBR03 multi-purpose disinfection solution and/or its components. The results support the safety of the formulation for the further evaluation for the proposed use.

The clinical procedures required in Protocol 914 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. Risk mitigation includes periodic assessments of ocular health by vision care specialists throughout the study, oversight by the study Sponsor, its representatives and the Medical Monitor, and well-defined procedures for the management of adverse events, should they occur.

Anticipated serious adverse device effects are presented in Section 7.1.4.1. Additional descriptions of the risks and benefits to subject safety associated with wearing contact

lenses, use of the contact lens care products, use of the investigational test articles is presented in the BL-3100-NBR03 multi-purpose solution Investigator's Brochure.

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 ICF, including HIPAA, 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.

Eligible subjects will be required to complete and initial the subject-completed forms while at the visits listed below. The data will then be transcribed into electronic Case Report Forms (eCRFs) by qualified site personnel. The original subject-completed forms will be retained by the site in the study files.

Visit Name	Subject-Completed Forms
Screening/Dispensing Visit	• Informed Consent • Initial Lens Performance (Worn Lenses Lens Performance) • Lens Performance (Abbreviated Study Lenses Lens Performance)
2-Week Follow-up Visit	• Lens Performance (Study Lenses Lens Performance)
1-Month Follow-up Visit	• Lens Performance (Study Lenses Lens Performance)
2-Month Follow-up Visit	• Lens Performance (Study Lenses Lens Performance)
3-Month Follow-up Visit	• Lens Performance (Study Lenses Lens Performance)
Unscheduled Visit(s)	• Lens Performance (Study Lenses Lens Performance)

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.

The Screening/Dispensing Visit will proceed as follows:

a. Collect demographic information as required by the RTSM system

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

- Average daily wearing time
- Hours lenses worn on the day of this visit

- Average hours per day of comfortable wear
- Current lens brand, sphere power and base curve
- Current lens care products

c. For females of child-bearing potential, inform the potential subject they must use an effective method for birth control during the study and for 2 weeks following the last visit, in a manner that risk of contraceptive failure is minimized. Abstinence is allowed as a birth control method.

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

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

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

e. Perform a slit-lamp examination (remove the lenses if the subject wore lenses to the visit). Record and sketch any scars and slit-lamp findings greater than Grade 2 in the subject's source document.

f. If the subject continues to be eligible, have the subject complete and initial the following form:

- The Initial Lens Performance Assessment Form (Worn Lens Performance Rating Scales), including use of rewetting drops.

g. Complete the Initial Symptoms/Complaints Form (Worn Lenses Symptoms/Complaints Form).

h. Dispense three pairs (two for back up only) of the subject's habitual contact lenses. Explain to the subject that the used lenses will be removed at the follow-up visits and returned to the Sponsor.

i. Instruct subject to insert study lenses

NOTE: wait 2-3 minutes for the new contact lenses to settle on the eye before proceeding

j. Instruct subject to complete Lens Performance Assessment Form (Abbreviated version: Study Lenses Lens Performance Rating Scale).

k. Complete the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints).

l. Record the following:

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

- Dispensed lens type (brand), sphere power, base curve
- High contrast distance lens VA
- Over-refraction and distance VA
- Lens wettability
- Lens centration
- Lens movement

- For each eye, compare the distance lens VA to the Distance Best Spectacle-Corrected VA obtained at this visit. If the VA has decreased by 5 letters (0.1 logMAR) or more, provide an explanation.
- *If the subject meets all Eligible requirements,* log into RTSM system to randomize the subject.
- *If the subject is a "Screen Fail"*, the reason for screen failure must be entered in the RTSM system and maintain a copy of their ICF.

m. Following randomization, designated study site staff should dispense one Study Kit to the subject via the RTSM system and record in the subject's individual Product Accountability Log.

n. The unmasked designee will explain to the subject that:

- Carton and bottle are NOT to be opened in front of any other site personnel.
- The subject should retain all study materials and bring these items back to the study site at each visit. Place the cartons containing the multi-purpose solution bottles and contact lens cases into the opaque bag provided and return it to the unmasked designee.

o. The unmasked Designee can dispense the Other Supplies, as needed by the subject (refer to Section 4.4.3).

p. Complete the following visit eCRFs:

- Screening/Dispensing Visit
- Exit Visit (to be completed if the subject is discontinued after randomization)
- Collect Adverse Events

6.1.2 2-Week Follow-up Visit

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

a. Collect the following lens wear parameters from the subject:

- Average daily wearing time (since last visit)
- Average hours of comfortable wear (since last visit)
- Hours lenses worn on the day of this visit
- Did subject replace their lenses? (If so, when)

b. Complete the Symptoms/Complaints Form (Study Symptoms/Complaints Rating Scales).

c. Have the subject complete and initial the Lens Performance Assessment Form (Study Lenses Performance Rating Scales, including use of rewetting drops.)

d. Collect any relevant medical treatment information, including any adverse events, including whether a culture may have been taken.

e. If the subject did not come to the visit wearing one or more study lenses, go to Step f (below, slit-lamp assessment). Otherwise, evaluate the lenses (while on eye) and record the following assessments:

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

- High contrast distance lens VA

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

f. Perform a slit-lamp examination (remove and store the lenses if the subject wore lenses to the visit). A lens case must be filled with *Bausch + Lomb Sensitive Eyes® Saline Solution* (NOT dispensed study solution) for storage of subject's lenses during the exam. If a corneal infiltrate is noted record details according to Corneal Infiltrates, Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation.

g. Record and sketch any scars and slit-lamp findings greater than Grade 2 in the subject's source document.

h. Return the lenses to the subject to wear until the next study visit.

i. If an unscheduled lens replacement is required, dispense a new pair of the subject's habitual contact lenses and go to Unscheduled Visits Section 6.1.6.

j. Complete the following visit eCRFs:

- 2-Week Follow-up Visit
- Exit Visit (to be completed if the subject is discontinued or exited at this visit)
- Collect Adverse Events

6.1.3 1-Month and 2-Month Follow-up Visits

The 1-Month and 2-Month Follow-up Visits will proceed as follows:

a. If a subject misses either the 1-Month or 2-Month 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:

- Average daily wearing time (since last visit)
- Average hours of comfortable wear (since last visit)
- Hours lenses worn on the day of this visit
- Did subject replace their lenses? (If so, when)

c. Complete the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints Rating Scales)

d. Have the subject complete and initial the Lens Performance Assessment Form. (Study Lenses Performance Rating Scales, including use of rewetting drops.)

e. Collect any relevant medical treatment information including any adverse events, including whether a culture may have been taken.

