A Safety and Effectiveness Study of a New Contact Leos Cleaning and Disinfecting Solution

PROTOCOL

STUDY#932

Sponsor.

Bausch + Lomb, lncorporated

This clinical investigation is being conducted in accordance with 21CFR Paru SO, S4, Sfi and 812, 42 USC 212(j). The protocol was developed with consideration of the provision in: ISO 1415S-1:2011 Clinical investigation of medical devices for human subjects - **Part** I: Official requirements 14ISS-2:2011 Part 2: Clinical investigation of medical devices for human subjects - **Part** 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Oplit:3 - Contact tenses and contact lens care products • Guidance for clinical investigations; ICH GCPs; and applicable local regulations.

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Original	06FEB2019
Amendment I	l3FEB2019

INVESTIGATOR STATEMENT OF APPROVAL

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

PROTOCOL

STUDY #932

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

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

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

I understand that my 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 IRBs, direct access to my medical records for study subjects.

_____

Principal Investigator, Printed Name

_____ _____

Principal Investigator, Signature Date

PERSONNEL AND FACILTIES

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

Sponsor
Bausch + Lomb, Inc.
1400 North Goodman Street
Rochester, NY 14609
US

[redacted]

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APPENDICES

LIST OF ABBREVIATIONS

Abbreviation /Acronym	Term
AADE	Anticipated Adverse Device Effect
ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CRA	Clinical Research Associate
D	Diopter
DOB	Date of Birth
eCRF	Electronic Case Report Form
FDA	United States Food and Drug Administration
GCPs	Good Clinical Practices
GP	Gas Permeable
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Identification
IRB	Institutional Review Board
ISO	International Standards Organization
ITT	Intent-to-Treat
logMAR	Logarithm of the Minimum Angle of Resolution
MCMC	Markov chain Monte Carlo
mm	Millimeter
OD	Right Eye
ORS	Oracle Randomization System
OS	Left Eye
PP	Per Protocol
PMMA	Polymethylmethacrylate
SAE	Serious Adverse Event
Tel	Telephone
USADE	Unanticipated Serious Adverse Device Effect
US	United States
VA	Visual Acuity

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

1.0 INTRODUCTION

Bausch + Lomb is evaluating an investigational cleaning and disinfecting solution, BL-ABT12 Multi-Purpose Solution ("ABT12 Multi-Purpose Solution"), for use with soft contact lenses. The aim of this study is to evaluate the safety and effectiveness of the investigational ABT12 Multi-Purpose Solution when compared to a currently marketed COMPLETE® Multi-Purpose Solution Easy Rub® Formula ("COMPLETE Multi-Purpose Solution").

ABT12 Multi-Purpose Solution is a sterile isotonic aqueous solution [containing polyaminopropyl biguanide (0.00005%), polyquaternium-1 (0.00015%), and alexidine dihydrochloride (0.00025%)] for disinfecting, cleaning, conditioning, rinsing, protein removal, and storing soft (hydrophilic) and silicone hydrogel contact lenses.

2.0 OBJECTIVE

The objective of this study is to evaluate the safety and effectiveness of ABT12 Multi-Purpose solution (Test) compared to COMPLETE® Multi-Purpose Solution Easy Rub® Formula ("COMPLETE Multi-Purpose Solution") when used by habitual contact lens wearers to bilaterally clean and disinfect their contact lenses for approximately three months.

3.0 STUDY DESIGN

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

3.1 Description of Study Design

The study is designed to examine whether ABT12 Multi-Purpose Solution cleaning and disinfecting solution is non-inferior to COMPLETE Multi-Purpose Solution in several primary endpoints.

Approximately 252 subjects (504 eyes) will be enrolled in this three-month multicenter, randomized, masked, parallel, bilateral study at approximately 18 investigative sites in the United States (US). Approximately one-half of the subjects will be randomized to receive Bausch + Lomb investigational ABT12 Multi-Purpose Solution (Test), and approximately one-half of the subjects will be randomized to receive COMPLETE® 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 (sufficient for the entire study) according to the subject's unique randomization schedule. Subjects may also be dispensed a supply of Sensitive Eyes® Rewetting 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 cleaning and disinfecting 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 on a 1:1 basis within each lens group per site to receive either the Test or Control cleaning and disinfecting 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 1: 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**	**Optix Aqua**	**Alcon**
5-Cr	**Senofilcon C**	**Vita**	**Vistakon**

3.2 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 they participate in the study or not. Bausch + Lomb will provide a Screening and Enrollment Log on which to enter information for each subject who signs an ICF. Once a potential subject is consented and their initials are entered onto the Screening and Enrollment Log, the Investigator should proceed with screening procedures.

Potential subjects are deemed either “Screen Pass” or “Screen Fail.” “Screen Fail” subjects have not met the study inclusion criteria or have met the exclusion criteria. “Screen Fail” subjects cannot participate in the study. Electronic case report forms (eCRFs) must not be completed for “Screen Fail” subjects; 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.

“Screen Pass” subjects have met all of the study inclusion criteria and have not met any of the exclusion criteria. Only “Screen Pass” subjects are eligible to participate in the study and will be assigned a subject identification (ID) number from the randomization system.

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

3.2.1 Eligibility

3.2.1.1 Inclusion Criteria

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

1. Is of legal age (at least 18) on the date the Informed Consent Form (ICF) is signed and has the capacity to provide voluntary informed consent.
2. Is able to read, understand, and provide written informed consent on the Institutional Review Board (IRB) approved ICF and provide authorization as appropriate for local privacy regulations.
3. Is a habitual wearer (at least 3 months) of one of the 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**	**Optix Aqua**	**Alcon**
5-Cr	**Senofilcon C**	**Vita**	**Vistakon**

4. Is correctable through spherocylindrical refraction to 32 letters (0.3 logMAR) or better (distance, high contrast) in each eye with soft spherical contact lenses.
5. Has clear central corneas and is free of any anterior segment disorders.
6. Is a habitual user of a lens care product for cleaning, disinfecting, and storage of lenses.
7. Requires lens correction in both eyes.
8. Wears the same manufacturer and brand of lens in both eyes.
9. Agrees to wear study lenses on a daily wear basis for approximately three months.
10. Is willing and able to comply with all treatment and follow-up/study procedures.

3.2.1.2 Exclusion Criteria

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

1. Subjects who currently use a hydrogen-peroxide cleaning and disinfecting solution
2. Participating in any drug or device clinical investigation within 30 days prior to entry into this study and/or during the period of study participation.

3. Females of childbearing potential (those who are not surgically sterilized or postmenopausal) if they meet any one of the following conditions:
   - they are currently pregnant
   - they plan to become pregnant during the study
   - they are breastfeeding
4. Has worn gas permeable (GP) lenses within the last 30 days.
5. Has worn polymethylmethacrylate (PMMA) lenses within the last three months.
6. Has any systemic disease currently affecting ocular health or which in the Investigator's opinion may have an effect on ocular health during the course of the study.
7. Has any ocular disease or is using any ocular medication.
8. Is using any systemic or topical medications that will, in the Investigator's opinion, affect ocular physiology or lens performance.
9. Currently wears monovision, multifocal, or toric contact lenses.
10. Has ocular astigmatism of 1.00D or greater in either eye.
11. Is not correctable through spherocylindrical refraction to 32 letters (0.3 logMAR) or better (distance, high contrast) in each eye with soft spherical contact lenses.
12. Has anisometropia (spherical equivalent) of greater than 2.00D.
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. Subjects with any "Present" 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. *Note that subjects with minor peripheral corneal scarring (that does not extend into the central area), that, in the Investigator's judgment, does not interfere with contact lens wear, are eligible for this study.*
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.

3.2.2 **Subject Completion**

The subject has completed the study when the Exit Visit is concluded at the 3-Month Follow-up Visit. Subjects who require further follow-up for an adverse event (AE) will be followed according to Section 6.2.

3.2.3 **Subject Discontinuation**

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

- An adverse event (AE) occurring during the course of the study, which precludes continued treatment or follow-up
- Persistent grade 3 or 4 slit lamp findings (must be reported to the Sponsor within 24 hours)
- Persistent study related symptoms/complaints
- Unacceptable distance lens visual acuity (VA)
- Unacceptable lens centration
- Unacceptable lens movement
- Other reasons related to 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
- Ineligible at baseline - does not meet the eligibility criteria in the protocol
- Inability to maintain recommended wearing schedule
- Lack of motivation
- Continued failure to follow subject instructions
- Misses any follow-up visit
- Lost to follow-up (refer to Section 3.2.4)
- Instillation of non-medically indicated solution not specified in the protocol
- 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 will 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 that are discontinued from the study following randomization will not be replaced.

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

3.2.4 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. 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.

3.3 Investigators

The study will be conducted at approximately 18 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. Principal Investigators will sign the Device Investigator Agreement form prior to the start of the study.

Each Investigator will enroll approximately 14 subjects, 28 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.

3.4 Study Duration

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

Subjects will be followed for approximately 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	10 - 18 Days
1-Month Follow-up Visit	30 Days	26 – 34 Days
2- Month Follow-up Visit	60 Days	53 – 67 Days
3-Month Follow-up Visit	90 Days	83 – 97 Days

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

3.5 Treatments

Eligible subjects will be randomized to use ABT12 Multi-Purpose Solution (Test) or COMPLETE Multi-Purpose Solution (Control). At the initial Screening/Dispensing Visit, each subject will be provided with a Study Kit (containing Test or Control solution sufficient for the full study duration, study lens cases, and Subject Instructions), and with other study supplies as needed (e.g., Sensitive Eyes® Rewetting 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 (non B+L brands) are to be purchased through the site's normal ordering process and will be reimbursed by the Sponsor. All other materials will be provided to the site prior to the start of the study. Refer to Product Replacement Section 4.7 for ordering replacement test or control product in case of loss or damage.

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

4.1 Description of Test Article-(Test)

ABT12 Multi-Purpose Solution cleaning and disinfecting solution is a sterile isotonic aqueous solution containing polyaminopropyl biguanide (0.00005%), polyquaternium-1 (0.00015%), and alexidine dihydrochloride (0.00025%) for disinfecting, cleaning, conditioning, rinsing, protein removal, and storing soft (hydrophilic) and silicone hydrogel contact lenses.

4.2 Description of Comparator Product (Control)

COMPLETE® Multi-Purpose Solution Easy Rub® Formula ("COMPLETE Multi-Purpose Solution") cleaning and disinfecting solution (Control) is indicated for the care of soft contact lenses. COMPLETE Multi-Purpose Solution is a sterile, isotonic, buffered solution, preserved with polyhexamethylene biguanide (0.0001%), a phosphate buffer, Poloxamer 237, edetate disodium, sodium chloride, potassium chloride, and purified water.

