Title

# Clinical Safety and Effectiveness Assessment of an Investigational Frequent Replacement Silicone Hydrogel Lens

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| Protocol Number: | CLL949-C010 / NCT04085328 |
| Development Stage of Project: | Development |
| Sponsor Name and Address: | Alcon Research, LLC and its affiliates ("Alcon")<br>6201 South Freeway<br>Fort Worth, Texas 76134-2099 |
| Test Product: | LID015385 |

Investigator Agreement:

- I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practice (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and any conditions of approval imposed by the Institutional Review Board and/or the FDA, and all applicable regulatory requirements including 21 CFR Parts 50 (Protection of Human Subjects), 54 (Financial Disclosure), 56 (Institutional Review Boards), and 812 (Investigational Device Exemptions).
- I will supervise all testing of the device involving human subjects and ensure that the requirements relating to obtaining informed consent and IRB review and approval are met in accordance with applicable local and governmental regulations.
- I have read and understand the appropriate use of the investigational product(s) as described in the protocol, current Investigator's Brochure, product information, or other sources provided by the Sponsor.
- I understand the potential risks and side effects of the investigational product(s).
- I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.
- I agree to comply with all other requirements regarding the obligations of clinical Investigators and all other pertinent requirements of the Sponsor and government agencies.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments.

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| Have you ever been disqualified as an Investigator by any Regulatory Authority?<br>☐ No ☐Yes |
| Have you ever been involved in a study or other research that was terminated?<br>☐ No ☐Yes<br>If yes, please explain here: |

Principal Investigator:

Signature Date

Name and professional position:

Address:

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# 1 GLOSSARY OF TERMS

| | |
|---|---|
| Names of test product(s) | Throughout this document, test product(s) will be referred to as [redacted] soft contact lenses or [redacted] contact lenses [redacted] |
| Name of Control Product(s) | CooperVision® BIOFINITY® soft contact lenses (Biofinity contact lenses or Biofinity) |
| Adverse Device Effect (ADE) | Adverse event related to the use of an investigational medical device (test product) or control product. *Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the test product or control product.* |
| Adverse Event (AE) | Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device (test product). *Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product.*<br><br>Requirements for reporting Adverse Events in the study can be found in Section 11. |
| Anticipated Serious Adverse Device Effect | Serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the risk management file. |
| Device Deficiency | Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.*<br><br>Requirements for reporting Device Deficiencies in the study can be found in Section 11. |

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| Enrolled Subject | Any subject who signs an informed consent form for participation in the study. |
| Interventional Clinical Trial | A research trial that prospectively assigns, whether randomly or not, human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, and/or a research trial in which diagnostic or monitoring procedures beyond standard of care are conducted and generate outcomes for use in analysis of data. |
| Investigational Product (IP) | Is defined as a preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or control product in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form. |
| Malfunction | Failure of a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan. |
| Non-serious Adverse Event | Adverse event that does not meet the criteria for a serious adverse event. |
| Randomized Subjects | Any subject who is assigned a randomized treatment. |
| Serious Adverse Device Effect (SADE) | Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. |
| Serious Adverse Event (SAE) | Adverse event that led to any of the following:<br>• Death. |

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| | • A serious deterioration in the health of the subject that either resulted in:<br>a. a life-threatening illness or injury.<br>*Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.*<br>*b.* any potentially sight-threatening event or permanent impairment to a body structure or a body function.<br>c. in-patient hospitalization or prolonged hospitalization.<br>*Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.*<br>*d.* a medical or surgical intervention to prevent a) or b).<br>*e.* any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use.<br>• Fetal distress, fetal death, or a congenital abnormality or birth defect.<br>*Refer to Section 11 for additional SAEs.* |

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| Significant Non-Serious Adverse Event | Is a symptomatic, device-related, non-sight threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks.<br><br>*Refer to Section 11 for additional Significant Non-Serious AEs.* |
| Unanticipated Serious Adverse Device Effect | Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk management file. |
| Use Error | Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. *Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.* |

# 2 LIST OF ACRONYMS AND ABBREVIATIONS

**Table 2–1 List of Acronyms and Abbreviations Used in This Protocol**

| Abbreviation | Definition |
|---|---|
| ADE | Adverse device effect |
| AE | Adverse event |
| Apps | Applications (ie, smartphone software applications) |
| [redacted] | [redacted] |
| Biofinity contact lens | Biofinity (comfilcon A) soft contact lenses |
| CFR | Code of Federal Regulations |
| CLEAR CARE | CLEAR CARE Cleaning & Disinfecting Solution |
| CLVA | Contact lens corrected visual acuity |
| COL | Clinical operations lead |
| CRF | Case report form |
| CSM | Clinical site manager |
| CTT | Clinical trial team |
| d | Days |
| D | Diopter(s) |
| D/C | Discontinue |
| eCRF | Electronic case report form |
| EDC | Electronic data capture |
| FDA | US Food and Drug Administration |
| GCP | Good Clinical Practice |
| hrs | Hours |
| IB | Investigator's brochure |
| ICF | Informed consent form |
| ICH | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use |
| IEC | Independent ethics committee |
| [redacted] | [redacted] |
| IP | Investigational product |
| IRB | Institutional review board |
| IRT | Interactive response technology |
| ISO | International Organization for Standardization |
| LacriPure | Menicon LacriPure, Preservative Free Saline |
| [redacted] | [redacted] |
| logMAR | Logarithm of the minimum angle of resolution |
| [redacted] contact lens | [redacted] soft contact lenses |
| mm | Millimeter |
| [redacted] | [redacted] |
| MOP | Manual of procedures |
| N/A | Not applicable |
| NCT | National Clinical Trial |
| OFPM MPDS | OPTI-FREE® PureMoist® Multi-Purpose Disinfecting Solution |

| Abbreviation | Definition |
|---|---|
| O/R | Over-refraction |
| OU | Both eyes |
| PI | Principal Investigator |
| PMA | Premarket approval |
| [redacted] | [redacted] |
| SAE | Serious adverse event |
| SADE | Serious adverse device effect |
| SiHy | Silicone hydrogel |
| SOP | Standard operating procedure |
| Systane | Systane Preservative-Free Eye Drops |
| UCL | Upper confidence limit |
| US / USA | United States of America |
| USV | Unscheduled visit |
| VA | Visual acuity |
| vs | Versus |

# 3 PROTOCOL SUMMARY

This will be a prospective, randomized, [redacted] controlled, double-masked, parallel-group, extended wear clinical study.