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):

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

   - distance lens VA
   - For each eye, compare the distance lens VA obtained at the Screening / Dispensing visit with the distance lens VA obtained at this visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, provide an explanation.
   - Over-refraction and distance VA
   - Lens wettability
   - Lens deposits (type, percent, and degree)
   - Lens centration
   - Lens movement

g. Perform a slit-lamp examination (remove the lenses if the subject wore lenses to the visit). Record and sketch any scars and slit-lamp findings greater than Grade 2 in the subject's source document. If a corneal infiltrate is noted record details according to Corneal Infiltrates, Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation.

h. Unmasked designee to collect the worn lenses from the subject. All worn lenses will be returned to the Sponsor in lens cases filled with *Bausch + Lomb Sensitive Eyes® Saline Solution* at the end of the study. Place the lens case in a labeled zippered bag.

i. Unmasked designee to collect used Study Kit (bottle and carton) dispensed at the subject's previous visit.

j. Unmasked designee to place the lens case in the labeled zippered bag and the used Study Kit (bottle and carton) in subject's bag. DO NOT seal subject bags until there is a full accountability by a Clinical Monitor at the end of the study.

k. Dispense a new pair of subject's habitual lenses, instruct the subject to insert the lenses, and record the following information:

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

   - Dispensed lens type (brand), sphere power, base curve
   - distance lens VA
   - For each eye, compare the distance lens VA obtained at the Screening / Dispensing visit with the distance lens VA obtained at this visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, provide an explanation
   - Over-refraction and distance VA
   - Lens wettability
   - Lens centration
   - Lens movement

l. Unmasked designee to dispense a new Study Kit through the RTSM system, and record in the subject's individual Product Accountability Log. If needed, dispense any other supplies.

m. Complete the following visit eCRFs:

   - 1-Month or 2-Month Follow-Up Visit

- Exit Visit (to be completed if subject is discontinued at this visit)
- Collect Adverse Events

6.1.4 3-Month Follow-up

The 3-Month Follow-up will proceed as follows:

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

a. Collect the following lens wear parameters from the subject:

- Average daily wearing time (since last visit)
- Average hours of comfortable wear (since last visit)
- Hours lenses worn on the day of this visit
- Did subject replace their lenses? (If so, when)
- Last date that lenses were worn after cleaning and storing them in study solution
- Number of days on study that the subject did not wear the study lenses
- Percentage of days on study that the subject used study solution and wore their lenses on average (less than 80% = fewer than four out of five days, or 80% or more = at least four out of five days)

b. Complete the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints Rating Scales).

c. Have the subject complete Lens Performance Assessment Form (Study Lenses Performance Rating Scales), including use of rewetting drops.

d. Collect any relevant medical treatment information, including any adverse events, including whether a culture may have been taken.

e. 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):

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

- High contrast distance lens VA
- For each eye, compare the distance lens VA obtained at the Screening / Dispensing visit with the distance lens VA obtained at this visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, provide an explanation.
- Over-refraction and distance VA
- Lens wettability
- Lens deposits (type, percent, and degree)
- Lens centration
- Lens movement

f. Perform a slit-lamp examination (remove the lenses if the subject wore lenses to the visit). Record and sketch any scars and slit-lamp findings greater than Grade 2 in the subject's source document. If a corneal infiltrate is noted record details according to Corneal Infiltrates, Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation.

g. Unmasked designee to collect all worn dispensed lenses from the subject. All worn lenses will be returned to the Sponsor in lens cases filled with *Bausch + Lomb Sensitive*

Eyes® Saline Solution at the end of the study. Place the lens case in a labeled zippered bag.

h. Unmasked designee to collect used Study Kit (carton and bottle) dispensed at the subject's previous visit.

i. Unmasked Designee to place the lens case in the labeled zippered bag and the used Study Kit (bottle and carton) in the subject's bag. DO NOT seal the subject's bags until a full accountability is performed by a Clinical Monitor at the end of the study.

j. All study materials (refer to Sections 4.4.2 and 4.4.3) must be returned to the Sponsor at the end of the study.

k. Complete the following visit eCRFs:

- 3-Month Follow-up Visit
- Exit Visit (if there is an ongoing AE at the time of the 3-month visit, do not complete the Exit Visit and follow up via Unscheduled visit (s) instead
- Collect Adverse Events

6.1.5 Exit Visit

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 3-Month Follow-up Visit will be followed according to the AE and/or Unscheduled Visit Section until the AE is resolved or stabilized.

The Exit Visit will proceed as follows:

a. Indicate status of the subject on the Subject Exit Form. If the status is "Discontinued" or "Non-dispensed," indicate the PRIMARY exit reason for each eye on the Subject Exit Form.

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

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

- Spherocylindrical refraction
- BSCVA Contrast Distance Lens VA
  - Compare the Exit Visit distance BSCVA to the distance BSCVA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, explain.
- Keratometry
  - For each eye, compare the Exit visit Horizontal and Vertical keratometry readings to the Screening/Dispensing Visit Horizontal and Vertical keratometry readings. If there is a change of 1.00 D or more, explain.

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

d. Unmasked designee to collect all worn lenses from the subject. All worn lenses will be returned to the Sponsor in lens cases filled with *Bausch + Lomb Sensitive Eyes® Saline Solution* at the end of the study. Place the lens case in a labeled zippered bag.

e. Unmasked designee to collect used Study Kit (bottle and carton) dispensed at the subject's previous visit.

f. Unmasked designee to place the lens case in the labeled zippered bag and the used Study Kit (bottle and carton) in the subject's bag. DO NOT seal subject bags until a full study accountability is performed by a Clinical Monitor at the end of the study.

g. All study materials (refer to Section 4.4.2) must be returned to the Sponsor at the end of the study.

h. Have the subject complete the Subject Assessment Questionnaire.

6.1.6 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. Refer to Section 7.2 for the procedures required should an AE be present at an Unscheduled visit. 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 eCRFs.

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.

Procedures to be followed during an Unscheduled Visit will depend on the reason for the visit:

a. Indicate the reason for the Unscheduled Visit.

b. If the subject is experiencing problems, assessments will be performed according to the Investigator's judgement.

c. If the exclusive purpose of the visit is to dispense study lens/ Study Kit and the subject is not experiencing any problems (refer to Section 6.1.8.).

d. Collect the following lens wear parameters from the subject:

   - Average daily wearing time (since last visit)
   - Average hours of comfortable wear (since last visit)
   - Hours lenses worn on the day of this visit
   - Did subject replace their lenses? (If so, when)

e. Complete the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints), including use of rewetting drops

f. Have the subject complete and initial the Lens Performance Assessment record (Study Lenses Performance Rating Scales).

g. Collect any relevant medical treatment information, including any adverse events, including whether a culture may have been taken.

h. If the subject did not come to the visit wearing one or more study lenses, go to Step i. Otherwise, evaluate the lenses (while on eye):

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

- High contrast distance lens VA
- Over-refraction and distance VA
- Lens wettability
- 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.

i. Perform a slit-lamp examination (remove the lenses if the subject wore lenses to the visit). Record and sketch any scars and slit-lamp findings greater than Grade 2 in the subject's source document and transcribe this information to the visit eCRF. If a corneal infiltrate is noted record details according to Corneal Infiltrates, Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation.

j. If a new Study Kit is required, designated site staff will log into RTSM system to dispense a new Study Kit (refer to Section 4.4.2) to the subject according to RTSM notification email and record in the Product Accountability Log.

k. If an unscheduled lens replacement is required at this visit, dispense a new pair of subject's habitual lenses and collect the following information:

- Primary (one) reason for replacement
- Dispensed lens type (brand), sphere power, base curve
- Distance lens VA
- Over-refraction and distance VA
- Lens wettability
- Lens centration
- Lens movement
- For each eye, compare the distance lens VA to the distance lens VA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, provide an explanation.

l. If Study Lenses were replaced, unmasked designee to collect the worn lenses from the subject. All worn lenses will be returned to the Sponsor in lens cases filled with *Bausch + Lomb Sensitive Eyes® Saline Solution* at the end of the study. Place the lens in a labeled zippered bag.

m. Unmasked designee to place the lens case in the labeled zippered bag and the used Study Kit (bottle and carton) in the subject's bag. DO NOT seal subject bags until a full accountability is performed by a Clinical Monitor at the end of the study.

n. All study materials (refer to Sections 4.4.2 and 4.4.3) must be returned to the Sponsor at the end of the study.

o. If the subject needs to exit the study at this visit,

- Complete the Exit Visit as per Section 6.1.5.
- Unmasked designee to collect the Study Kit (bottle and carton) dispensed to the subject.