4.3 Instructions for Use and Administration

Based on the randomization assignment, each randomized subject will be assigned a unique subject ID number. Each subject will be issued a Study Kit labeled with a unique Study Kit number. Subjects will be dispensed 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. 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 with their study lens care solution carton for 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.

Subjects are to be instructed not to discuss or show the dispensed study products or lens care system to the Investigator or masked site staff during the study.

4.3.1 Storage Requirements

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

4.3.2 Subject Instructions

a. All subjects must be given Subject Instructions for the use of study articles (refer to Appendix C for Subject Instructions). Subjects must comply with the instructions provided to them. Subject Instructions will be included with each carton of study solution.

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

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

4.4 Packaging and Labeling

4.4.1 Lenses

The site is responsible for ordering all habitual contact lenses needed for the study and submitting an invoice for reimbursement. 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 that 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:

- **5 bottles 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 Study Kit number (a unique 5-digit number) and a bottle number (1, 2, 3, 4 or 5). Cartons containing bottles 1, 2, 3 and 4 will be provided to subjects at the Screening/Dispensing Visit, and the carton containing bottle 5 will serve as a reserve bottle to be retained at the site for each dispensed subject in the event that an unscheduled replenishment is required. The subject number may be written on the outside carton ONLY. The bottles should not be written on or labelled.

- **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.** Will be included with each carton of study solution.

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 drawstring bags and pre-printed labels for return of Test and Control articles (full, partially full, and empty bottles) to the Sponsor.
- **Lens Return Materials**. Comprised of sealable plastic bags and pre-printed labels for return of worn lenses to the Sponsor (in a fresh lens case with the approved saline solution). The unmasked designee will place worn lenses in Sensitive Eyes Saline Solution in a supplied fresh lens case (not the lens case that was used by the subject in between visits). The case will be put in a sealable plastic bag. The preprinted label is to be adhered to the sealable plastic bag. Label will identify such information as study number, site identification number, subject number, subject initials, lens type, date dispensed, date removed, quantity of lenses returned (should be one lens for each eye).
- ***Sensitive Eyes*® Rewetting Drops**

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

4.5 Accountability

The unmasked designee will be responsible for keeping current and accurate records of study materials during the course of the study. The records will include an inventory of the quantity and disposition of study test articles and habitual contact lenses received by the site, an inventory of all test articles and habitual contact lenses dispensed to or returned by the subject, including subject ID and Study Kit identifiers. Accountability logs will be provided to the sites to maintain records of the study articles, including the habitual contact lenses, assigned to each enrolled subject.

The study articles must be stored under the appropriate conditions (room temperature) in a secure area and are to be dispensed only to subjects enrolled in the study, in accordance with the conditions specified in this protocol.

Upon completion of the study, the field Clinical Research Associates (CRAs) will review and verify the Investigator's accountability records.

Following verification, and as directed by the Sponsor, all used and unused study supplies (study solutions, unused contact lenses, and lens cases including worn lenses) must be returned to the Sponsor at the address below:

Bausch + Lomb, Inc.

4.6 Masking/Unmasking

The Investigator and Sponsor/Sponsor's representatives involved in the conduct of the study will be masked to the study cleaning and disinfecting solutions. The randomization schedule will be produced prior to study enrollment and uploaded into ORS.

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

Study solutions will be provided in sealed opaque white boxes with Study Kit numbers preprinted on them. Subjects are not to show the study solution to or discuss their care regimen 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.

While there will be unique features of each of the solution bottles, efforts will be made to keep subjects masked to their solution by removing or covering the manufacturer's label.

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 (Dan Donatello, see Personnel and Facilities Page 3) and obtain approval to grant permission to unmask. Upon receipt of authorization from the Sponsor designee, the Medical Monitor will advise the Investigator (or other qualified designee) to log into the randomization system and unmask the subject. If the Medical Monitor cannot be contacted, the Investigator (or other qualified designee) should 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 ORS without authorization and unmask the subject. Whether unmasking occurs inadvertently or intentionally, the Investigator must notify the Medical Monitor or Sponsor designee as soon as possible after unmasking. In addition, the Investigator must record the date, time, and reason for unmasking the study treatment in the source documentation.

4.7 Product Replacement

As described in Section 4.4.2, a labeled reserve bottle of Test or Control product, in a labeled and sealed carton, will be retained in-office for each dispensed subject in the event that unscheduled study kit replenishment is required. These reserve cartons/bottles will be labeled with an investigational label including a Study Kit number (a unique 5-digit number) and bottle number (bottle 5).

Any additional/replacement (in the case of loss or damage) Test or Control product must be ordered through the randomization system according to the subject randomization.

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

5.0 SAFETY AND EFFECTIVENESS VARIABLES

Safety and effectiveness endpoints are also shown in Section 8.1.

5.1 Safety Variables

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

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

5.2 Primary Effectiveness Variables

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

- Overall comfort averaged over all follow-up visits
- Dryness averaged over all follow-up visits
- Optimal (none or light) lens deposits at all follow-up visits

5.3 Risk Assessment

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

6.0 STUDY METHODS

6.1 Study Visits

Refer to APPENDIX A for a Schedule of Visits and Parameters and APPENDIX B for Methods of Clinical Evaluation.

Prior to enrollment into the study, the Investigator (or designee) will explain the purpose of the study, procedures, risks/benefits, and subject responsibilities to the potential participant. The subject's willingness and ability to meet the follow-up requirements of the study will be determined. If the subject chooses to participate in the investigation, written 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	Initial Symptoms/Complaints (Worn Lenses Symptoms/Complaints) Symptoms/Complaints (Abbreviated Study Lenses Symptoms/Complaints)
2-Week Follow-up Visit	Symptoms/Complaints (Study Lenses Symptoms/Complaints)
1-Month Follow-up Visit	Symptoms/Complaints (Study Lenses Symptoms/Complaints)
2-Month Follow-up Visit	Symptoms/Complaints (Study Lenses Symptoms/Complaints)
3-Month Follow-up Visit	Symptoms/Complaints (Study Lenses Symptoms/Complaints)
Unscheduled Visit(s)	Symptoms/Complaints (Study Lenses Symptoms/Complaints)

6.1.1 Screening/Dispensing Visit

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

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

The Screening/Dispensing Visit will proceed as follows:

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

a. Enter the following information on the next available line of the Screening and Enrollment Log:
   - Subject Number
   - Subject Initials
   - Subject Date of Birth (DOB)
   - Gender
   - Habitual Lens Group
   - Visit 1 (Screening/Dispensing) Date

b. Collect demographic information and record in the subject's source document.

c. Collect the following baseline lens/lens care history information and lens wear parameters from the subject and record in the subject's source document:
   - Average daily wearing time
   - Hours lenses worn on the day of this visit
   - Average hours of comfortable wear
   - Current lens brand, sphere power and base curve
   - Current lens care products

d. Perform the following baseline assessments (without lenses; remove the lenses if the subject wore lenses to the visit) and record in the subject's source document:

   - Spherocylindrical refraction
   - High contrast distance best 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 Symptoms/Complaints Form (Worn Lenses Symptoms/Complaints Form), including use of rewetting drops.

   Site personnel will transcribe this information to the Visit electronic Case Report Form (eCRF), and will retain the original in the study files.

g. Complete the Initial Lens Performance Assessment Form (Worn Lenses Performance Rating Scales).

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.

j. Instruct subject to complete Symptoms/Complaints Form (Abbreviated version: Study Lenses Symptoms/Complaints).

k. Complete the Lens Performance Assessment Form (Study Lenses Performance Rating Scales).

l. Record the following into the subject's source documentation:

   - 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 high contrast distance lens VA to the high contrast Distance Best Spectacle-Corrected VA obtained at this visit. If the VA has decreased by 5 letters (0.1 logMAR) or more, explain.

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

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

- *If the subject is a "Screen Fail"*: the reason for screen failure must be documented on the Screening and Enrollment Log and in the subject record, and maintained with a copy of their ICF.

n. If the subject is a "Screen Pass" the Unmasked Designee should then dispense Study Kit bottles 1, 2, 3, and 4 only (keeping bottle 5 as a reserve at the site) (refer to Section 4.4.2) to the subject and record in the subject's individual Product Accountability Log.

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

- Cartons and bottles are NOT to be opened in front of any other site personnel.
- The subject should retain all study materials during the course of the study.
- Prior to coming to the site for the 3-month, exit or early study termination/suspension visits, follow-up visit or exit visit the subject should: (i) place all used and unused study solution bottles into their original white cartons, (ii) place the cartons and all lens cases into the opaque white drawstring return bag, (iii) close the bag, and (iv) return it to the unmasked designee.

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

q. If the Subject was randomized (a subject ID has been assigned in ORS) and needs to be exited during this visit, complete the Exit Visit as per Section 6.1.5.

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

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

6.1.2 **2-Week Follow-up Visit**

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

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

a. If a subject misses the scheduled follow-up visit and cannot be seen prior to the start of the visit window for the next scheduled follow-up visit, then the visit is considered missed, and the subject must be exited from the study (see Section 3.2.3).

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 Lens Performance Assessment Form (Study Lenses Performance Rating Scales).

d. Have the subject complete and initial the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints Rating Scales), including use of rewetting drops.

- Site personnel will transcribe this information to the visit eCRF, and will retain the original in the study files.

e. Collect any relevant medical treatment information, including any adverse events, on the 2-Week Follow-up Visit Form, 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) and record the following assessments into the subject's source document:

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

g. Perform a slit lamp examination (remove and store the lenses if the subject wore lenses to the visit). A lens case must be filled with Sensitive Eyes saline (NOT dispensed study solution) for storage of subject's lenses during the exam. Record the results in the subject's source document. If a corneal infiltrate is noted fill out the Corneal infiltrate form.

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

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

j. 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, k.

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

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

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

m. If needed, dispense a new labeled reserve bottle of Test or Control product according to the subject's ID number, and record in the subject's individual Product Accountability Log. If needed, dispense any other supplies.

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

<u>The 1-Month and 2-Month Follow-up Visits will proceed as follows:</u>

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

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 and subject must be exited from the study (see Section 3.2.3)

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 Lens Performance Assessment Form. (Study Lenses Performance Rating Scales).

d. Have the subject complete, and initial the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints Rating Scales), including use of rewetting drops.

- Site personnel will transcribe this information to the visit eCRF, and will retain the original in the study files.

e. Collect any relevant medical treatment information, including any adverse events, on the 1- or 2-Month Follow-up Visit Form, 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), and record the following assessments on the subject's source documentation:

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

g. Perform a slit lamp examination (remove 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 fill out the Corneal infiltrate form.

h. Collect the worn lenses from the subject and return all worn study lenses to the Sponsor or designee using the return materials provided (refer to Section 4.4.3). Worn lenses will be returned in lens cases filled with Bausch + Lomb Sensitive Eyes Saline Solution.

i. Dispense a new pair of subject's habitual lenses, instruct the subject to insert the lenses, and collect the following information in the subject's source documentation:

- 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 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.

j. If needed, dispense a new labeled reserve bottle of Test or Control product according to the subject's ID number, and record in the subject's individual Product Accountability Log. If needed, dispense any other supplies.