This clinical trial will engage approximately 45 clinic sites to enroll approximately 812 subjects [redacted]

- [redacted]
- [redacted]

Subjects will be randomized to wear either the test contact lens [redacted] or the control contact lens (Biofinity) throughout the duration of the study.

Subjects will be expected to attend 9 office visits: Baseline/Dispense, 24-hour follow-up, 1-week follow-up, 1-month follow-up, 2-month follow-up, 3-month follow-up, 6-month follow-up, 9-month follow-up and 12-month follow-up/Exit. The total expected duration of participation for each subject is approximately 12 months in this extended wear study.

At the Baseline/Dispense Visit, study lenses will be trial fit using the fitting sets supplied by the Sponsor, and the correct contact lens power for the individual subject will be determined. Subjects achieving optimal/acceptable fits with **both pairs** of study lenses and desired visual

acuity as specified in the inclusion criteria, will then be randomized in a 1:1 manner to either receive [redacted] or Biofinity lenses for use throughout the duration of the study.

Following randomization, study lenses will be dispensed to the subject. Subjects will be provided with sufficient lens supplies to follow a weekly replacement schedule until the next visit.

All subjects will wear the study lenses in an extended wear modality, while awake and asleep for up to 6 nights/7 days of continuous wear with one night of no lens wear. This wearing schedule will be repeated throughout the course of the trial. Subjects assigned to [redacted] or Biofinity contact lenses will insert a new pair of study lenses each week and discard them at the end of the week.

Problem lenses (if any) will not be discarded but collected by the subject and returned to the investigational site. Regardless of whether the subject is randomized to the test or the control group, CLEAR CARE® Cleaning & Disinfecting Solution (CLEAR CARE) and Menicon LacriPure, Rinsing & Insertion Saline (LacriPure or equivalent) will be permitted for use if the subject must remove the lens for any reason. Systane® Preservative-Free Eye Drops (Systane) will also be permitted but should only be used if necessary and is the only product permitted for use in the eye.

[redacted]

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| **Investigational product type** | Device |
| **Study type** | Interventional |

| | |
|---|---|
| **Investigational products** | Test Product: [redacted] soft contact lens<br>Control Product: Biofinity soft contact lens |
| **Purpose and rationale** | The purpose of this clinical trial is to evaluate the safety and performance of the [redacted] soft contact lens compared to the commercially available Biofinity soft contact lens, by assessing ocular serious and significant non-serious adverse device effects as the primary safety variable and visual acuity as the primary effectiveness variable. |
| **Objective(s)** | The objective of this study is to demonstrate safety and effectiveness of [redacted] soft contact lenses as compared to Biofinity soft contact lenses, when both study lenses are worn for extended wear (6 nights/7 days of continuous wear followed by 1 night of no lens wear) and replaced on a weekly basis. |
| **Endpoint(s)** | Primary Effectiveness<br>• Distance VA (Snellen)<br>Primary Safety<br>• Proportion of ocular serious and significant non-serious ADEs<br>[redacted] |

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| | [redacted]<br>Other Safety<br>• AEs (non-serious, non-significant)<br>• Biomicroscopy findings<br>• Device deficiencies |
| **Assessment(s)** | Effectiveness<br>• Distance VA with study lenses (Snellen)<br>• Distance VA with habitual correction (Snellen)<br>• Manifest refraction<br>[redacted] |

| | |
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| | [redacted] |
| | Safety<br>• AEs<br>• Biomicroscopy findings<br>• Device deficiencies |

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|---|---|
| **Study Design** | This will be a prospective, randomized, [redacted], controlled, double-masked, parallel-group, extended wear clinical study. The total expected duration of participation for each subject is approximately 12 months in this extended wear study. |
| **Subject population** | Volunteer subjects aged 18 or over who are adapted daily wear or extended wear frequent replacement soft contact lens wearers, have at least 3 months of soft contact lens wearing experience, and who wear their habitual lenses at least 5 days per week.<br><br>Subjects must have regularly worn their habitual lenses for at least **10 hours** per day. Additionally, extended wear lens wearers must have regularly worn their habitual lenses for at least 1 night per week. Subjects must require contact lens correction in the power range available for this study as specified in the inclusion criteria.<br><br>[redacted] Pregnant and breastfeeding women are excluded from this study.<br><br><u>Planned number of subjects for the study: ~812 (total)</u><br><br>• **Primary Cohort**<br>[redacted]<br>• Enrolled/consented: ~632<br>• Randomized: ~568 (~284 each in test and control)<br>• Completed: at least 426 (minimum 213 completed each in test and control)<br><br>[redacted] |

| | |
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| | [redacted] |
| **Key inclusion criteria**<br>(See Section 8.1 for a complete list of inclusion criteria) | • Successful wear of spherical daily wear or extended wear frequent replacement soft contact lenses in both eyes during the past 3 months for a minimum of 5 days per week. Habitual daily or extended wear subjects must have regularly worn their lenses for at least 10 hours per day. Additionally, extended wear lens wearers must have regularly worn their lenses for a minimum of 1 night per week.<br>• Manifest cylinder ≤ 0.75 D in each eye.<br>[redacted] |
| **Key exclusion criteria**<br>(See Section 8.2 for a complete list of exclusion criteria) | • Currently pregnant or breast-feeding<br>• Monovision contact lens wearers |
| **Data analysis and sample size justification** | In adherence to the reporting format as specified in the ISO clinical standard and FDA 510(k) guidance documents, effectiveness and safety data of the primary cohort will be presented separately based upon subject study status of Completed or Discontinued.<br>The primary safety analysis is to assess noninferiority of [redacted] contact lenses when compared to Biofinity contact lenses for the proportion of ocular serious and significant non-serious ADEs, with a pre-defined margin of 0.05 (5%). A generalized linear model with a logit link function will be used, and a one-sided 95% upper confidence limit (UCL) will be calculated for the difference in proportions between treatments ([redacted] minus Biofinity). |