- Complete the form(s) listed below and transcribe the information to the eCRF as appropriate:
  - Unscheduled Visit Form
  - Exit Visit Form (to be used if the subject is discontinued or exited at this visit)

6.1.7 Missed Visits

Missed Visits will be handled as follows:

a. If a subject misses any scheduled follow-up 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.

6.1.8 Product Dispensing Only Visit

Product Dispensing Only Visits will proceed as follows:

a. If a subject is seen exclusively for resupply or replacement of study materials, a complete exam is not required, as long as the subject is not experiencing any problems. If any assessment is performed, then an Unscheduled Visit Form must be completed (see section 6.1.6).
   - If additional study solution is required at this visit, go to Unscheduled Visit Section 6.1.6, j.
   - If a lens replacement is required, go to Unscheduled Visit Section 6.1.6, k.

6.2 Study Completion / Early Study Terminations / Suspensions

6.2.1 Study Completion

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

6.2.2 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, 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.

6.3 Concomitant Medications/Therapy

Study subjects are not allowed to use other lens care products, ocular solutions, ocular medications, or eye drops (over-the-counter or prescription) during the study unless specifically approved by the Investigator following consultation with the Sponsor. Use of other contact lenses is not allowed.

Ocular medications, 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. If used during the course of the study, these medications must be recorded in the appropriate eCRF.

6.4 Treatment Compliance

Treatment compliance will be assessed using lens wear parameter data.

6.5 Protocol Deviations

A deviation from the protocol is an unintended and/or unanticipated departure from the procedures and/or processes approved by the Sponsor and the IRB and agreed to by the Investigator. It is a Sponsor expectation that Investigators will follow the protocol and procedures as written. The Sponsor will not grant protocol waivers for this study. The Investigator may implement a deviation from the protocol to eliminate an immediate hazard to study subjects without prior IRB/EC approval. As soon as possible after such an occurrence, the implemented deviation, as well as the reasons for it should be submitted to the IRB/EC for review and approval. It should also be submitted to the Sponsor for agreement, and to the regulatory authorities, if required.

In the event a protocol deviation occurs, the date of and reason for deviations must be documented in all cases. Significant or major protocol deviations impacting the rights or safety of the subject or the integrity of the study must be reported by the Investigator to the IRB/EC and Medical Monitor immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB/EC. Unless the protocol deviations put the subject at risk or the subject's condition requires that they be discontinued from the study, subjects may continue to participate until the end of the study.

Site Corrective Action Plans will be developed and completed as deemed necessary by the Sponsor, Sponsor Designee (e.g., Contract Research Organization, 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 Introduction to Adverse Event Definitions

AEs, Serious AEs (SAEs), Significant Non-Serious AEs, Non-Significant Non-Serious Adverse Events, Adverse Device Effects and Anticipated Serious Adverse Device Effects are defined in this section and in the Protocol's Glossary.

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or 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.

7.1.1 Serious Adverse Event (SAE) Definitions

An AE that (related or not related to the investigational test articles, comparator products or study procedures):

- 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 may include but are not limited to any hazardous, sight-threatening conditions occurring after exposure to the investigational test article or control product including, but not limited to, 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 the central 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.

7.1.2 Significant Non-Serious Adverse Event Definitions

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 to the Sponsor (see Section 7.2.1.). These events include but are not limited to:

- 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 (if not within 6 mm of the cornea)
- Any ocular event that necessitates temporary lens discontinuation of greater than or equal to 2 weeks.

7.1.3 Non-Significant Non-Serious Adverse Events Definitions

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.

7.1.4 Adverse Device Effect (ADE) Definitions

An adverse device effect (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.

7.1.4.1 Anticipated Serious Adverse Device Effect (ASADE) Definition

An anticipated serious adverse device effect (ASADE) is an ADE that first meets the serious criteria (see Section 7.1.1) 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 but are not limited to:

- 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

7.1.4.2 Unanticipated Serious Adverse Device Effect (USADE) Definitions

An unanticipated serious ocular or non-ocular adverse device effect (USADE) is an adverse event related to the use of an investigational medical device that has resulted in any of the consequences characteristic of a serious adverse event as described in section 7.1.1 and

which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

This definition includes but is not limited to 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. USADEs include but are not limited to:

- 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.

7.1.5 Relationship Definition: Study Device and/or Other Study Materials

- **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.
- **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.

7.1.6 Severity Definitions

- **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

7.2 Procedures for Evaluating Adverse Events

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. All SAEs, ocular and systemic, must be recorded and reported as required.

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. 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.

Ocular AEs of possible clinical significance should be photo-documented and shared with the Medical Monitor in electronic form.

When evaluating for reportable AEs, the Investigator should refer to the definitions for AEs to determine:

a) whether the event is serious (refer to Section 7.1.1 and 7.1.2.)
b) whether the event is severe (refer to Section 7.1.6.)
c) whether the event is significant (refer to Sections 7.1.2 and 7.1.3.)
d) whether the event is related to the study device (refer to Section 7.1.5.)

7.2.1 Procedures for Reporting Serious or Significant Adverse Events

An AE classified as a SAE or a Significant Non-Serious Ocular 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 ([redacted] 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 will email a copy of the form (within 24 hours) to all parties listed below:
  - [redacted]

  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 by the site to the Medical Monitor within 24 hours. The Medical Monitor should distribute the updated reports to appropriate Sponsor personnel. Whenever

possible, it is suggested that the Investigator take photographs of all ocular AEs of possible clinical significance 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 USADEs to the reviewing IRB within 10 working days following awareness of the USADE 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.

7.2.2 Procedures for Reporting Off-Site Unanticipated Serious Adverse Device Effects

When participating in multicenter clinical investigations, Investigators may receive off-site USADE reports. These are Sponsor reports of USADEs which occurred at other clinical sites for the same trial, or in different trials using the same investigational test article or comparator, 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.

7.2.3 Device Deficiencies: Definition and Reporting Procedures

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 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:

- [redacted]

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

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.

7.2.4 Procedures for Culturing of Corneal Ulcer or Suspected Ocular Infection

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 B, Section 8.0).

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.

7.2.5 Guidelines for Reporting Pregnancies

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 Pregnancy Report 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 report to the Sponsor as per the distribution listed below.

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 and submitted to the Medical Monitor via facsimile or email transmission once the outcome is learned. The Medical Monitor will distribute the completed report to the Sponsor as per the distribution listed below.

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 are:

[redacted]

8.0 STATISTICAL METHODS

Changes to these statistical plans that are made prior to unmasking of study treatments will be documented in protocol amendments and/or the statistical analysis plan. Changes made after unmasking will be described in the clinical study report.

8.1 Study Endpoints

8.1.1 Primary Effectiveness Endpoints

The primary effectiveness endpoints are as follows.

a. Overall comfort averaged over all scheduled follow-up visits (Appendix B, Section 6.0, Rating Scale #3)

b. Vision averaged over all scheduled follow-up visits (Appendix B, Section 6.0, Rating Scale #12)

c. The proportion of eyes with a maximum degree of front surface deposits grade of ≤ 2 over all scheduled follow-up visits.

8.1.2 Secondary Effectiveness Endpoints

There are no predefined secondary effectiveness endpoints.

8.1.3 Supportive Effectiveness

The supportive effectiveness outcomes are the percentages of subjects agreeing with the consumer survey statements.

8.1.4 Primary Safety Endpoint

The primary safety endpoint is the proportion of eyes with any slit-lamp findings greater than Grade 2 over all follow-up visits.