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

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

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

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 use the cleaning and disinfecting 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 five days)

b. Complete the Lens Performance Assessment Form (Study Lenses Performance Rating Scales).

c. Have the subject complete Symptoms/Complaints Form (Study Lenses Symptoms/Complaints Rating Scales), including use of rewetting drops.

- Site personnel will transcribe this information to the visit eCRF, and will retain the original in the study files.

d. Indicate if a Post-study Follow-up Visit is required and, if necessary, schedule the subject accordingly.

e. Collect any relevant medical treatment information, including any adverse events, on the 3-Month Follow-up Visit Form, 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) and record the following assessments on the subject's source documentation:

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

g. Perform a slit lamp examination (remove 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 fill out the Corneal infiltrate form.

h. Collect all worn dispensed lenses and used and unused bottles of study solution from the subject and return all to the Sponsor or designee using the return materials provided (refer to Section 4.4.3). Worn lenses will be returned in lens cases filled with Bausch + Lomb Sensitive Eyes Saline Solution. It is important that the site personnel do not observe the contents of the study solution return bag.

i. Complete the Exit Visit as per Section 6.1.5.

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

- 3-Month Follow-up Visit Form
- Exit Visit Form (if there is an ongoing AE at the time of the 3 month visit, do not complete the Exit Visit and schedule a Post Study Visit instead)

6.1.5 **Exit Visit**

<u>The Exit Visit will proceed as follows:</u>

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

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

- Spherocylindrical refraction
- High contrast distance BSCVA
- Keratometry

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

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

e. Collect all worn dispensed lenses and Study Kits (if not collected previously) from the subject and return all to the Sponsor or designee using the return materials provided (refer to Section 4.4.3). Worn lenses will be returned in lens cases filled with Bausch + Lomb Sensitive Eyes Saline Solution.

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. Visits intended to fulfill scheduled visit requirements that fall outside the designated scheduled visit range are not Unscheduled Visits. In these cases, the visit data will be collected and transcribed to the appropriate scheduled visit eCRF.

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

Unscheduled Visits will proceed as follows:

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

a. Indicate the reason for the Unscheduled Visit.

b. If the subject is experiencing problems, complete the Unscheduled Visit Form.

c. If this visit is to dispense study materials only 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 Lens Performance Assessment Form (Study Lenses Performance Rating Scales).

f. Have the subject complete and initial the Symptoms/Complaints Form (Study Lenses Symptoms/Complaints), including use of rewetting drops.

- Site personnel will transcribe this information to the visit eCRF, and will retain the original in the study files.

g. Collect any relevant medical treatment information, including any adverse events, on the Unscheduled Visit Form, 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) and record the following assessments on the source documentation:

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

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 fill out the Corneal infiltrate form.

j. If additional study solution is required at this visit, dispense a new labeled reserve bottle of Test or Control product according to the subject's ID number, and record in the Product Accountability Log. If a new Study Kit is required, log into ORS to dispense a new Study Kit (refer to Section 4.4.3) to the subject according to ORS notification email and record in the Product Accountability.

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 in the subject's source documentation:

- Primary (one) reason for replacement
- Dispensed lens type (brand), sphere power, base curve
- High contrast distance lens VA
- Over-refraction and distance VA
- Lens wettability
- Lens discoloration
- 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.

l. If Study Lenses were replaced, collect the worn lenses from the subject and return all worn study lenses to the Sponsor or designee using the return materials provided (refer to Section 4.4.2). Worn lenses will be returned in lens cases filled with Bausch + Lomb Sensitive Eyes Saline Solution.

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

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

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

6.1.7 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, and the subject must be exited (see Section 3.2.3).

6.1.8 Product Dispensing Only Visit

Product Dispensing Only Visits will proceed as follows:

a. If a subject is seen for resupply or replacement of study materials only, 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).

b. If additional Study Solution is required at this visit, go to Unscheduled Visit Section 6.1.6, j.

c. If a lens replacement is required, go to Unscheduled Visit Section 6.1.6, k.

6.2 Post-study Follow-up

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

a. If a subject requires further follow-up upon discontinuation or completion of the study, the Investigator must schedule post-study follow-up visits, as necessary. The Investigator is required to follow the subject until the condition no longer warrants further follow-up for study purposes. A Post-study Follow-up Visit eCRF must be completed for each of these visits.

b. 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 to the eCRF as appropriate. If a corneal infiltrate is noted fill out the Corneal infiltrate form.

c. Complete an ocular examination without lenses on the eyes, including spherocylindrical refraction and high contrast distance BSCVA.

d. Compare the high contrast distance BSCVA to the high contrast distance BSCVA obtained at the Screening/Dispensing Visit. If the VA has decreased by 10 letters (0.2 logMAR) or more, explain.

e. If the subject is exiting the study at this visit, complete Exit Visit as per Section 6.1.5.

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

- Post-study Follow-up Visit Form
- Exit Visit Form

6.3 Study Completion

6.3.1 Study Completion

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

6.3.2 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, the study will be terminated and appropriate notification will be given to the Investigator(s), IRBs, and FDA, as applicable. Bausch + Lomb will instruct the Investigators to stop/restart dispensing study materials and will arrange for study closeout, if applicable, at each site.

6.4 Concomitant Medications/Therapy

Other ocular solutions, medications or drops are not allowed to be used by subjects during the study. Use of other contact lenses are 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 source document and the appropriate eCRF.

6.5 Treatment Compliance

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

6.6 Protocol Deviations

The date of and reason for deviations (failure to comply with the protocol, eligibility or randomization errors, not done visits, out of window study visits, worn lenses not returned, habitual lenses not worn daily, etc.) will be documented in all cases. Significant or major protocol deviations impacting the safety of the subject or the integrity of the study must be reported by the Investigator to the IRB and Medical Monitor immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB.

A subject may continue to participate until the end of the study, unless the protocol deviations put the subject at risk, the subject's condition requires that the subject be discontinued from the study or other sections of this protocol state that the subject must be discontinued due to the deviation (see Section 3.2.3).

7.0 ADVERSE EVENTS

7.1 Adverse Event Definitions

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

7.1.1 Adverse Event (AE)

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

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

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

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

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

7.1.2 Adverse Device Effect (ADE)

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

7.1.2.1 Anticipated Serious Adverse Device Effect (ASADE)

An anticipated serious adverse device effect (ASADE) is an ADE that first meets the serious criteria (see Section 7.1.3) or significant non-serious criteria (see Section 7.1.4) and which, by its nature, incidence, severity or outcome, has been previously identified in the investigational plan or application (including a supplementary plan or application) and/or in the risk analysis report. ASADEs include:

- Corneal Ulcer (infectious or non-infectious)
- Keratitis
- Sensitivity to light (photophobia)
- Excessive eye secretions including mucopurulent discharge

- Blurred vision, rainbows or halos around objects
- Poor visual acuity (reduced sharpness of vision)
- Moderate to severe eye pain not relieved by removing the lens

7.1.2.2 Unanticipated Serious Adverse Device Effect (USADE)

An unanticipated serious adverse device effect (USADE) is an ADE that first meets the serious criteria (see Section 7.1.3) or significant non-serious criteria (see Section 7.1.4) and has an effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.1.3 Serious Adverse Event (SAE)

An AE that:

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

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

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

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

- A presumed infectious ulcer (defined as a progressive erosion of the corneal tissue). For the purposes of reporting, this includes:
  - Central or para-central location;
  - Penetration of Bowman's membrane;
  - Infiltrate ≥2 mm diameter;
  - Associated with iritis;
  - Associated with any increase in intraocular pressure;
  - Culture positive for microorganisms;
  - Increasing size or severity at subsequent visits;

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

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

7.1.4 Significant Non-Serious Adverse Events

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

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

7.1.5 Non-Significant Non-Serious Adverse Events

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

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

7.2 Adverse Event Treatment and Culturing

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

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

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

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

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

7.3 Evaluations

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

7.3.1 Severity

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

7.3.2 Relationship to Study Device and/or Rewetting Drops

- **Related:** There is at least a reasonable possibility that the AE is related to the study device (study solution) and/or rewetting drops. Reasonable possibility means that there is evidence to suggest a causal relationship or association between the study device and/or rewetting drops and the AE. Also referred to as an ADE.
- **Unrelated:** There is little or no reasonable possibility that the AE is related to the study device (study solution) and/or rewetting drops. This assessment implies that the AE has no evidence to suggest either a causal relationship

or association to the study device and/or Rewetting Drops and a more likely or certain alternative etiology exists.

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

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

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

representatives may contact the Investigator to request further information concerning the treatment.

- Report all 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.

7.4.1 Off-Site Unanticipated Serious Adverse Device Effect Reporting

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 test article, that met the criteria for reporting to a regulatory agency. These should be reported to the reviewing IRB within 10 working days or per their established reporting procedures, whichever is shorter.

7.4.2 Reporting Device Deficiencies

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

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

Report device deficiencies within 24 hours of knowledge to:

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

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

7.4.3 Guidelines for Reporting Pregnancies

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

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

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

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

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

The contact for reporting pregnancies and pregnancy outcomes are:

8.0 STATISTICAL METHODS

8.1 Study Endpoints

8.1.1 Primary Effectiveness Endpoints

a. Overall comfort averaged over all follow-up visits.

b. Dryness averaged over all follow-up visits.

c. Lens deposits at all follow-up visits.

8.1.2 Secondary Effectiveness Endpoints

There are no secondary effectiveness endpoints.

8.1.3 Primary Safety Endpoint

Slit lamp findings greater than Grade 2.

8.2 Hypotheses

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 Dryness Averaged Over All Follow-up Visits

The null hypothesis (H_0) is that the difference in mean dryness 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 Lens Deposits at All Follow-up Visits

The null hypothesis (H_0) is that the difference in the proportion of eyes with None or Light ratings of lens deposits at all Follow-up Visits (test group proportion [rr_T] minus standard group proportion [rr_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%).

$$H_0: rr_T - rr_S \leq -0.1$$

$$H_1: rr_T - rr_S > -0.1$$

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 [rr_T] minus standard group proportion [rr_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%).

$$H_0: rr_T - rr_S \geq 0.05$$

$$H_1: rr_T - rr_S < 0.05$$

8.3 Sample Size

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

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

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

8.3.1 Overall Comfort

When the sample size in each group is 226, a two group 0.025 one-sided t-test will have 96.82% power to reject the null hypothesis that the test is not non-inferior to the standard (the difference in means, μ_T - μ_S, is -5 or farther from zero in the same direction) in favor of the alternative hypothesis that the test is non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 13.9.