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| | No formal hypotheses are formulated for the primary effectiveness endpoint of distance VA; hence, no inferential testing will be performed. Descriptive summary statistics will be provided for the Snellen categories as well as the converted logMAR values.<br>[redacted]<br>The sample size calculation was based on previous extended wear clinical studies which evaluated five currently marketed silicone hydrogel lenses. Assuming that the expected difference between test and control is 0 and that the control proportion is 0.045, a sample size of 213 per group will provide 80% power to reject the null hypothesis of inferiority in test compared to control, with a noninferiority margin of 0.05 (5%). |
| **Key words** | [redacted] Biofinity, extended wear |
| **Associated materials** | CLEAR CARE and LacriPure (or equivalent) will be permitted if the subject must remove their lens(es) for any reason. Systane will be also be permitted but should only be used if necessary. |

**Table 3–1 Schedule of Study Procedures and Assessments[α]**

| Procedure/Assessment | Baseline | Follow-Up Visits | | | | | | | Exit | Early Exit | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 | Visit 2 | Visit 3 | Visit 4 | Visit 5 | Visit 6 | Visit 7 | Visit 8 | Visit 9 | | |
| | Day 1 Dispense | 24 hrs Day 2 ± 4 hrs | 1-week Day 7 ± 2 d | 1-month Day 30 ± 4 d | 2-months Day 60 ± 7 d | 3-months Day 90 ± 7 d | 6-months Day 189 -7 / + 14 d | 9-months Day 270 ± 14 d | 12-months Day 365 ± 14 d | | |
| Informed Consent | ✓ | - | - | - | - | - | - | - | - | - | - |
| Demographics | ✓ | - | - | - | - | - | - | - | - | - | - |
| Medical History including pregnancy[1] | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | (✓) |
| Concomitant Medications | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | (✓) |
| Inclusion/Exclusion | ✓ | - | - | - | - | - | - | - | - | - | - |
| Habitual lens information (brand / manufacturer, modality, power, wear success, habitual lens care brand) | ✓ | - | - | - | - | - | - | - | - | - | - |
| Distance VA w/ habitual correction (Snellen) | ✓ | - | - | - | - | - | - | - | ✓ | ✓ | (✓) |
| Manifest refraction | ✓ | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | ✓ | ✓ | (✓) |
| [redacted] | | | | | | | | | | | |
| Keratometry | ✓ | - | - | - | - | - | ✓ | - | ✓ | ✓ | (✓) |
| Biomicroscopy[2] | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Determine study lens fit and power for each eye using Sponsor provided trial fitting sets. O/R as necessary. | ✓ | - | - | - | - | - | - | - | - | - | - |
| Order study lenses | ✓ | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | - | - | (✓) |

| Procedure/Assessment | Baseline | Follow-Up Visits | | | | | | | Exit | Early Exit | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 | Visit 2 | Visit 3 | Visit 4 | Visit 5 | Visit 6 | Visit 7 | Visit 8 | Visit 9 | | |
| | Day 1 Dispense | 24 hrs<br>Day 2 ± 4 hrs | 1-week<br>Day 7 ± 2 d | 1-month<br>Day 30 ± 4 d | 2-months<br>Day 60 ± 7 d | 3-months<br>Day 90 ± 7 d | 6-months<br>Day 189 -7 / + 14 d | 9-months<br>Day 270 ± 14 d | 12-months<br>Day 365 ± 14 d | | |
| IP Dispense | ✓ | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | - | - | (✓) |
| Distance VA w/ study lenses (Snellen) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| [redacted] | | | | | | | | | | | |

| Procedure/Assessment | Baseline | Follow-Up Visits | | | | | | | Exit | Early Exit | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 | Visit 2 | Visit 3 | Visit 4 | Visit 5 | Visit 6 | Visit 7 | Visit 8 | Visit 9 | | |
| | Day 1 Dispense | 24 hrs<br>Day 2 ± 4 hrs | 1-week<br>Day 7 ± 2 d | 1-month<br>Day 30 ± 4 d | 2-months<br>Day 60 ± 7 d | 3-months<br>Day 90 ± 7 d | 6-months<br>Day 189 -7 / + 14 d | 9-months<br>Day 270 ± 14 d | 12-months<br>Day 365 ± 14 d | | |
| [redacted] | | | | | | | | | | | |
| Symptoms, problems & complaints[4] | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| [redacted] | | | | | | | | | | | |
| Study lens and accessories return log | (✓) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | (✓) |
| Adverse events | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | (✓) |
| Device deficiencies | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | (✓) |
| Exit Form | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | (✓) | ✓ | ✓ | (✓) |
| [redacted] | | | | | | | | | | | |

[α] See Section 26 of the MOP (Manual of Procedures) for a chronological order of procedures per visit

(✓) assessment performed as necessary, eg, decrease of VA by 2 lines or more with IP.

USV=Unscheduled Visit

[1] Pregnancy to be self-reported by subject

[redacted]