8.2 Hypotheses

The noninferiority margins that follow are commonly used values in the industry for the corresponding endpoints. The study will be statistically successful if the Test lens is statistically successful in all primary endpoints.

8.2.1 Overall Comfort Averaged Over All Follow-up Visits

The null hypothesis (H_0) is that the difference in mean overall comfort (test group mean [μ_T] minus standard group mean [μ_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.

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

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

8.2.2 Vision Averaged Over All Follow-up Visits

The null hypothesis (H_0) is that the difference in mean vision score (test group mean [μ_T]

minus standard group mean [μ_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 Front Surface Deposits at All Follow-up Visits

The null hypothesis (H_0) is that the difference in the proportion of eyes with maximum front surface deposits grade of ≤ 2 at all Follow-up Visits (test group proportion [π_T] minus standard group proportion [π_S]) is less than or equal to -0.1 (-10%). The alternative hypothesis (H_1) is that the difference is greater than -0.1 (-10%).

$$H_0: \pi_T - \pi_S \leq -0.1$$

$$H_1: \pi_T - \pi_S > -0.1$$

8.2.4 Slit-Lamp Findings Greater than Grade 2

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 [π_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%).

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

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

8.2.5 Subject Assessments

Each of the following hypotheses will be evaluated for each of twelve statements in the Subject Assessment Questionnaire.

8.2.5.1 Proportion of Test Group Respondents Agreeing

The null hypothesis (H_0) is that the proportion of respondents in the Test group agreeing with the statement (π_T) is less than or equal to 0.5. The alternative hypothesis (H_1) is that the proportion agreeing is less than 0.5.

$$H_0: \pi_T \leq 0.5$$

$$H_1: \pi_T > 0.5$$

8.2.5.2 Comparison Between Groups of the Proportion of Respondents Agreeing

The null hypothesis (H_0) is that the proportion of respondents in the Test group agreeing with the statement (π_T) is less than or equal to the proportion of respondents in the Control group (π_T). The alternative hypothesis (H_1) is that the proportion agreeing in the Test group is greater than the proportion agreeing in the Control group.

$$H_0: \pi_T \leq \pi_C$$

$$H_1: \pi_T > \pi_C$$

8.3 Sample Size

Estimates of standard deviations and proportions were obtained from Bausch + Lomb Study #872.[5]

The sample size calculations assume that the unit of analysis will be the eye and that the outcomes from each subject's eyes will be independent.

Sample size calculations were completed using nQuery software, Version 9.

8.3.1 Overall Comfort

When the sample size in each group is 300 eyes (150 subjects), a two-group one-sided 0.025 significance level t-test will have 99% power to reject the null hypothesis that the test is not non-inferior to the standard (the difference in means, μT-μS, 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 13.264.

8.3.2 Vision

When the sample size in each group is 300 eyes (150 subjects), a two-group one-sided 0.025 significance level t-test will have 99% power to reject the null hypothesis that the test is not non-inferior to the standard (the difference in means, μT-μS, is -5 or farther from zero in the same direction) in favor of the alternative hypothesis that the non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 11.7.

8.3.3 Front Surface Deposits

With 300 eyes (150 subjects) in each group, the observed one-sided 97.5% confidence interval will be expected to exceed -0.1 with 99% power when the Standard proportion, π_0, is 0.942 and the Test expected proportion, π_1, is 0.942; results are based on 100,000 simulations using the Newcombe-Wilson score[6] method to construct the confidence interval.[6]

8.3.4 Slit-Lamp Findings Greater than Grade 2

With 300 eyes (150 subjects) in each group, the observed one-sided 97.5% confidence interval will be expected to be less than 0.05 with 99% power when the Standard proportion, π_0, is 0.008 and the Test expected proportion, π_1, is 0.008; results are based on 100,000 simulations using the Newcombe-Wilson score method to construct the confidence interval.

8.3.5 Lens Groups

For each lens group in Table , at least approximately 30 test group subjects will complete the study. For a sample size of 30, the probability of observing at least one complication will be at least 95% when the true complication rate is 10% or greater.

8.3.6 Overall Power

If the four primary endpoints are independent, then the overall power of the study is 99% x 99% x 99% x 99% = 96%.

8.3.7 Enrollment Targets

Approximately 300 subjects (150 in each treatment group) will complete the trial. Allowing for up to 10% losses and for equal enrollment across sites, the enrollment target will be approximately 340 subjects (680 eyes).

To allow for approximately 30 completed test group subjects per lens group, each lens group will enroll approximately 34 test group subjects.

8.4 Randomization

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

Each subject will be randomized to one of the treatment arms in a 1:1 ratio (Test to Control). Randomization will be managed using a RTSM system. The randomization will be stratified by lens group and investigational site.

Efforts will be made to enroll subjects in at least three of the lens strata within each site to minimize confounding between site and lens group. While the target enrollment for each lens group is approximately 68 subjects, some lens strata may be difficult to enroll.

8.5 Study Populations

8.5.1 Intent-to-Treat (ITT) Population

The ITT Population will consist of all randomized subjects for subject level summaries and, for eye level summaries, 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 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 8.6.5 below. Subjects will be included in PP Population summaries according to the treatment group to which they were randomly assigned. The membership of the PP population will be determined prior to 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 sample size (n), mean, standard deviation (SD), 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 unless otherwise indicated.

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

Listings of data will be produced in addition to tables of summary statistics.

8.6.1.2 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 ITT Set in a table. A one-sided lower 97.5% confidence limit around the difference in means between the Test and Control treatment groups, computed using an analysis of variance model including the fixed factors of treatment, site, and lens group will be displayed. If the lower confidence limit is greater than -5.0, then the null hypothesis that the test solution is not noninferior will be rejected, and the test solution will be statistically successful in this outcome.

As a sensitivity analysis, the PP Population will be analyzed for this endpoint.

8.6.1.3 Vision

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

8.6.1.4 Front Surface Deposits

At each follow-up visit, the degree of front surface deposits will be graded for each eye as 0, 1, 2, 3, or 4. Using only the non-missing observations from scheduled follow-up visits without imputation, each eye will be classified with respect to the maximum grade of front surface deposits (≤ 2, > 2) observed over all follow-up visits. Maximum Front Surface Deposits Over All Follow-up Visits (≤ 2, > 2) will be summarized at the eye level by treatment using categorical summary statistics for the ITT Set in a table. A one-sided lower 97.5% confidence limit around the difference in "≤ 2" proportions between the Test and Control treatment groups will be constructed using the Newcombe-Wilson score method. If the lower confidence limit is greater than -10.0% or if no deposits with grade greater than 2 are observed in either treatment group, then the null hypothesis that the Test solution is not noninferior will be rejected, and the Test solution will be statistically successful in this outcome.

As a sensitivity analysis, the PP Population will be analyzed for this endpoint.

8.6.1.5 Graded Slit-Lamp Findings > Grade 2

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, each eye will be classified with respect to findings greater than grade 2 at any visit (Absent, Present). 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 97.5% confidence limit around the difference in "Present" proportions between the Test and Control treatment groups will be constructed using the Newcombe-Wilson score method. If the upper confidence limit is less than 5.0% or if no findings greater than grade 2 are observed in either treatment group, then the null hypothesis that the Test solution is not noninferior will be rejected, and the Test solution will be statistically successful in this outcome.

8.6.1.6 Subject Assessment

At the Exit visit, subjects will report their level of agreement with each of a series of twelve statements in the Subject Assessment Questionnaire. Responses will be on a scale of one (strongly disagree) through six (strongly agree). These values will be dichotomized for analysis, with responses of one through three being mapped to the category of "Disagree" and responses of four through six being mapped to "Agree."