8.3.2 Dryness

When the sample size in each group is 226, a two group 0.025 one-sided t-test will have 96.62% power to reject the null hypothesis that the test is not non-inferior to the standard (the difference in means, μ_T - μ_S, is -5 or farther from zero in the same direction) in favor of the alternative hypothesis that the test is non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 14.0.

8.3.3 Lens Deposits

With 226 eyes in each group, the lower limit of the observed one-sided 97.5% confidence interval will be expected to exceed -0.100 with 97.38% power when the Standard proportion, π_S, is 0.925 and the Test expected proportion, π_T, is 0.925; results are based on 100,000 simulations using the Newcombe-Wilson score method to construct the confidence interval.[2]

8.3.4 Slit Lamp Findings Greater than Grade 2

With 226 eyes in each group, the upper limit of the observed one-sided 97.5% confidence interval will be expected to be less than 0.050 with 99.00% power when the Standard proportion, π_S, is 0.005 and the Test expected proportion, π_T, is 0.005; results are based on 100000 simulations using the Newcombe-Wilson score method to construct the confidence interval.[2]

8.3.5 Overall Power

If the four primary endpoints are independent, the overall power of the study is 96.82% x 96.62% x 97.38% x 99.00% = 90.18%.

8.3.6 Enrollment Target

Allowing for up to 10% losses, the enrollment target in each treatment group will be $\mathrm{r}113 \div (1 - 0.1)1 = 126$. Consequently, the total enrollment target will be approximately 252 subjects (504 eyes).

8.4 Randomization

Subjects will be randomized to one of two treatment arms in a 1:1 ratio, using Test solution or Control solution for the duration of the study. Randomization will be managed using ORS. The randomization will be stratified by lens group within investigational site. The lens group will be determined by the subjects' habitual lens material at baseline and will be one of the groups shown in Table 1 above (page 9).

Efforts will be made to enroll subjects in at least four of the lens strata within each site to minimize confounding between site and lens strata. It should be noted that while the target enrollment for each lens strata is approximately 50 subjects (approximately 25 per treatment arm), some lens strata may be difficult to enroll.

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

8.5 Study Populations

8.5.1 Intent-to-Treat (ITT) Population

The ITT Population will consist of all randomized subjects 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 be the primary population used for analysis of the primary effectiveness endpoints. The PP Population will consist of all ITT Population subjects without important (major) protocol deviations for subject level summaries and, for eye level summaries, both of their eyes. Important protocol deviation categories are defined in Section 8.6.4 below (page 41). Subjects will be included in PP Population summaries according to the treatment group to which they were randomly assigned. The PP population will be determined prior to study unmasking.

8.5.3 Safety Population

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

8.6 Statistical Analysis

8.6.1 Methods of Analysis

8.6.1.1 General Methods

Continuous data will be summarized using descriptive statistics: sample size (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 at the given visit for each respective study treatment, 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.

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

8.6.1.2 Overall Comfort

At each follow-up visit, overall comfort will be assessed for each eye on a scale from 0 to 100, with 100 denoting the most favorable response. For each eye, mean overall comfort over all follow-up visits will be computed as the average of the non-missing values over all scheduled follow-up visits. Missing data will not be imputed for the primary analysis. Mean overall comfort over all follow-up visits will be summarized at the eye level by treatment using continuous summary statistics for the Per Protocol Set in a table. A one-sided lower 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 factor of treatment and the fixed blocking factor of site, will be displayed. If the lower confidence limit is greater than -5.0, then the null hypothesis that the test solution is not non- inferior will be rejected, and the test solution will be statistically successful in this outcome.

As a sensitivity analysis, the ITT Population will be analyzed for this endpoint. Summaries by treatment and a confidence interval around the difference in means will be provided as described above using the available data. Twenty-five imputations of missing overall comfort data will be produced using the Markov chain Monte Carlo (MCMC) method with a seed of 1674236965. The variables used to create the imputed datasets will be the randomized treatment assignments (categorical), the subject identification numbers (categorical), and the overall comfort scores observed at each scheduled visit. The differences and standard errors estimated by imputation will be combined to create an estimated difference and confidence limit.

8.6.1.3 Dryness

At each follow-up visit, dryness will be assessed for each eye on a scale from 0 to 100, with 100 denoting the most favorable response. Dryness will be analyzed using the methods described above for overall comfort. The seed for multiple imputation will be 1975251391.

8.6.1.4 Lens Deposits

At each follow-up visit, lens deposits degree will be assessed for each eye as none, light, medium, or heavy. Using only the non-missing observations from scheduled follow-up

visits without imputation, each eye will be classified with respect to the maximum observed grade of Deposits at All Follow-up Visits (None or Light, Medium or Heavy). Missing data will not be imputed for the primary analysis. Maximum Deposits over All Follow-up Visits (None or Light, Medium or Heavy) will be summarized at the eye level by treatment using categorical summary statistics for the Per Protocol Set in a table. A one-sided lower 97.5% confidence limit around the difference in None or Light Deposits proportions between the test and control treatment groups will be constructed using the Newcombe-Wilson score method.[2] If the lower confidence limit is greater than -10.0%, then the null hypothesis that the test solution is not non-inferior will be rejected, and the test solution will be statistically successful in this outcome.

As a sensitivity analysis, the ITT Population will be analyzed for this endpoint. Summaries by treatment and a confidence interval around the difference in means will be provided as described above using the available data. The effects of missing data will be explored by considering best case and worst-case imputation scenarios. If the statistical conclusion differs between the best and worst-case scenarios, then a tipping point analysis will be completed.

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 without imputation, each eye will be classified with respect to findings greater than grade 2 at any visit (Absent, Present). Missing data will not be imputed. Greater than grade 2 findings (Absent, Present) will be summarized at the eye level by treatment using categorical summary statistics for the Safety Set in a table. A one-sided upper 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.[2] If the upper confidence limit is less than 5.0%, then the null hypothesis that the test solution is not non-inferior will be rejected, and the test solution will be statistically successful in this outcome.

8.6.2 Subject Demographics and Baseline Characteristics

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

8.6.3 Subject Discontinuation

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

8.6.4 Protocol Deviations

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

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

- Ineligibility
- Not dispensed study treatment
- 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.

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

8.6.5 Treatment Compliance

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

8.6.6 Treatment Exposure

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

8.6.7 Missing Data

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

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

8.6.8 Interim Analyses

No interim analyses are planned.

9.0 DATA QUALITY ASSURANCE

9.1 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, 21CFR Parts 50, 54, 56 and 812, 42 USC 282(j) and with consideration of the provision in: ISO 14155-1:2009 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2009 Part 2:

Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2009 Ophthalmic Optics – Contact Lenses and contact lens care products – Guidance for clinical investigations; ICH GCPs; 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
- 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.

9.2 Source Documentation

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

Examples of source documents include: hospital records, clinical and office charts, laboratory notes, memoranda, signed 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.

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

The CRA will be responsible for reviewing and verifying 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.

9.4 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 and by initials. 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 approvals for the study protocol, all amendments, ICF(s), and advertisements
- IRB annual study review
- IRB correspondence and reports (e.g., AE reports, protocol deviations, and safety updates)
- regulatory documents (e.g., financial disclosure and delegation of authority forms)
- 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.

9.5 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, the Investigator must inform the Sponsor immediately that this request has been made.

9.6 Institutional Review Board

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

- 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 approval of the study protocol and informed consent must be provided to the Sponsor prior to initiation of the study. In addition, the Investigator must

ensure that the reviewing IRB has provided approval for any protocol amendments prior to implementation. If the amendment necessitates a revision to the ICF, the Investigator should ensure the revised form is also submitted to and approved by the Sponsor and the IRB and implemented as directed.

9.7 Publication of Results

All study data generated as a result of this study will be regarded as confidential, until appropriate analysis and review by the Sponsor or its designee and the Investigator(s) are completed. The results of the study may be published or presented by the Investigator(s) after 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

[1] 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)

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

APPENDIX A: SCHEDULE OF VISITS AND PARAMETERS

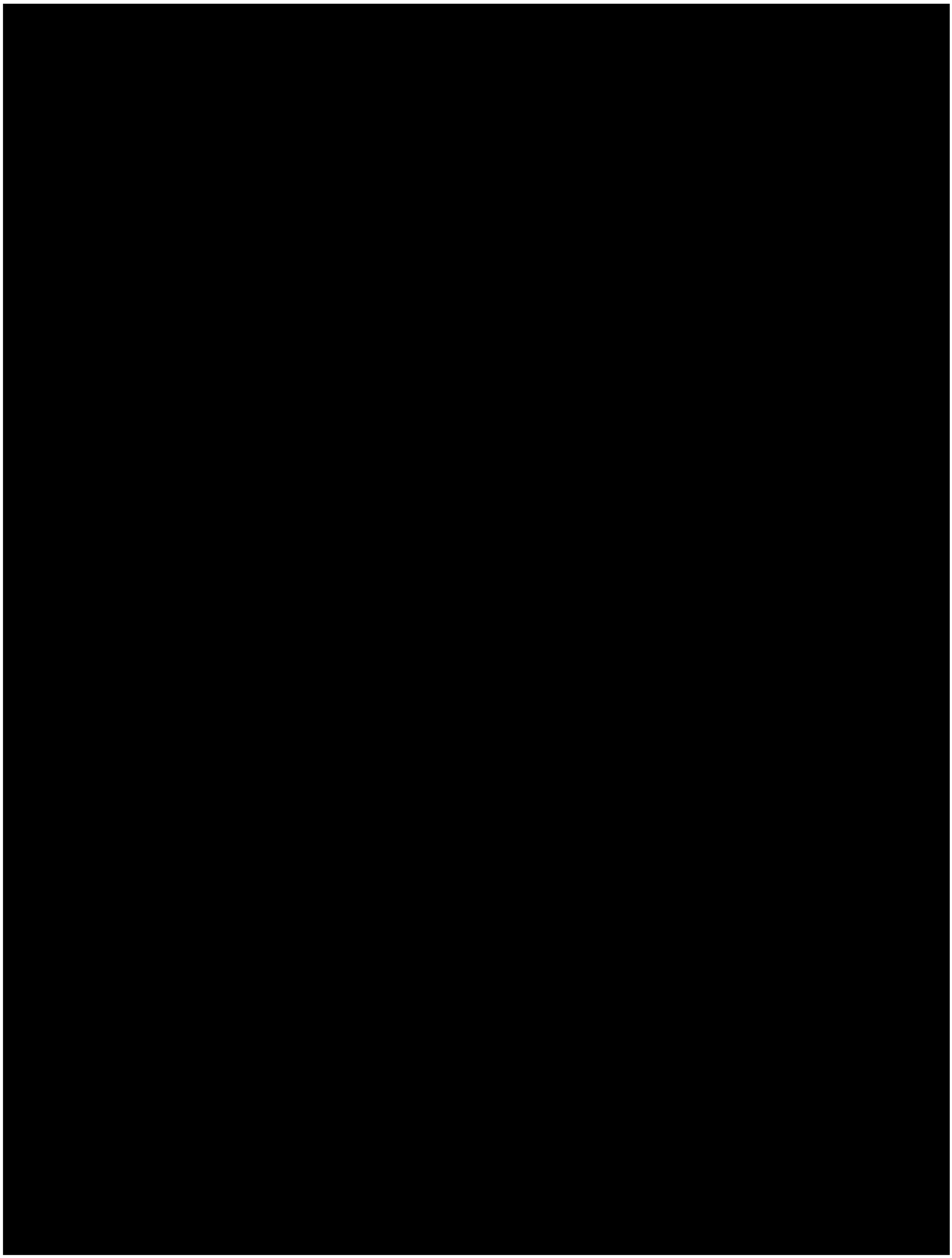
All study tasks should be performed by qualified study site personnel as indicated on the delegation of authority log under the supervision of the Principal Investigator.