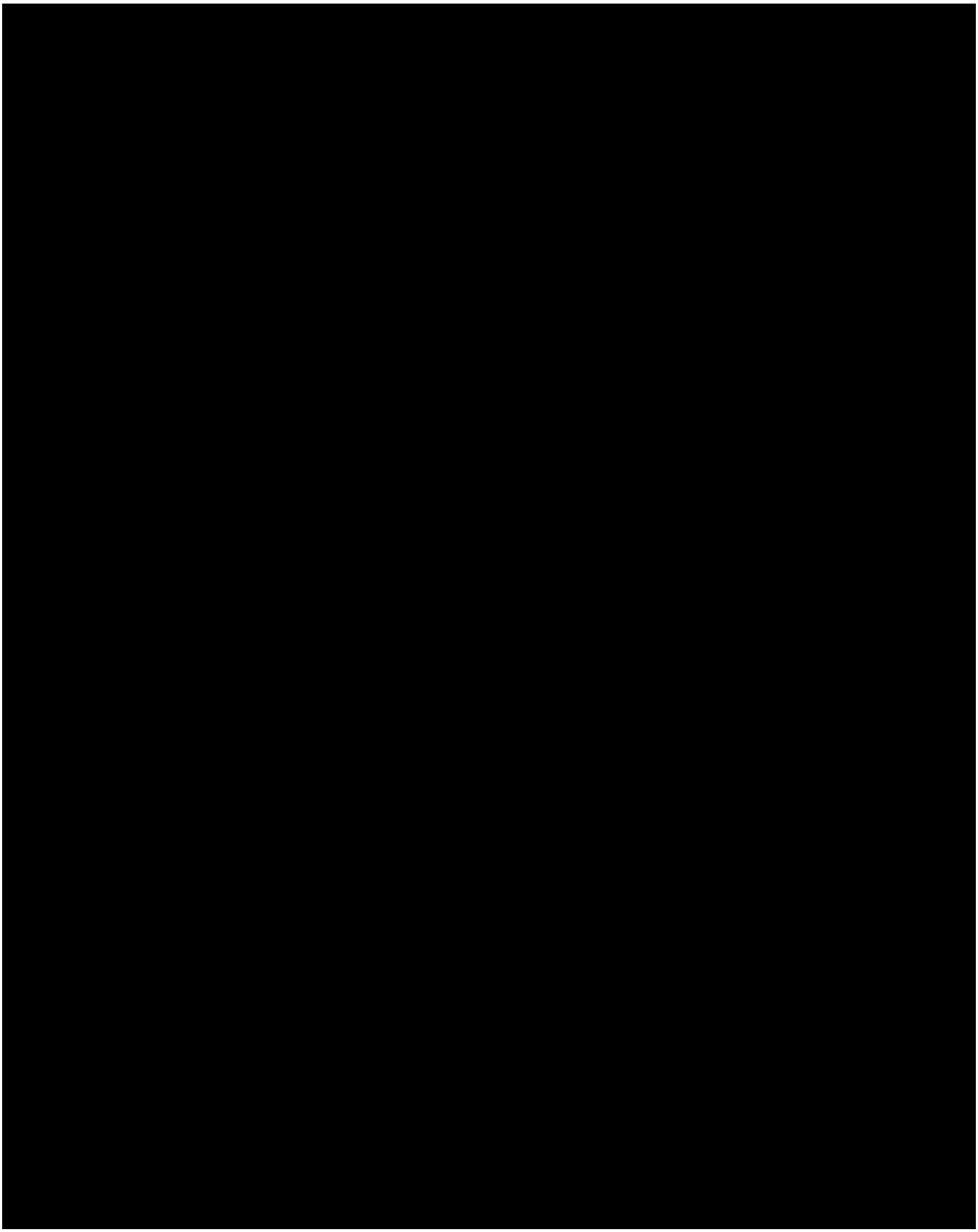
[4] Symptoms, problems, and complaints will include burning/stinging, itching, lens awareness, dryness, discomfort, blurred vision, fluctuating/variable vision, halo, lens needs cleaning, redness, excessive tearing, secretions, photophobia, and other (description required). The response will be recorded as "present" or "absent".

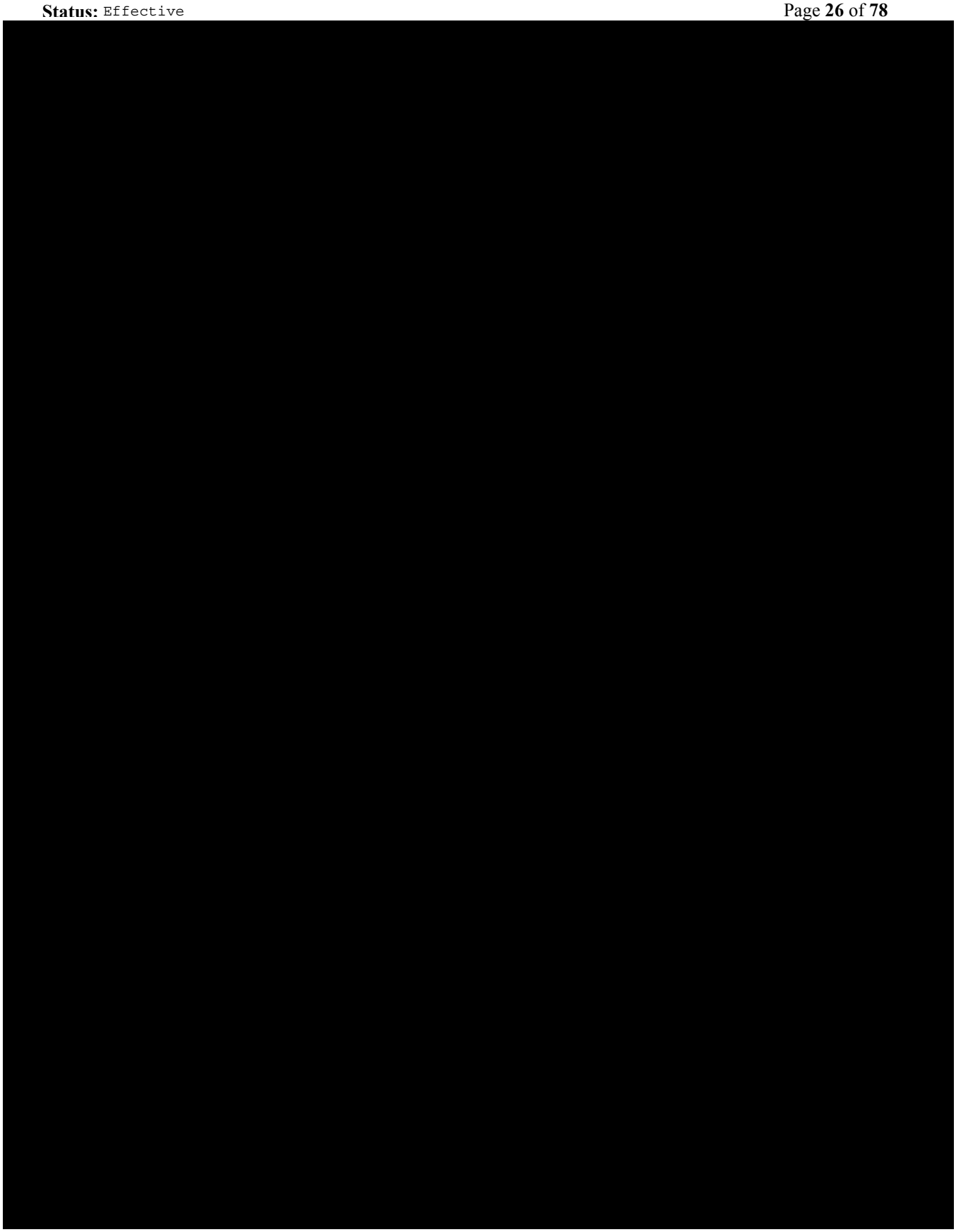
[redacted]