Statistical testing will proceed in two hierarchical families of twelve statistical tests each (one test per statement), with the null hypotheses of the first family eligible for rejection if all the primary endpoints are met.

The first family will employ a one-sided exact binomial test to compare the proportion of respondents in the Test group agreeing with each statement to 0.5.

The second family will employ a one-sided chi-square test to compare the proportion of respondents agreeing with each statement between the treatment groups.

Within each family of hypothesis tests, the *P*-values will be adjusted for multiplicity using the Holm method. Adjusted one-sided *P*-values less than 0.025 will show statistical significance.

The responses to each statement will be summarized categorically (1, 2, 3, 4, 5, 6, Agree, Disagree) by treatment group in a table for the ITT Set. The adjusted *P*-values from the statistical tests will also be displayed along with an indicator of statistical significance. If the statistical tests in a family are not eligible for rejection due to hierarchy, then the adjusted *P*-values for that family will not be displayed.

8.6.2 Adverse Events

All AEs occurring during the study will be recorded and classified on the basis of Medical Dictionary for Regulatory Activities (MedDRA) terminology. Descriptions of AEs will include the date of onset, the date the AE ended, the severity of the AE, the relationship to the study device, the action taken regarding study medication usage, the action taken to treat the AE, and the outcome. All reported treatment-emergent AEs (TEAEs) will be summarized by the number of subjects reporting AEs, system organ class, severity, seriousness, and relationship to study device. TEAEs are those AEs with an onset on or after the date of the first study device use.

Adverse events will be summarized by treatment group and severity. Each subject will be counted only once within a system organ class or a preferred term by using the AEs with the highest severity within each category.

Adverse events will be summarized by treatment group and relationship to study medication. Each subject will be counted only once within a system organ class or a preferred term by using the AEs with the greatest relationship within each category.

All information pertaining to AEs noted during the study will be listed by subject, detailing verbatim given the Investigator, preferred term, system organ class, start date, stop date, severity, action taken, and device relatedness. The AE onset will also be shown relative (in number of days) to the day of initial use of the randomized study device.

Serious adverse events (SAEs) will be tabulated by subject within treatment groups.

In addition, a list of subjects who discontinued from the study and a list of subjects who experienced SAEs will also be provided.

8.6.3 Subject Demographics and Baseline Characteristics

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

8.6.4 Subject Discontinuation

The reasons for study discontinuation will be summarized by treatment and overall, for the ITT Population.

8.6.5 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.

- Ineligibility at screening/dispensing but randomized
- Not dispensed study treatment
- Misrandomization
- Dispensing of the incorrect solution
- 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.

8.6.6 Treatment Compliance

As is customary for contact lens solution trials, treatment compliance will not be summarized.

8.6.7 Treatment Exposure

As is customary for contact lens solution trials, treatment exposure will not be summarized.

8.6.8 Missing Data

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

The effects of missing data on the primary effectiveness endpoint analyses will be explored by considering best- and worst-case imputation scenarios and tipping point analysis with the ITT Set.[7]

8.6.9 Multiplicity Issues

The overall Type I error will be controlled by requiring the four co-primary endpoints to be statistically significant for overall success to be achieved. Failure of any one of the primary endpoints will invalidate the statistical significance of the secondary effectiveness endpoints. If the primary endpoints are met, then statistical testing of the supportive effectiveness endpoints will proceed in two hierarchical families with Holm multiplicity adjustments applied within each family.

8.6.10 Interim Analyses

No interim analyses are planned.

9.0 DATA QUALITY ASSURANCE

9.1 Subject Confidentiality

All personal subject data collected and processed for the purposes of this trial will be maintained by the Investigator and his/her staff with adequate precautions as to ensure that the confidentiality of the data is in accordance with local, state, and federal laws and regulations.

Monitors, auditors, and other authorized representatives of CRO, the Sponsor, the IRB approving this trial, the FDA, the Department of Health and Human Services, other domestic government agencies, and other foreign regulatory agencies will be granted direct access to the trial subject's original medical and trial records for verification of the data and/or clinical trial procedures. Access to this information will be permitted to the aforementioned individuals to the extent permitted by law.

A report of the results of this trial may be published or sent to the appropriate health authorities in any country in which the product may ultimately be marketed, but the subject's identity will not be disclosed in these documents.

Suspected data breaches involving Personnel Health Information will be escalated to Bausch + Lomb Data Privacy representative per B+L SOP CLN-035 - Privacy of Clinical Data and Related Protection.[8]

9.2 Study Monitoring

Bausch + Lomb Clinical Operations 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 Bausch + Lomb Clinical Operations.

Prior to the start of the study, member(s) of the Bausch + Lomb Clinical Operations, Clinical Affairs, and Global Regulatory Affairs 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
- the conduct of the investigation is in compliance with the currently approved protocol/amendment, 21 CFR Parts 11, 50, 54, 56 and 812; 42 CFR Part 11 – Clinical Trials Registration and Results Information Submission; EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good clinical practice*; Medical Device Regulation (MDR) 2017/745; International Council for Harmonization (ICH) Good Clinical Practice; the Declaration of Helsinki and applicable local regulations
- 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
- investigational 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.

Plans for monitoring study sites, designed to ensure compliance with Good Clinical Practice (GCP), study-specific procedures, human rights and applicable regulations, are described in the Monitoring Plan.[9]

9.3 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 ICFs, 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. 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 (e.g., 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.

9.4 Electronic 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. All information required on the eCRFs needs to be supplied, including subject identification, date(s), assessment values, etc., and any omission or discrepancy will require explanation. All information on eCRFs must be traceable to source documents.

A Clinical Monitor will be responsible for reviewing and verifying 100% of the data recorded on the eCRFs, utilizing the original source documentation, and will query discrepant findings. The Investigator and study site personnel will be responsible for answering all queries.

The eCRF data will be reviewed for completeness, accuracy, consistency, and medical sense. Programmed edit checks will be used to reduce data entry errors and identify unusual data for verification prior to statistical analysis.

A copy of the eCRF data will be retained at the conclusion of the study by the Investigator, who must ensure that it is stored in a secure place.

9.5 Recording of Data and Retention of Documents

Subject data recorded on eCRFs during the study will be documented to maintain subject confidentiality. The subject will only be identified by the subject number. Confidentiality of subject's records must be maintained to ensure adherence to applicable local privacy regulations.

The Investigators have to retain records for 2 years after the investigational product is approved by the FDA. 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:

- Device Investigator Agreement
- IRB/EC approvals for the study protocol, all amendments, ICF(s), and advertisements
- IRB/EC annual study review
- IRB/EC correspondence and reports (e.g., AE reports, protocol deviations, and safety updates)
- regulatory documents (e.g., financial disclosure and delegation of authority forms or records)
- all source documents
- eCRFs
- subject's signed ICF (including HIPAA)
- accountability records for the test article(s)
- 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 Bausch + Lomb Clinical Operations.

9.6 Auditing Procedures

Audits of clinical research activities in accordance with the Sponsor's internal Standard Operating Procedures 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.

9.7 Institutional Review Board

The Investigator should ensure that the following are approved by their institution's IRB/EC, or if not using their institution's IRB/EC, approved by the reviewing central IRB/EC prior to entering any subjects in the study:

- The protocol
- The Investigator's participation in the study
- Subject recruitment materials (written information or materials including web pages, radio advertisements, television spots or written text developed to encourage subject enrollment)
- The ICF to be used in this study.

Documentation of IRB/EC 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/EC 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.

9.8 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 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 products and activities receive fair, accurate, and reasonable presentation.