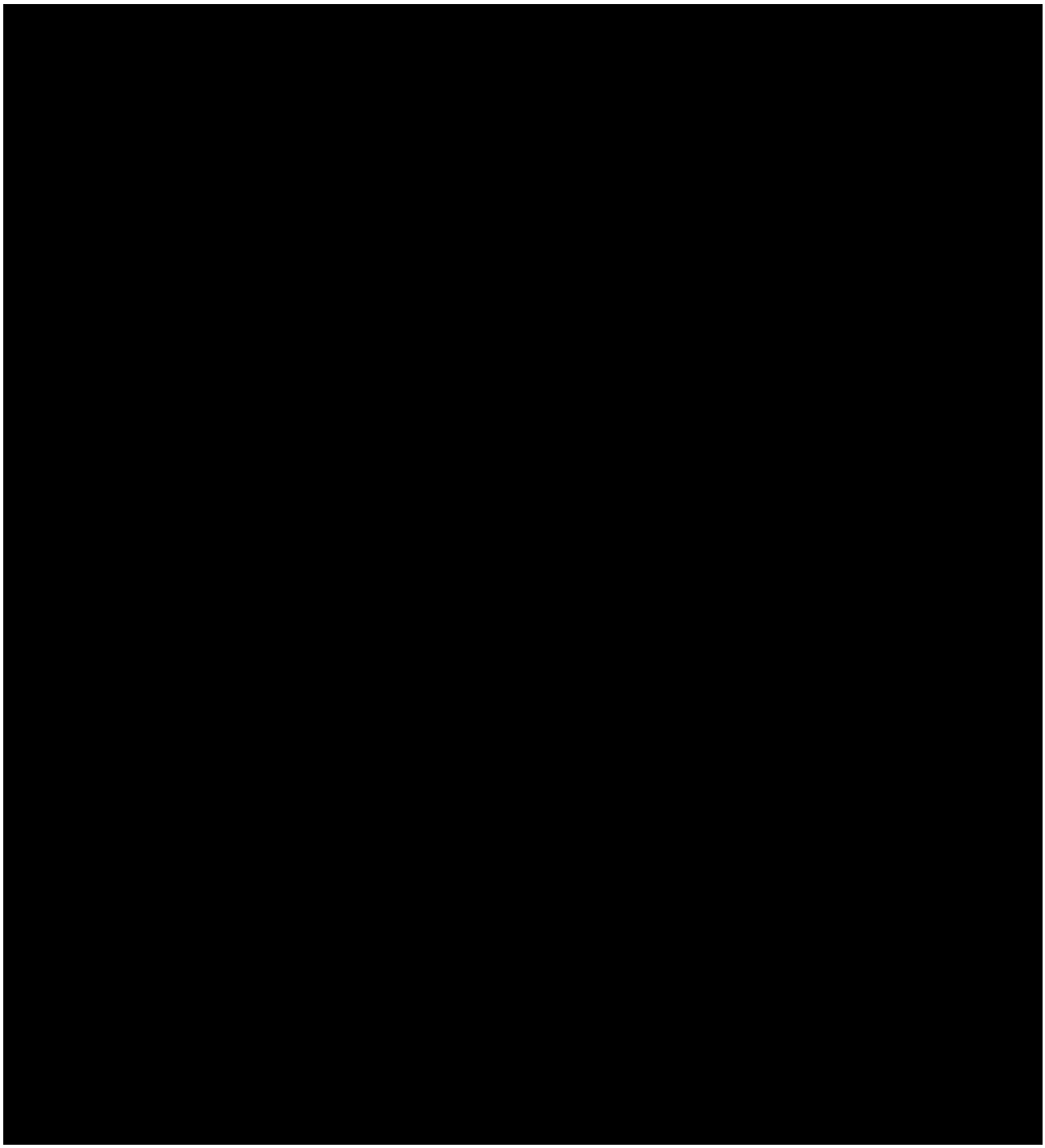
PROCEDURES / ASSESSMENTS	Screening/Dispensing	2-Week Follow-up Visit	1-Month Follow-up Visit	2-Month Follow-up Visit	3-Month Follow-up Visit	Exit Visit	Unscheduled Visit	Post Study Follow-Up Visit
	Day 0	Day 10-18	Day 26-34	Day 53-67	Day 83-97			
Informed Consent / HIPAA Authorization	X							
Eligibility	X							
Demographics	X							
Adverse events, Culture taken		X	X	X	X		X	
Baseline Lens / Lens Care History	X							
Lens Wear Parameters	X	X	X	X	X		X	
Initial Lens Performance Assessment Form (Worn Lenses Performance Rating Scales)	X							
Lens Performance Assessment Form (Study Lenses Performance Rating Scales)	X	X	X	X	X		X	
Exit Form (if an Exit Visit took place)	X[a]	X	X	X	X	X	X	X
Subject Completed Forms								
Initial Symptoms/Complaints[b] (Worn Lenses Symptoms/Complaints Form)	X							
Symptoms/Complaints (Abbreviated Study Lenses Symptoms/Complaints)	X							
Symptoms/Complaints Form[b] (Study Lenses Symptoms/Complaints)		X	X	X	X		X	
Without Lenses								
Spherocylindrical refraction	X					X		X
High contrast distance BSCVA	X					X		X

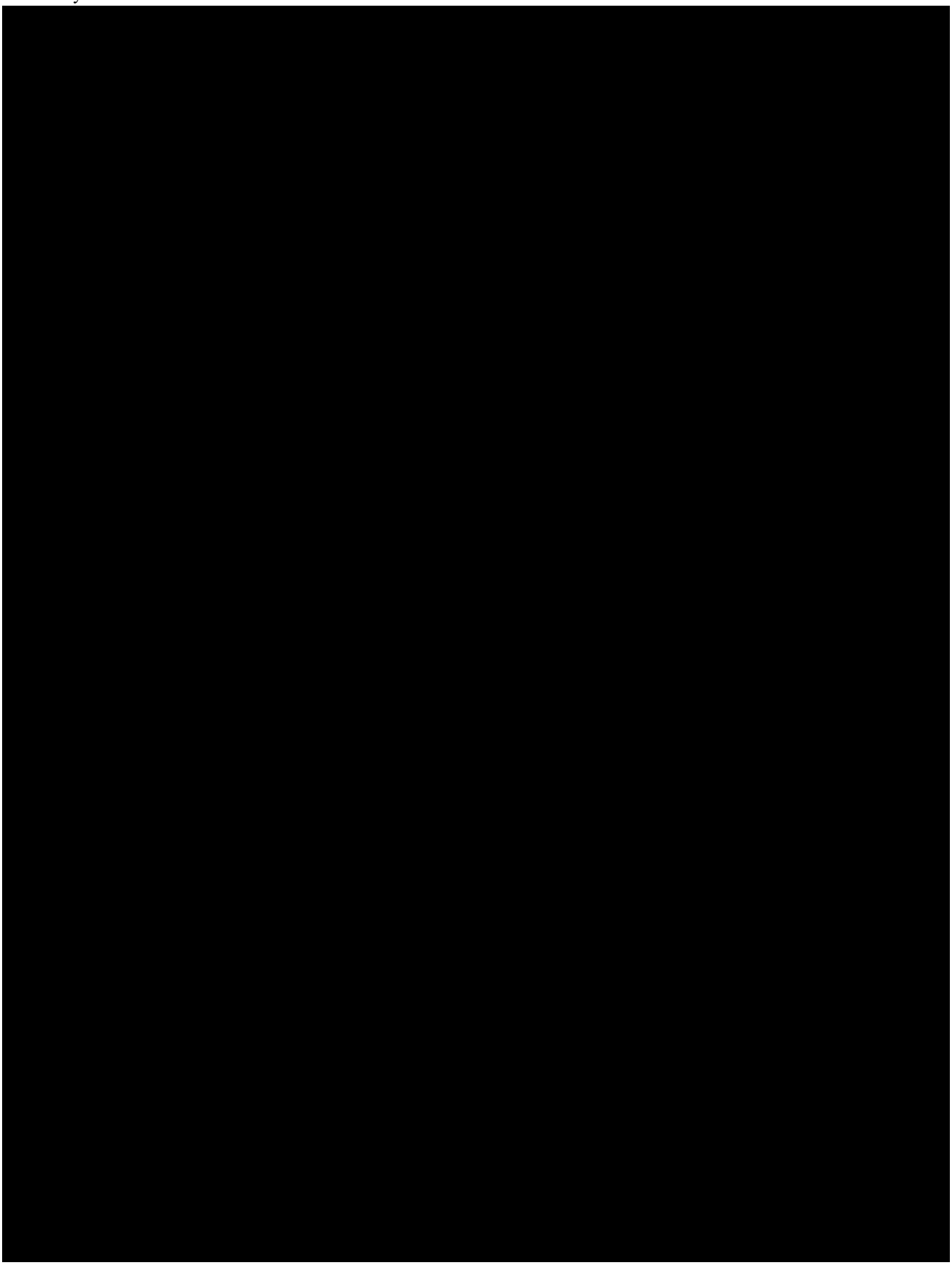
PROCEDURES / ASSESSMENTS	Screening/Dispensing	2-Week Follow-up Visit	1-Month Follow-up Visit	2-Month Follow-up Visit	3-Month Follow-up Visit	Exit Visit	Unscheduled Visit	Post Study Follow-Up Visit
	Day 0	Day 10-18	Day 26-34	Day 53-67	Day 83-97			
Keratometry	X					X		
Slit Lamp Examination	X	X	X	X	X		X	X
Compare high contrast distance BSCVA to screening high contrast distance BSCVA						X		X
Compare final keratometry to screening / dispensing keratometry						X		
With Lenses Worn to Visit								
High Contrast Distance lens VA		X	X	X	X		X	
Over-refraction and distance VA		X	X	X	X		X	
Lens wettability		X	X	X	X		X	
Lens discoloration		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 high contrast distance lens VA to high contrast distance VA at Screening / Dispensing Visit		X	X	X	X		X	
With Newly Dispensed Lenses								
High Contrast Distance lens VA	X		X	X			X	
Over-refraction and distance VA	X		X	X			X	
Lens wettability	X		X	X			X	
Lens centration	X		X	X			X	
Lens movement	X		X	X			X	
Compare high contrast distance lens VA to high contrast BSCVA	X							
Compare high contrast distance lens VA to high contrast VA at Screening/Dispensing Visit			X	X			X	