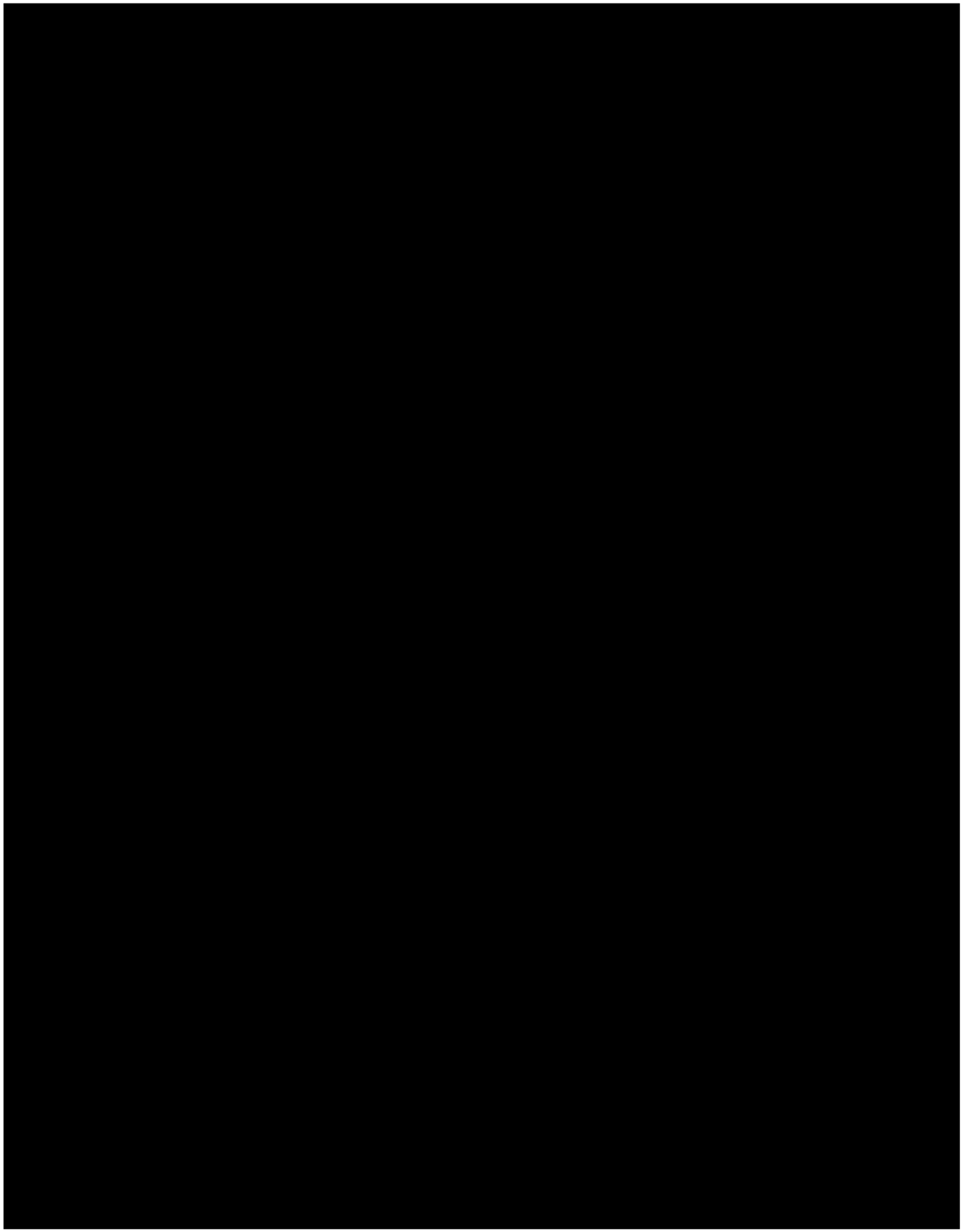
# 4 PROTOCOL AMENDMENTS

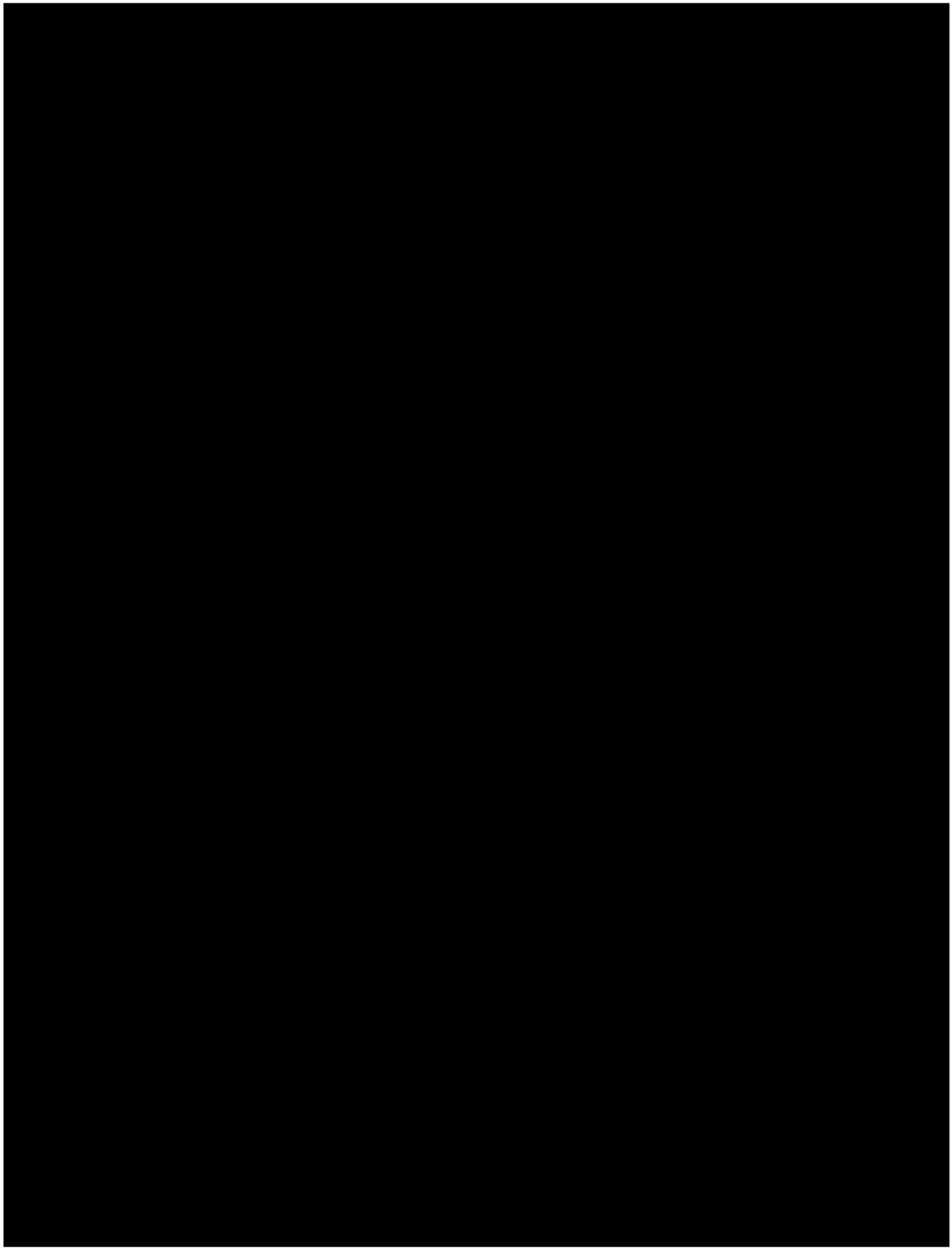
Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments must be created by the Study Sponsor and must be approved by the IRB/IEC and global and regional Health Authorities, as