10.0 REFERENCES

Global and Regional Regulatory References:

- EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good Clinical Practice*
- EN ISO 11980:2012 *Ophthalmic Optics – Contact Lenses and contact lens care products – Guidance for clinical investigations*
- 21 CFR Part 11 – Electronic Records; Electronic Signatures
- 21 CFR Part 50 – Protection of Human Subjects
- 21 CFR Part 54 – Financial Disclosure by Clinical Investigators
- 21 CFR Part 56 – Institutional Review Boards
- 21 CFR Part 812 – Investigational Device Exemptions
- 42 USC 282(j)
- MDR 2017/745 – Regulation of the European Union on the clinical investigation and sale of medical devices for human use

Literature References:

[1] Study 914 -Multi-Purpose Solution BL-3100-NBR03 -Investigator's Brochure

[2] Protocol 914 Investigator Contact List

[3] Protocol 914 Investigator Clinical Trial Agreements

[4] B&L SOP No. 20-D022-3 Investigational Material Release for Bausch Health Companies R&D Activities

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

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

[7] Yan X, Lee S, and Li N (2009) Missing Data Handling Methods in Medical Device Clinical Trials. Journal of Biopharmaceutical Statistics, 19: 1085-1098

[8] B&L SOP No. CLN 035 – Privacy of Clinical Data and Related Information

[9] Protocol 914 Monitoring Plan

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. **(Refer to important footnotes at the bottom of the table)**

PROCEDURES / ASSESSMENTS	Screening/ Dispensing	2-Week Follow-up Visit	1-Month Follow-up Visit	2-Month Follow-up Visit	3-Month Follow-up Visit	Exit Visit [e]	Unscheduled Visit [g]	
	Day 1	Day 11-19	Day 27-35	Day 54-68	Day 84-98			
Informed Consent / HIPAA Authorization	X							
Eligibility	X							
Demographics/ Medical History	X							
Concomitant Medications	X	X	X	X	X	X	X	
Adverse Events; Cultures Taken if Appropriate [d]	X	X	X	X	X		X	
Baseline Lens / Lens Care History	X							
Lens Wear Parameters	X	X	X	X	X		X	
Habitual Lens Symptoms/Complaints [b]	X							
Symptoms/ Complaints Form [b] (Study Lenses Symptoms/Complaints)		X	X	X	X		X	
Exit Form (if an Exit Visit took place)	X [a]	X	X	X	X	X	X	
Subject Completed Forms								
(Habitual Lens) Lens Performance Assessment [b]	X							
Abbreviated Lens Performance Assessment Form [b] (Study Lenses Performance Rating Scales)	X							
Study Lens Performance Assessment Form [b] (Study Lenses Performance Rating Scales)		X	X	X	X		X	
Subject Assessment Questionnaire						X		
Without Lenses								
Spherocylindrical Refraction [c]	X					X		

PROCEDURES / ASSESSMENTS	Screening/ Dispensing	2-Week Follow-up Visit	1-Month Follow-up Visit	2-Month Follow-up Visit	3-Month Follow-up Visit	Exit Visit [e]	Unscheduled Visit [g]	
	Day 1	Day 11-19	Day 27-35	Day 54-68	Day 84-98			
Distance BSCVA [c]	X					X		
Keratometry	X					X		
Slit-lamp Examination	X	X	X	X	X		X	
Compare Distance BSCVA to Screening / Dispensing Visit Distance BSCVA [c]						X [e]		
Compare Final Keratometry to Screening / Dispensing Visit Keratometry [c]						X		
With Lenses Worn to Visit								
Distance Lens VA [c]		X	X	X	X		X	
Over-Refraction and Distance VA [c]		X	X	X	X		X	
Lens Wettability		X	X	X	X		X	
Lens Deposits (type, percent, and degree)		X	X	X	X		X	
Lens Centration		X	X	X	X		X	
Lens Movement		X	X	X	X		X	
Compare Distance Lens VA to Distance Lens VA at Screening / Dispensing Visit [c]		X	X	X	X		X	
With Newly Dispensed Lenses								
Distance lens VA [c]	X		X	X			X	
Over-Refraction and Distance Lens VA [c]	X		X	X			X	
Lens Wettability	X		X	X			X	
Lens Centration	X		X	X			X	
Lens Movement	X		X	X			X	
Compare Distance Lens VA to Distance Lens VA at Screening/ Dispensing Visit [c]			X	X			X	

PROCEDURES / ASSESSMENTS	Screening/ Dispensing	2-Week Follow-up Visit	1-Month Follow-up Visit	2-Month Follow-up Visit	3-Month Follow-up Visit	Exit Visit [e]	Unscheduled Visit [g]	
	Day 1	Day 11-19	Day 27-35	Day 54-68	Day 84-98			
Compare Distance Lens VA to Distance BSCVA at Screening/ Dispensing Visit [c]	X							
Study Materials								
Dispense Lenses	X		X	X			X	
Randomization	X							
Dispense Study kit [h]	X		X	X			X	
Dispense other Supplies as Needed (Refer to Protocol Section 4.4.3)	X	X	X	X			X	
Collect Worn Lenses from Subject [h]			X	X	X	X	X	
Collect Study Kit [h]			X	X	X	X	X	
Return Study Materials to Sponsor at End of Study [f]						X		

a = At the Screening Visit, only complete the Exit Record for study participants who were randomized

b = Use rating scales provided

c = All VA measurements MUST be made using a phoropter

d = Reporting s begins when the informed consent form is signed by the study subject.

e = At any visit, if a randomized patient is exiting from study, perform the procedures listed in the Exit Visit column. In the presence of some adverse events, premature withdrawals and other rare situations, some Exit Visit procedures may be omitted. Document the reason for all omissions.

f = Sites need to keep all study materials until a full accountability is performed by study clinical monitor.

g = Perform assessments according to the Investigator's judgement

h = Unmasked designee

APPENDIX B: METHODS OF CLINICAL EVALUATION

Any changes to the procedures described in this appendix will be provided under separate cover. Equipment and Instrumentation used to perform clinical evaluations should be maintained and calibrated per the investigative site's procedures.

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. All VA/Refraction must be measured using a phoropter in 0.25 D steps. 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 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. 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 6 were read correctly. Line 7 had 4 correct responses, and line 8 had only 1 correct response. After line 8, the VA test would be considered complete. In this example, the total letters correctly identified is 32. 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	O K S V Z	K S X R H	4
20/32	0.2	K S N H O	X X K X X	1
20/25	0.1	H O V S N	N D V K O	
20/20	0	V C S Z H	D H O S Z	
20/16	-0.1	C Z D V R	V R N D O	
20/12.5	-0.2	S H R Z C	C Z H K S	
20/10	-0.3	D N O K R	O R Z S K	

TOTAL	32

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 bullae.

Epithelial Microcysts

0 - None: no microcysts; normal transparency.

1 - Trace: 1 to 20 microcysts; barely discernible local epithelial haziness.

2 - Mild: 21 to 50 microcysts; faint but definite localized generalized haziness.

3 - Moderate: 51 to 100 microcysts; significant localized or generalized haziness.

4 - Severe: > 100 microcysts; definite widespread epithelial cloudiness giving a dull glass appearance to the cornea or numerous coalescing bullae.

Stromal Edema

0 - None: no oedema.

1 - Trace: just detectable clouding.

2 - Mild: faint corneal striae (2 or fewer).

3 - Moderate: pronounced corneal striae (3).

4 - Severe: folds in Descemet's membrane pronounced striae.

Endothelial regularity

0 - None: regular endothelial mosaic.

1 - Minimal: isolated difference in cell size.