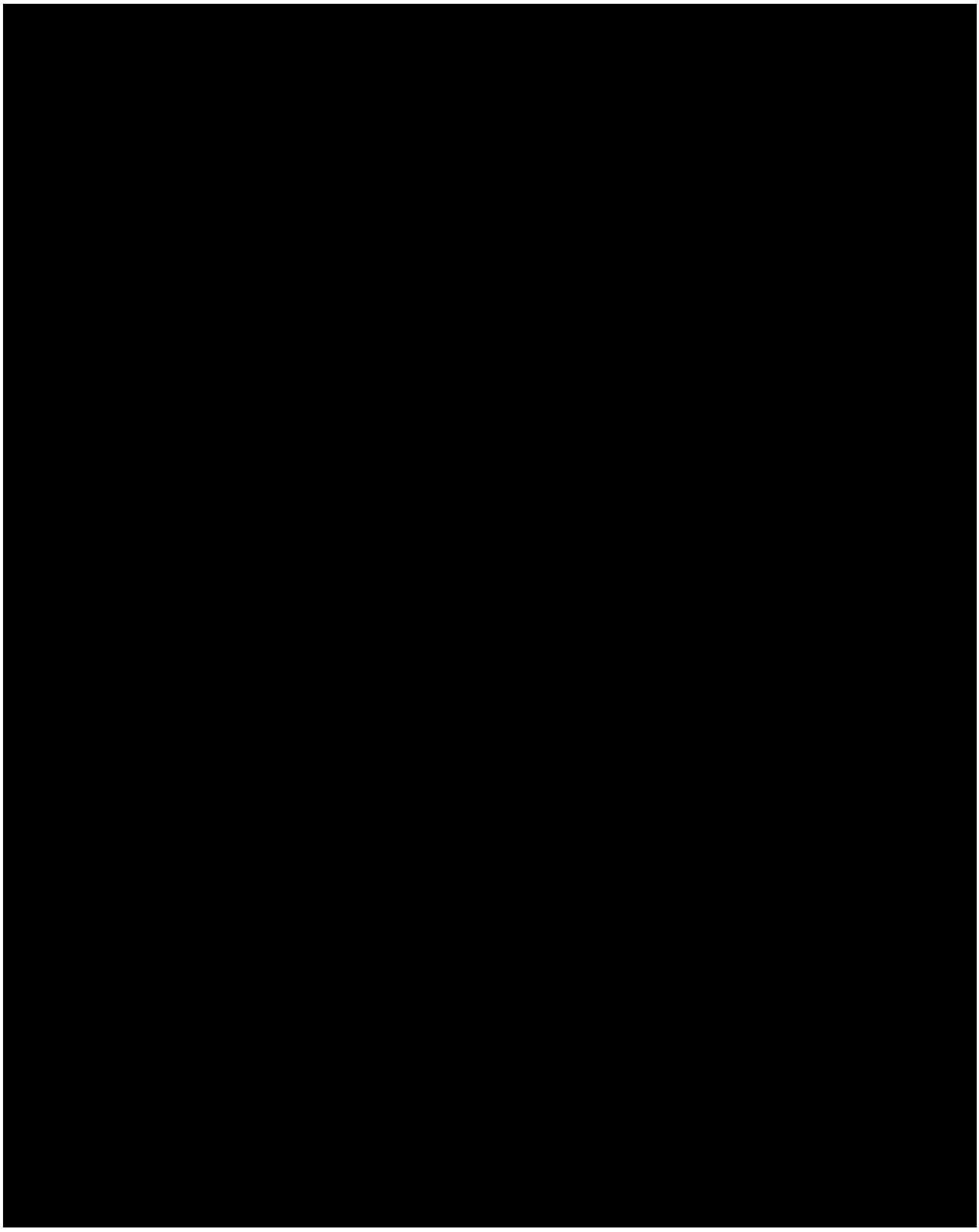
PROCEDURES / ASSESSMENTS	Screening/Dispensing	2-Week Follow-up Visit	1-Month Follow-up Visit	2-Month Follow-up Visit	3-Month Follow-up Visit	Exit Visit	Unscheduled Visit	Post Study Follow-Up Visit
	Day 0	Day 10-18	Day 26-34	Day 53-67	Day 83-97			
Study Materials								
Dispense Lenses (record lens brand, sphere power, base curve); If replacement lens, record reason for replacement	X		X	X			X	
Dispense Study kit bottles 1, 2, 3 and 4 (keep bottle 5 as a reserve at the site);	X							
Dispense Study Kit reserve (Bottle 5, if needed)		X	X	X			X	
Dispense other supplies as needed (see Protocol Section 4.4.3)	X	X	X	X			X	
Collect worn lenses from subject			X	X	X	X	X	
Collect used and unused bottles of study solutions					X	X		
Return study materials to sponsor					X	X		

[a] At the screening visit, only complete the Exit Form if the subject was randomized.
[b] Use provided rating scales (separate document).
Note: All VA measurements MUST be made using a phoropter.
Note: If this is an Exit Visit, also perform the procedures listed under the Exit Visit column.









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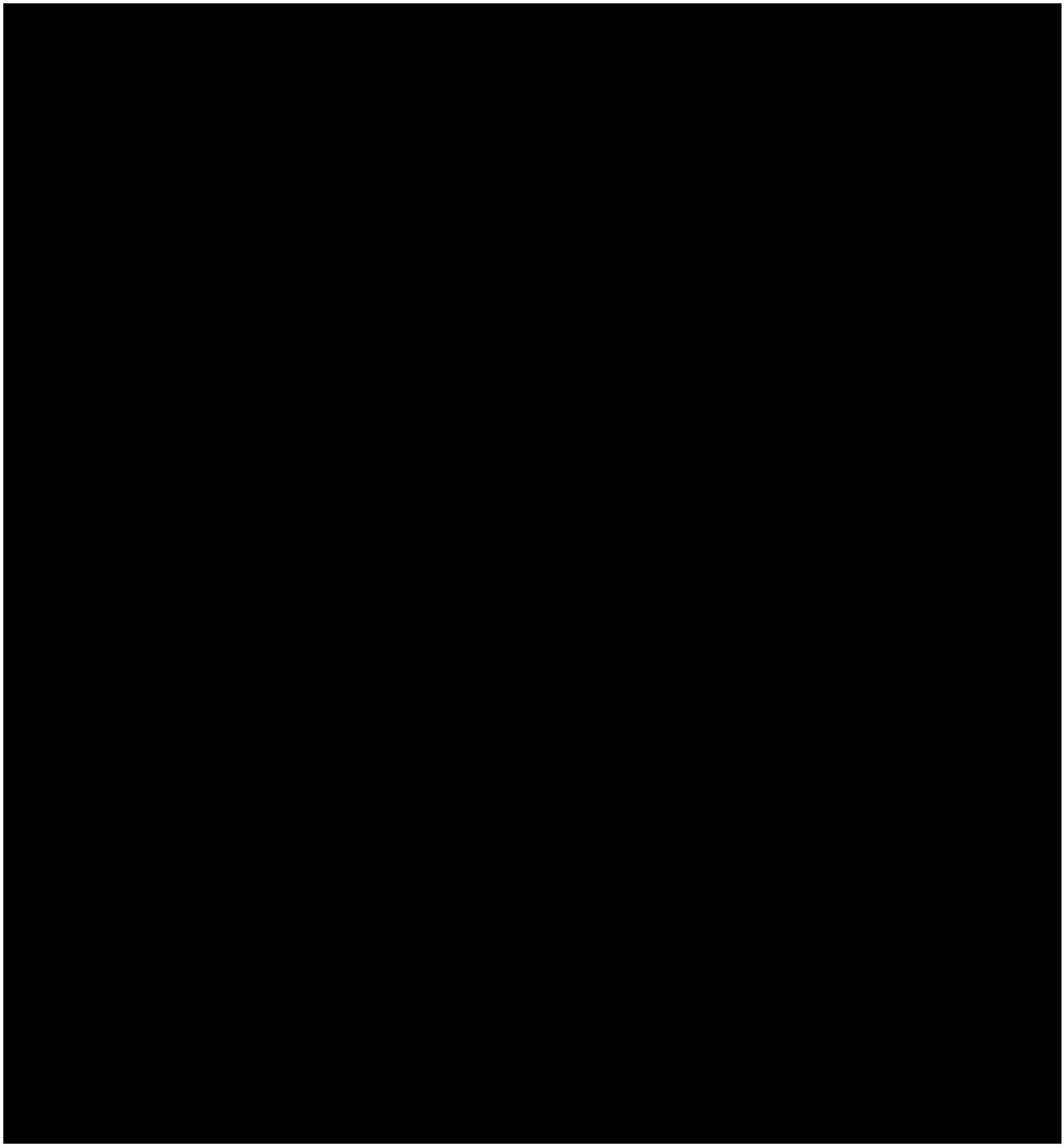