applicable, prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all subjects currently enrolled in the study must sign the approved, revised informed consent (re-consent), as required by the IRB/IEC.









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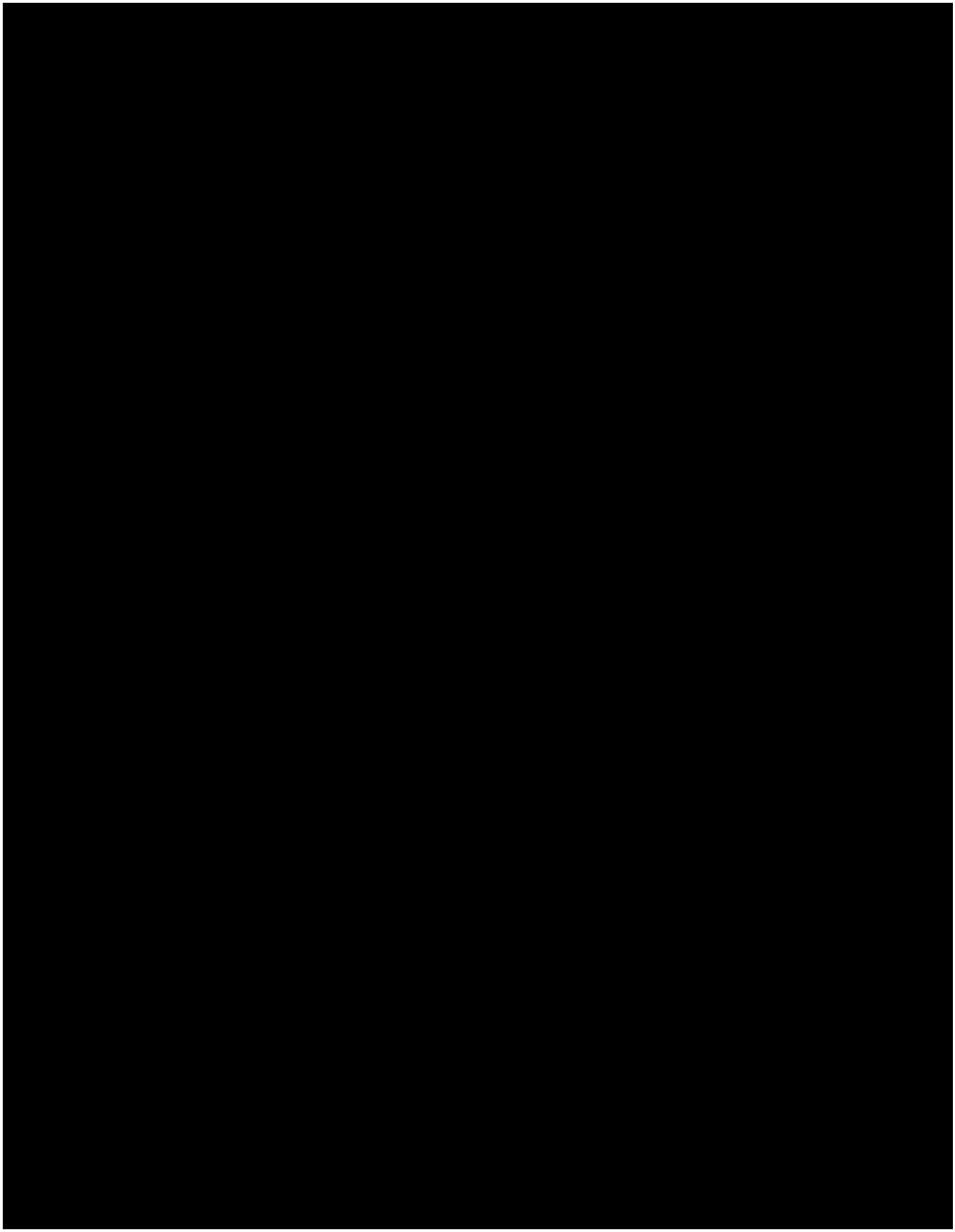