2 - Mild: just noticeable variation in cell size or bumpiness of cell layer.

3 - Moderate: easily detected difference in cell size or bumpiness of cell layer.

4 - Severe: noticeable cell layer bumpiness and loss of definition of cell borders.

Corneal Staining

Corneal staining must be assessed after the instillation of fluorescein. 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.

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 less than 1.0 mm in diameter.

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

4 - Severe: Localized or generalized giant papillae, larger than 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 less than 1.0 mm of advancement into cornea in one quadrant.

2 - Mild: Vascularization greater than 1.0 mm to less than 1.5 mm of advancement into cornea in more than one quadrant.

3 - Moderate: Vascularization greater than 1.5 mm to less than 2.0 mm of advancement into cornea in any quadrant.

4 - Severe: Vascularization more than 2.0 mm of advancement into cornea in any quadrant.

Corneal Infiltrates

0 - None - No infiltrates.

1 - Trace - single or multiple epithelial infiltrates < 1 mm in diameter.

2 - Mild - single or multiple epithelial infiltrates ≥ 1mm and < 2mm in diameter.

3 - Moderate - multiple infiltrates ≥ 2 mm and < 3 mm in diameter.

4 - Severe - multiple dense infiltrates ≥ 3 mm in diameter.

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

Infiltrate Depth (Deepest):

OD: _____ OS: _____

1. E - Epithelial
2. AS - Anterior Stroma
3. P - mid/posterior stromal

Infiltrate Density:

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

OD: _____ OS: _____

Infiltrate Type:

OD: _____ OS: _____

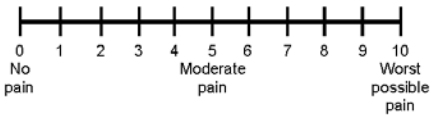
Grades

0 None
1 Micropunctate
2 Macropunctate
3 Coalesced Macropunctate
4 Patch
5 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)

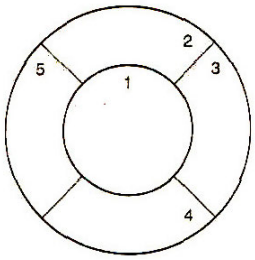
Location:

Check all that apply

OD:

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

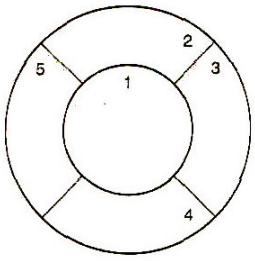
Draw:



OS:

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

Draw:



Bulbar Conjunctival Lens Compression/Indentation

OD:

Absent

Present

OS:

Absent

Present

Other Slit-Lamp Findings:

OD:

Absent

Present

_____ (specify).

OS:

Absent

Present

_____ (specify).

New Corneal Scar:

OD:

Absent

Present

OS:

Absent

Present

If present is selected, please indicate size and draw.

Size of any New Corneal scar:

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

Location:

Check all that apply

OD:

Central (central 6 mm, 3 mm from corneal center)

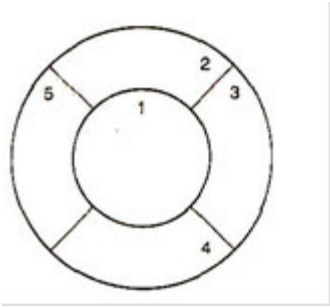
Nasal

Inferior

Temporal

Superior

Draw:



OS:

Central (central 6 mm, 3 mm from corneal center)

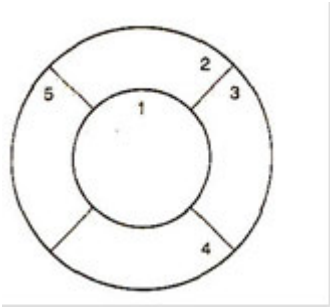
Nasal

Inferior

Temporal

Superior

Draw:



3.0 Method for the Examination, Description and Classification of Lens Deposits at Follow-up Visits

Introduction:

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 (Front and Back Surface)

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

Front Surface Deposits

0 - Absent, clean surface.

1 - Very slight, only visible after tear film drying.

2 - Slight, visible deposits easily removable.

3 - Moderate, deposits adherent and not removable.

4 - Severe, non-removable deposits and comfort affected.

Back Surface Deposits

0 - absent, clean surface.

1 - very slight, 3 spots or less of moving particles.

2 - slight, up to 10 spots of moving particles.

3 - moderate, 3 or less non-moving deposits adherent to lens.

4 - severe, 4 or more deposits adherent to the lens and/or corneal indentation.

IV. Wettability

0 - a smooth uniformly reflecting surface.

1 - a coarse hazy surface which seems resolved momentarily with each blink and becomes exacerbated with staring.

2 - one stable dry (non-wetting) area of some magnitude.

3 - more than one stable dry (non-wetting) area of some magnitude.

4 - non-wettable lens surface.

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

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

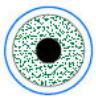
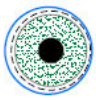
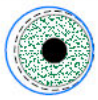
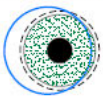
inferior portion of the lens.
  - All movement depicted in the diagram below is from the absolute centered position.
  - All movement descriptions apply from the various decentered positions.
  - Corneal exposure in any sector is an unacceptable fit.
  - If the inferior edge of the contact lens is not 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:

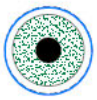
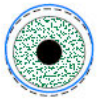
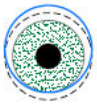
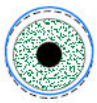
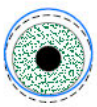
  -2 - No observable movement (perform Josephson push-up test, see below)
  -1 - Minimal; Just observable movement, lens returns to origin.
  0 - Optimal/Free movement, lens returns to origin.
  +1 - Substantial movement; but lens does not immediately return to origin.
  +2 - Excessive movement; lens does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

BAUSCH + LOMB™

PRIMARY GAZE
LENS CENTRATION

GRADE	0	1	2	3
	EQUAL OVERLAP 360 DEGREES	MAXIMUM OVERLAP ≤ 2/3 IN ANY SECTOR	MAXIMUM OVERLAP > 2/3 IN ANY SECTOR	ANY CORNEAL EXPOSURE
LIMBAL OVERLAP				

PRIMARY GAZE
LENS MOVEMENT

GRADE	-2	-1	0	+1	+2
PRE BLINK					
POST BLINK					
RETURN					
	NO OBSERVABLE MOVEMENT	MINIMAL/ JUST OBSERVABLE MOVEMENT	OPTIMAL/ FREE MOVEMENT	SUBSTANTIAL MOVEMENT	EXCESSIVE MOVEMENT

5.0 Symptoms/Complaints Rating Scales

For completion of the Symptoms/Complaints Rating Scale Form (conducted at Screening/Dispensing for the subject's habitual lenses and all follow-up visits with the study lenses), the Investigator or designee will obtain Subject responses according to the following procedure for the specific symptoms listed in the Symptoms/ Complaints Rating Table (below):

Step 1: Ask the Subject: "Are you experiencing any Symptoms or problems with the lenses?"

Step 2: If the Subject answers "*No*", enter "0" on the subject source documentation for all symptoms.

Step 3: If the Subject answers "*Yes*", then ask: "*What specifically are you noticing*". Note that the subject will *not* be shown the list of options / descriptions.

Step 4: From the Subject's response, select the most appropriate symptom (from the Symptoms/Complaints Rating Scale Table below) and ask the Subject to rate the symptom on the following scale:

0 - None
1 - Slight symptoms. The symptom is felt or noticed occasionally.
2 - Mild symptoms. The symptom is noticeable but not irritating or limiting use.
3 - Moderate symptoms. The symptom is moderately irritating or annoying; the use of device is limited by <25% (short wear time, etc.).
4 - Severe symptoms. The symptom is very irritating or annoying, and the lens cannot be tolerated.