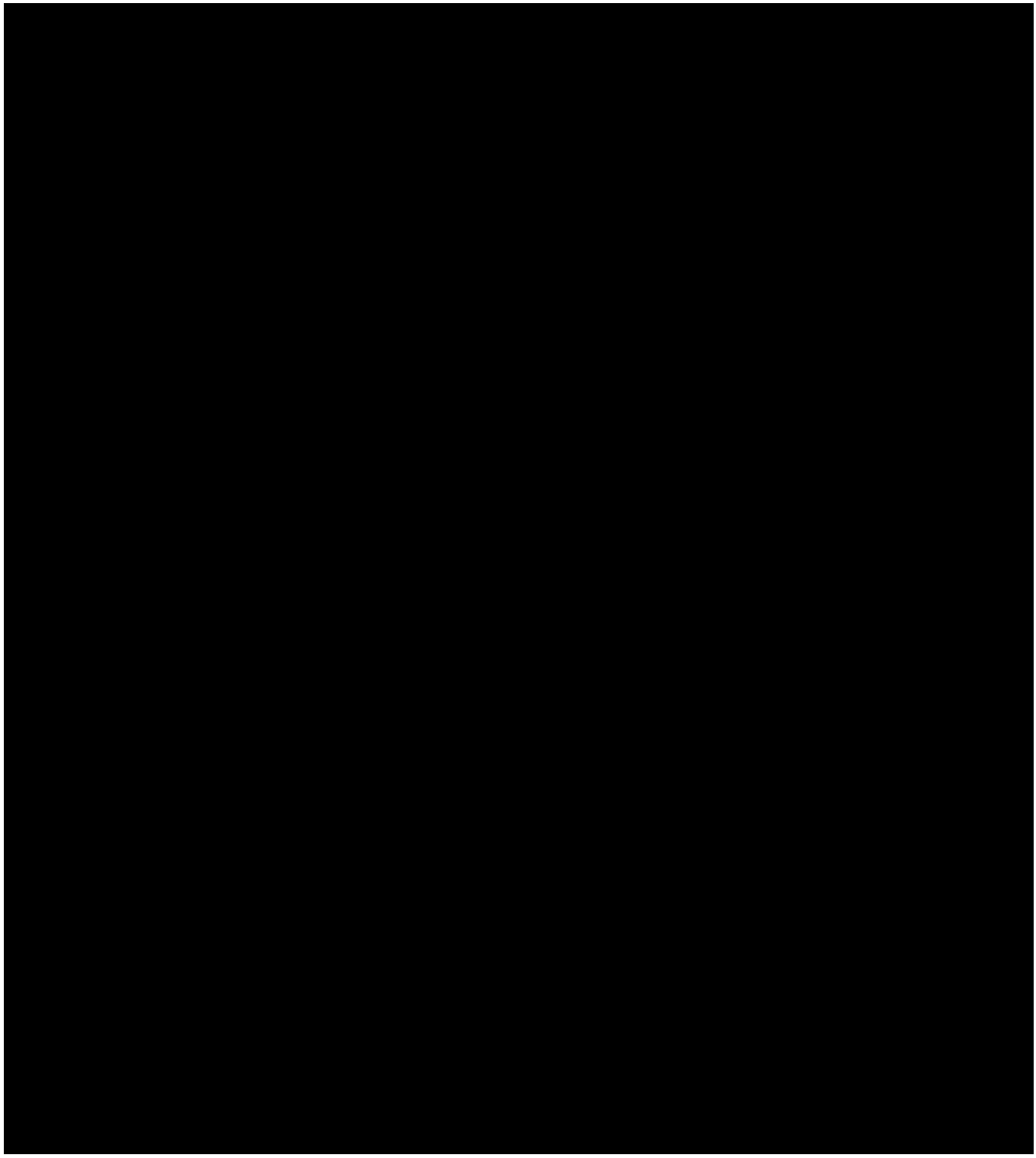

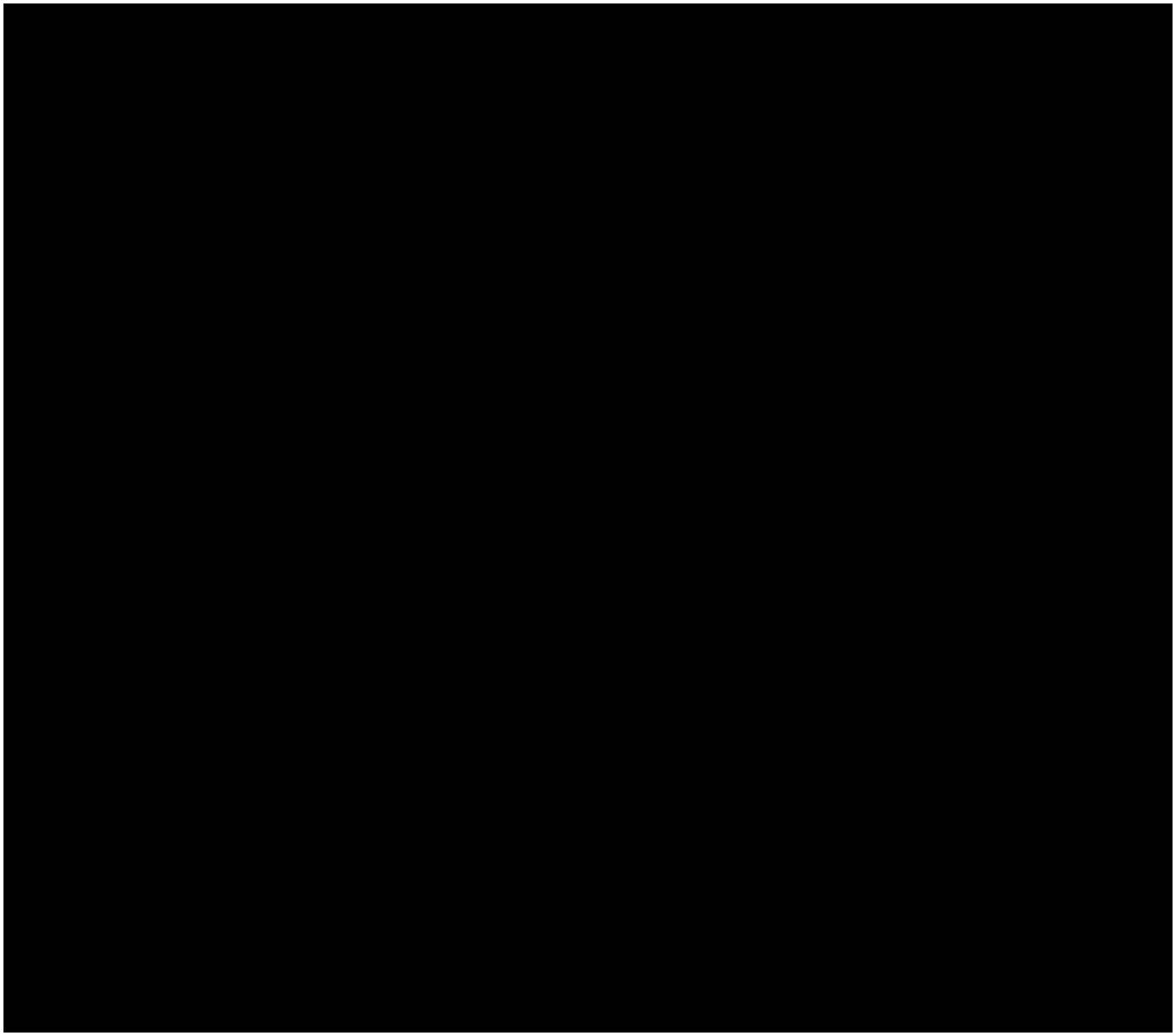

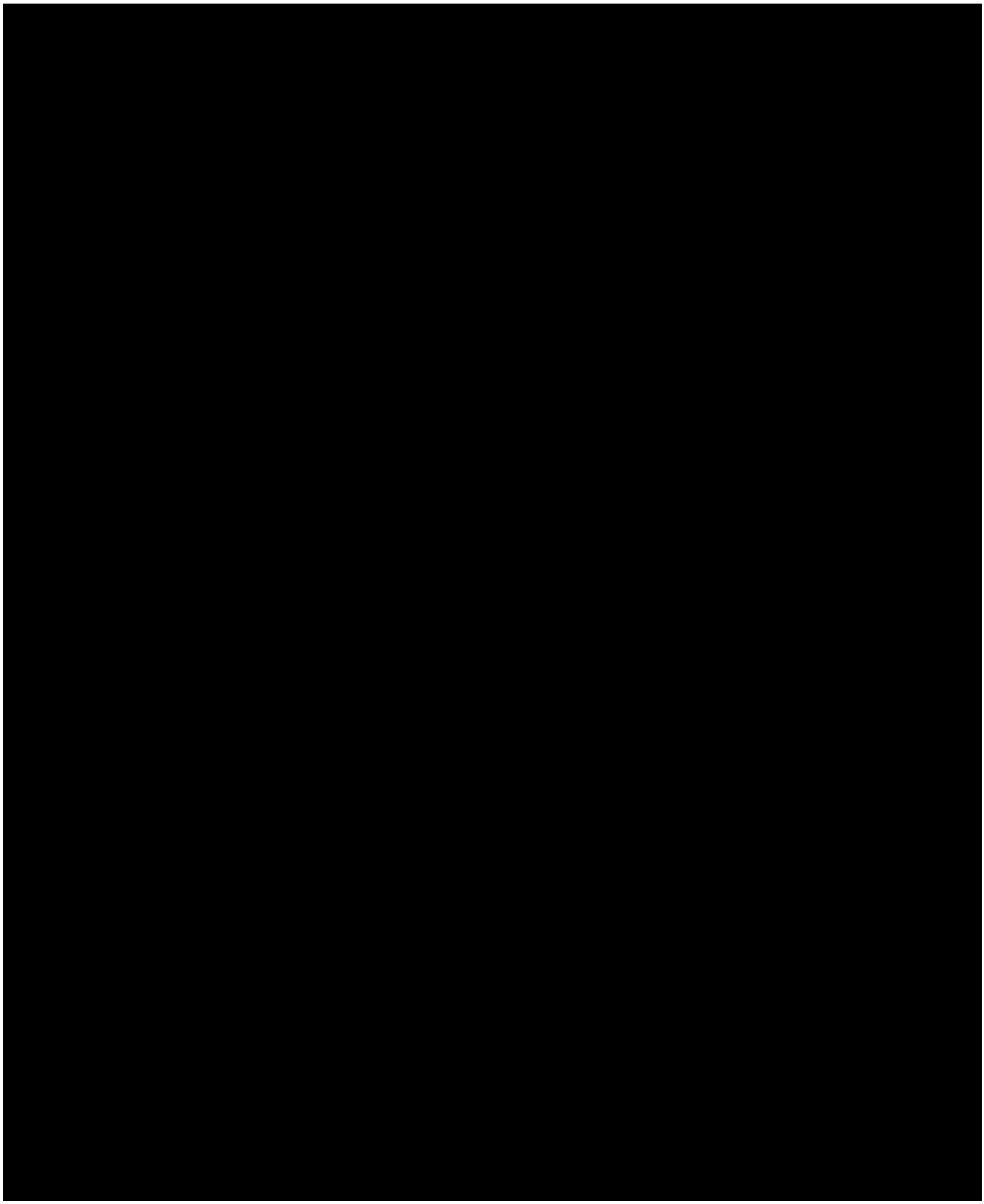

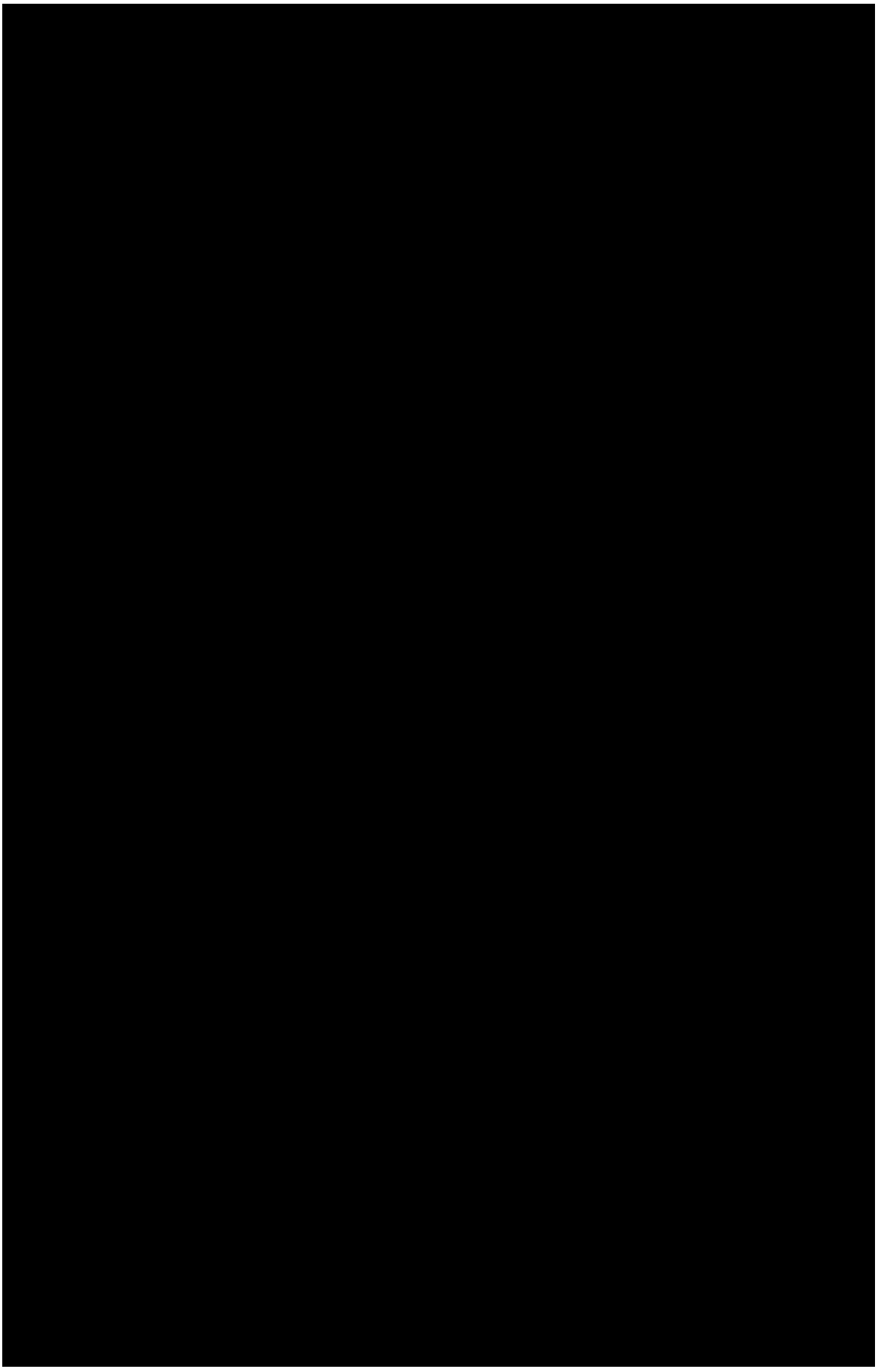

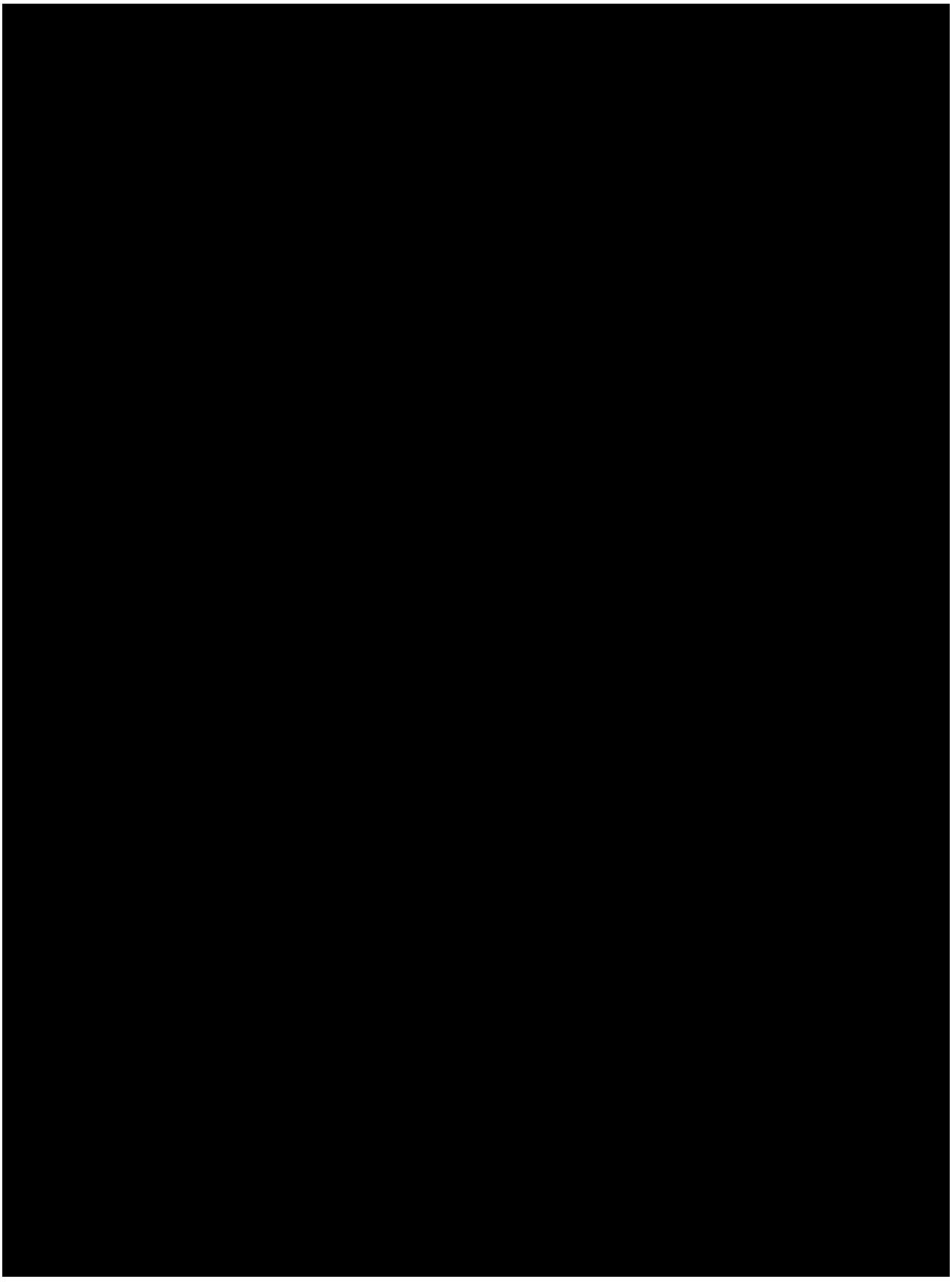

APPENDIX C: SUBJECT INSTRUCTIONS

SUBJECT INSTRUCTIONS (Page 1 of 3)

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 multipurpose soft contact lens care solutions. Please keep all appointments and **follow these instructions thoroughly**. If you have any questions or problems, call your study doctor. 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 that will contain:
  - **4 bottles of Study Solution each inside a white carton.** Each bottle and each carton will have an investigational label including the Study Kit number (a unique 5-digit number) and a bottle number (bottles 1, 2, 3 or 4). A fifth bottle will be retained at the site in case replenishment is required.
  - **Study Lens case.** A study lens case will be included *with each carton* of study solution for the subject to use for the month. *You are required to use the study lens case.*
  - **Subject Instructions.** Will be included with each carton of study solution.
- **Other Study Supplies.** The following supplies will be provided to you as needed:
  - **Carton/Bottle Return Materials.** Comprised of opaque drawstring bags and pre-printed labels for return of Study Solutions (full, partially filled, and empty bottles) to the Sponsor.
  - **Lens Return Materials.** Comprised of sealable plastic bags and pre-printed labels for return of worn lenses (in a fresh lens case with the approved saline solution) to the Sponsor.
  - ***Sensitive Eyes*® Rewetting Drops**

IMPORTANT SUBJECT INSTRUCTIONS:

This is a "masked" clinical study in which the Investigators and Coordinators cannot see the Study Solutions or Study Lens Cases 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 do not bring the study solutions or lens cases to the study site unless they are in the white opaque bag.

SUBJECT INSTRUCTIONS (continued)

SUBJECT INSTRUCTIONS (Page 2 of 3)

GENERAL INFORMATION:

- Do NOT use any products other than those listed above or dispensed to you by your study doctor for use in this study.
- Do NOT use any other care products other than those listed above.
- Do not use any topical ocular medications (eye drops) during this study.
- Do NOT discuss or show the dispensed study products or these Subject Instructions to the Investigator or site staff during the study.