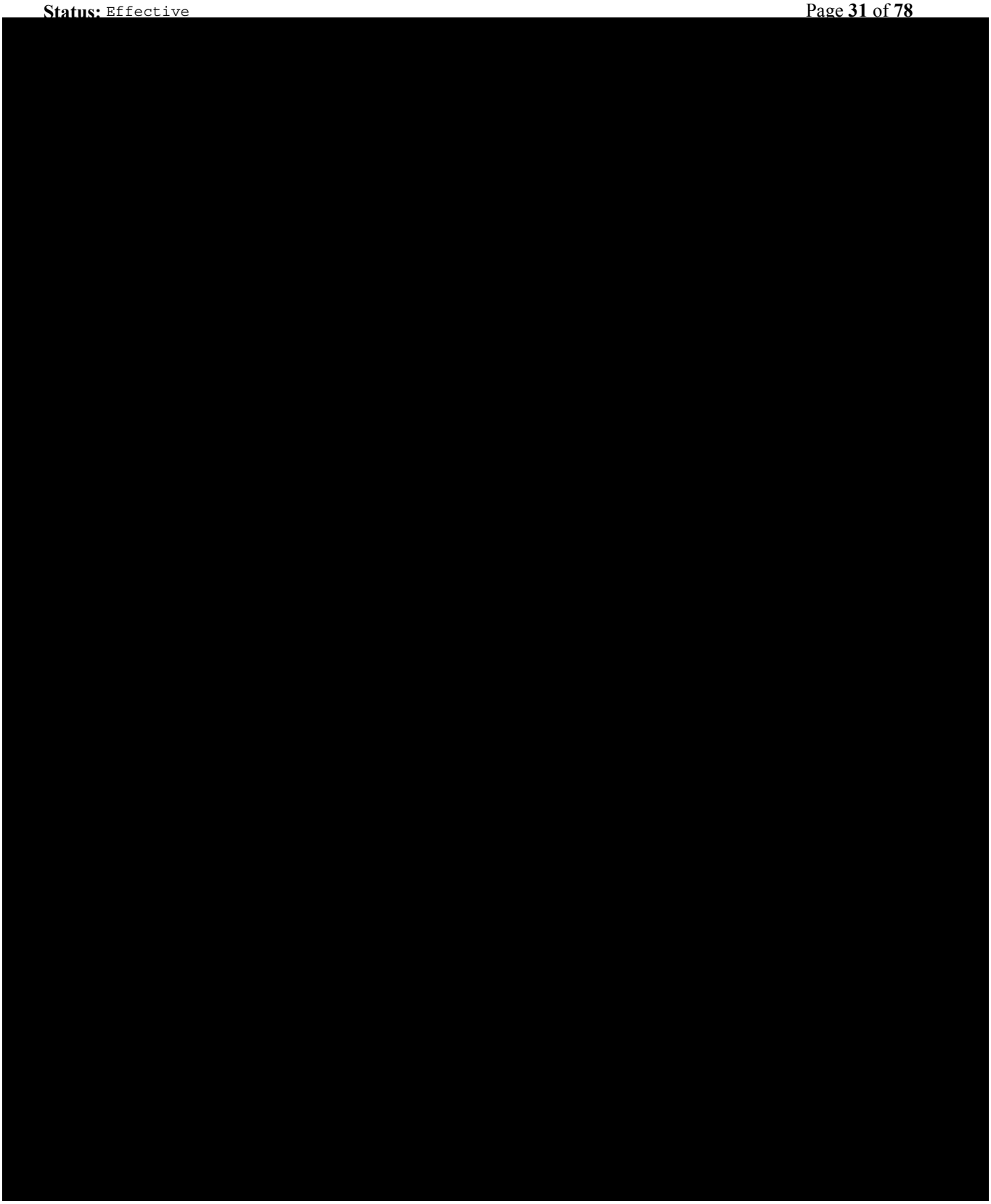

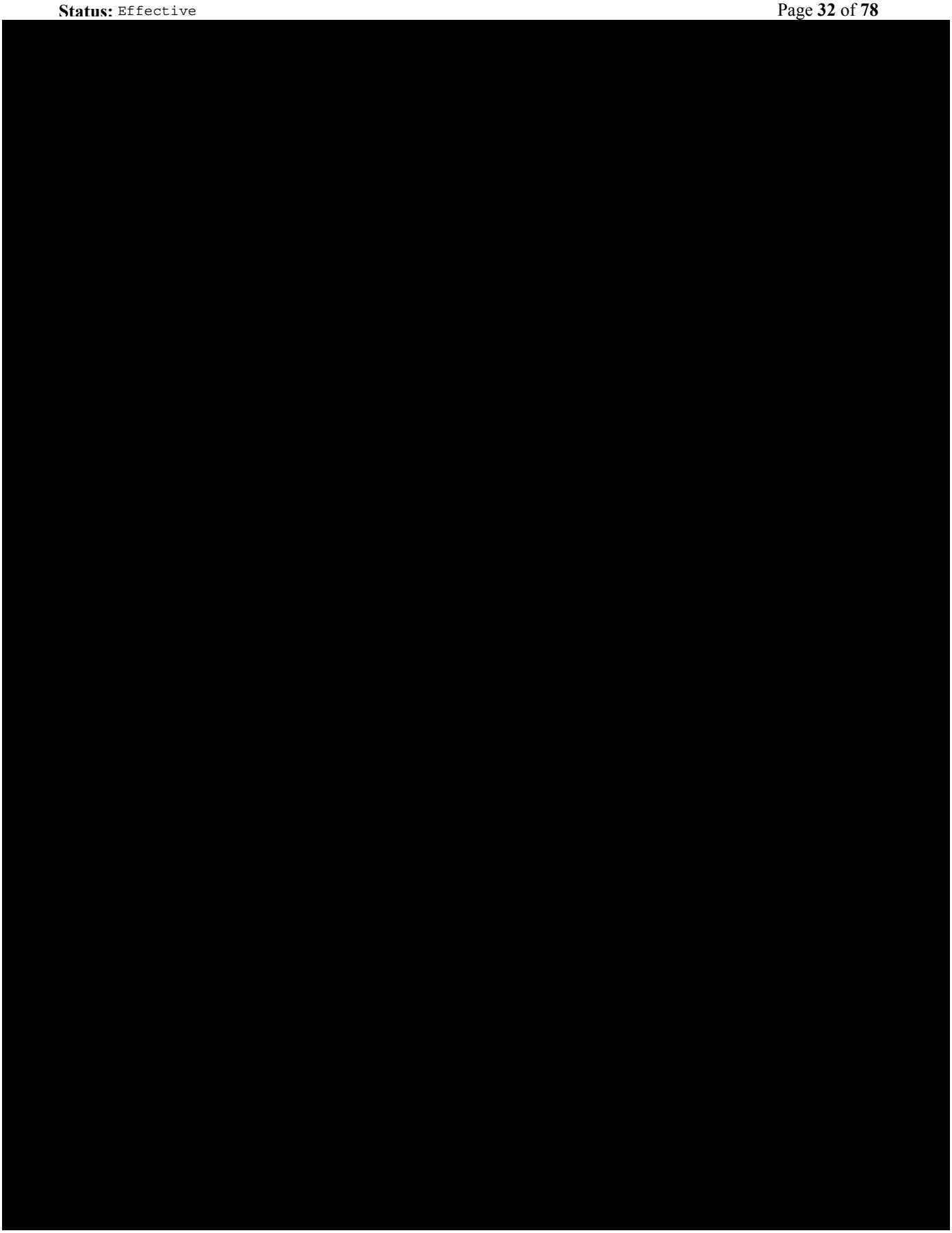