Symptoms/Complaint Rating Table

Symptom	OS (left eye)	OD (right eye)
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	0-4

6.0 Subject Assessment Questionnaire

For completion of the Subject Assessment Questionnaire (conducted at Exit Visit), the Investigator or designee will instruct the subject to complete the form according to the care system care system that they have been using during the study. For each statement, the subject will check the box next to the appropriate number from 1 to 6, with 1 = strongly disagree and 6 = strongly agree. Boxes one through three will also be visibly grouped into a category named "disagree," while boxes four through six will be labeled as "agree." The statements are as follows:

- My lenses feel clean upon insertion
- Makes my lenses feel clean throughout the day
- Makes my lenses feel comfortable upon insertion
- Makes my lenses feel comfortable throughout the day
- Helps prevent dryness and discomfort
- My vision remains clear throughout the day
- Feels as gentle as natural tears
- Makes my lenses feel moist throughout the day
- Makes my lenses feel like a fresh pair
- Keeps my eyes feeling healthy
- Gives me a feeling of freedom to wear my lenses worry-free
- Provides long lasting comfort

7.0 Lens Performance Rating Scales

For completion by Subjects. Refer to Rating Scales (separate document) that should be provided to subjects to reference while completing form. Enter rating from 0-100 (e.g., 90).

Lens Performance Rating Scale	Scale Number
Burning and Stinging Upon Lens Insertion	1
Comfort Upon Insertion	2
Overall Comfort	3
Comfort at the End of Day	4
Ease of Handling/Insertion	5
Ease of Handling/Removal	6
Dryness	8
Vision Upon Insertion	11
Vision	12
Vision in Low Light	13
Vision at End of Day	26
Lens Cleanliness Upon Removal	15
Overall Impression	19

Abbreviated Lens Performance Rating Scale	Scale Number
Burning and Stinging Upon Lens Insertion	1
Comfort Upon Insertion	2
Ease of Handling/Insertion	5

8.0 Culture Procedures

NOTE: The site must use their standard of care culture kit and ship specimens to their local laboratory for testing per the local labs 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 the culture collection kit (provided by the central laboratory) 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 the culture collection kit (provided by the central laboratory) 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 the culture collection kit (provided by the central laboratory) 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.

APPENDIX C: SUBJECT INSTRUCTIONS

SUBJECT INSTRUCTIONS

PLEASE READ THESE INSTRUCTIONS CAREFULLY AND KEEP FOR FUTURE USE. DO NOT BRING WITH YOU TO THE FOLLOW-UP VISITS.

You will be participating in a study evaluating the clinical performance of two multi-purpose soft contact lens care solutions. Please keep all appointments and **follow these instructions thoroughly**. If you have any questions or problems, call your eye care practitioner. Remember to bring your glasses to all examinations.

NOTE: ***Wear your study lenses to each of your follow-up visits.***

STUDY PRODUCT INFORMATION:

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

- **Study Contact Lenses.**
  - You will be provided with new pairs of your current contact lenses at the start of the study, and then again at the 1-Month and 2-Month Follow-Up Visits.
- **A Study Kit**. You will be provided with a Study Kit at each visit that will contain:
  - **1 bottle of Study Solution inside a white carton.** Each bottle and each carton will have an investigational label including the Study Kit number (a unique 5-digit number).
  - **Study Lens Case.** A study lens case will be included *with each carton* of study solution for you to use for the month. *You are required to use this study lens case.*
  - **Subject Instructions.** Will be provided by unmasked designee with each carton of study solution.
  - **All items, bottle, carton and lens case must be kept and returned at each visit.**
- **Other Study Supplies.** The following supplies will be provided to you as needed:
  - **Carton/Bottle Return Materials.** Comprised of opaque bags and pre-printed labels for return of Study Kit and worn lenses to the study Investigator.
  - **Rewetting Drops***: Bausch + Lomb renu® Contact Lens Moisture Drops*

IMPORTANT SUBJECT INSTRUCTIONS:

This is a "masked" clinical study in which the Investigators and Coordinators cannot see the Study Solutions 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 opaque bag and who will handle any questions you have related to the study materials.

It is very important that you bring the study solutions or lens cases to the study site in the white opaque bag.

SUBJECT INSTRUCTIONS (continued)

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 to the Investigator or site staff during the study.
- Please save all study materials, both bottles and cartons, during the course of the study, and plan to bring study solution with you to each visit. Place the solution bottle back into the carton. Place the carton containing the bottle and contact lens cases into the white opaque 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.
- Since you are wearing your lenses on a daily wear basis, you will be using the **Study Solution** daily to clean, rinse, disinfect and store your lenses.

PRECAUTIONS:

- Lens care procedures recommended by your practitioner must be followed.
- Failure to follow these procedures may result in the development of serious eye infections.
- Discard the **Study Solution** from the lens case after each use.
- Store **Study Solution** at room temperature.
- Use **Study Solution** before the expiration date marked on the bottle label and carton.
- Do not use any eye medication in conjunction with this **Study Solution** unless under medical supervision.
- Do not touch the bottle tip of the **Study Solution** to any surface or to your eye since this may contaminate the solution.
- Keep the **Study Solution** cap closed when not in use to avoid contamination or evaporation.
- Do not use **Study Solution** with a heat disinfection method.
- Keep **Study Solution** out of reach of children.
- Consult with your study eye care practitioner if you have any allergies that may affect your ability to use a 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 Investigator.

SUBJECT INSTRUCTIONS (continued)

When used as directed, the **Study Solution**: (1) Cleans, loosens, and removes accumulations of film, protein andother deposits from soft contact lenses, and (2) Rinses and stores your soft contact lenses.

GENERAL INSTRUCTIONS:

- Always wash and rinse your hands before you handle your contact lenses.
- Lenses must be thoroughly cleaned, rinsed, and soaked each time they are removed to achieve disinfection.
- Rinse each case well with the **Study Solution** before and after each use.

LENS CLEANING INSTRUCTIONS (RUB REGIMEN):

FOR DAILY CLEANING/PROTEIN REMOVAL DISINFECTION AND STORING

- Remove the right lens from your right eye.
- Place at least 3 drops of **Study Solution** on each side of lens surface and gently rub for 20 seconds.
- Thoroughly rinse each side of the lens for 5 seconds with **Study Solution**.
- Place the cleaned contact lens in the lens case and fill with fresh **Study 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 for wear. If any debris remains on contact lenses, rinse with **Study Solution** prior to insertion.*

STUDY LENS CASE CARE:

- Before first use, rinse lens case and caps thoroughly with **Study Solution** and allow to dry.
- Clean, rinse and air-dry your lens case each time you remove your lenses. To permit excess solution to drain, flip over your lens case while air drying.
- For visits to the clinic, you need to bring the lens case to the study site.
- Place the lens case in the opaque bag for transfer to the study site.

REWETTING:

- If necessary, you can use the supplied *Bausch + Lomb renu® Contact Lens Moisture Drops* while wearing your lenses. Simply place 2 or 3 drops of *Bausch + Lomb renu® Contact Lens Moisture Drops* on contact lens whenever needed. Blink several times.
- If the lens still does not feel comfortable, add another drop.
- If discomfort persists, IMMEDIATELY remove your lens and contact your study Investigator immediately.

WEEKLY CARE:

No separate protein remover is required to remove protein deposits from the lenses. Daily use of **Study Solution** as directed removes protein.