- Please save all study materials during the course of the study, and plan to bring all opened and unopened study solutions with you to the 3-month follow-up visit. Place the solution bottles back into the cartons. Place the cartons containing the bottles into the opaque drawstring bag provided. Seal the bag before going to the office.
- 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 study doctor 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 **Study 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 doctor if you have any allergies that may affect your ability to use the **Study solution**.

IMPORTANT:

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

SUBJECT INSTRUCTIONS (Page 3 of 3)

When used as directed, the **Study Solution**: (1) Cleans, loosens and removes accumulations of film, protein and other 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 lens in lens case first
- Thoroughly rinse each side of the lens for 5 seconds with multi-purpose solution
- Place cleaned contact lenses in the lens case and fill with fresh multi-purpose solution. Soak at least 4 hours. Remember to always use fresh solution - discard solution from lens case after each use. Be sure that the lens is completely immersed in fresh **Study Solution**.
- Secure the cap and repeat the procedure with the other lens.

*Your lenses are now ready for wear. No rinse is necessary. If any debris remains on your lenses, rinse with **Study Solution** prior to insertion.*

CARE OF THE STUDY LENS STORAGE CASE:

- When the study lens case is not in use for storage of lenses, pour the **Study Solution** out of the lens case and rinse the case with fresh **Study Solution**.
- Leave the case with the caps off to dry in the air.
- For visits to the clinic, you do not need to bring the lens case to the clinic.
- If there is a reason to bring the lens case to the clinic, PLACE THE LENS CASE IN THE WHITE OPAQUE BAG FOR TRANSFER TO THE CLINIC.

REWETTING:

- If necessary, you can use the supplied rewetting drops while wearing your lenses. Simply place one or two drops of the supplied Sensitive Eyes rewetting drops in each eye and blink 2 or 3 times.
- If your lenses become dry while you are wearing them, directly apply the Sensitive Eyes rewetting drops to restore moisture and maintain comfortable lens wear.
- If lens discomfort persists, discontinue use, remove your lenses and contact your study Investigator immediately.