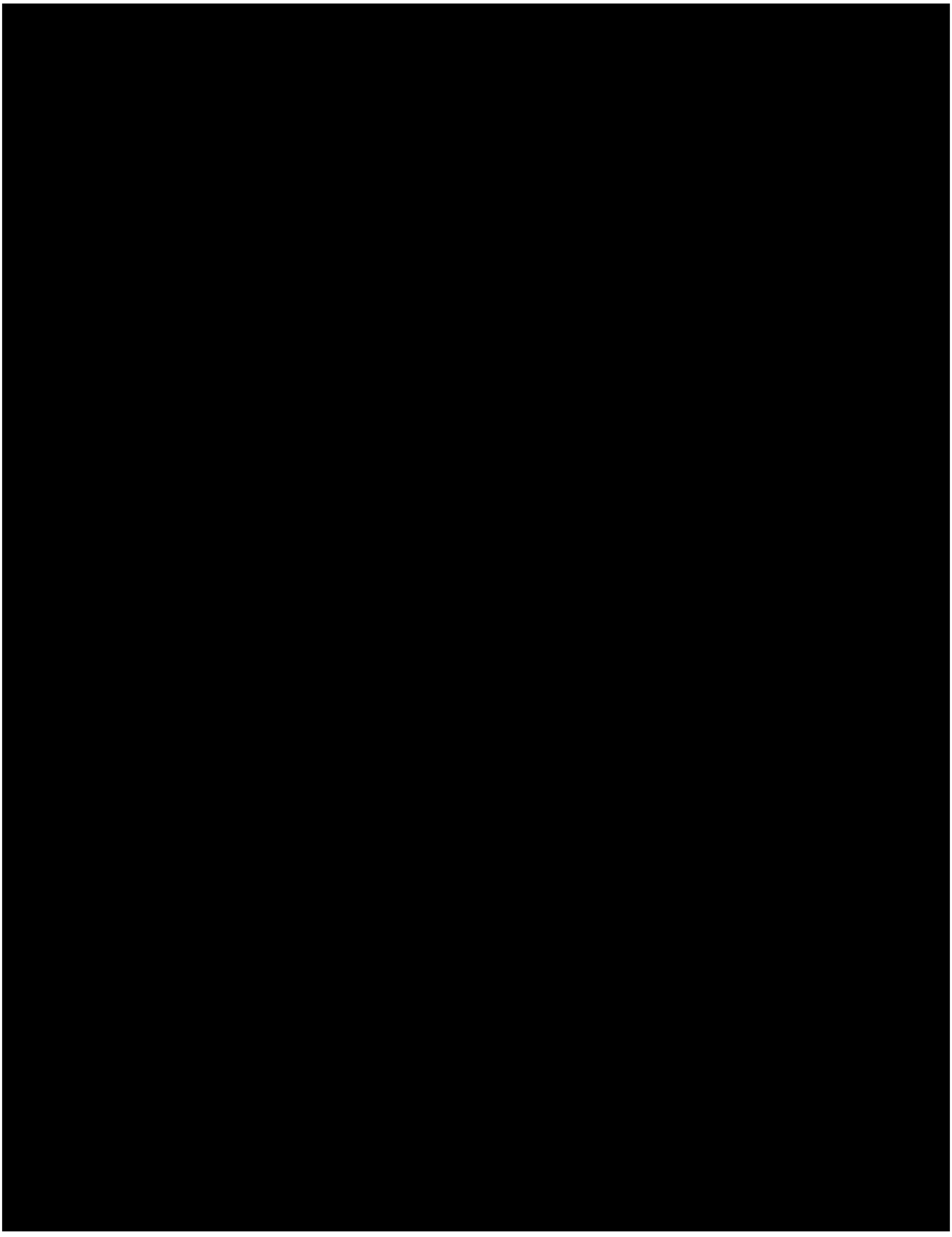

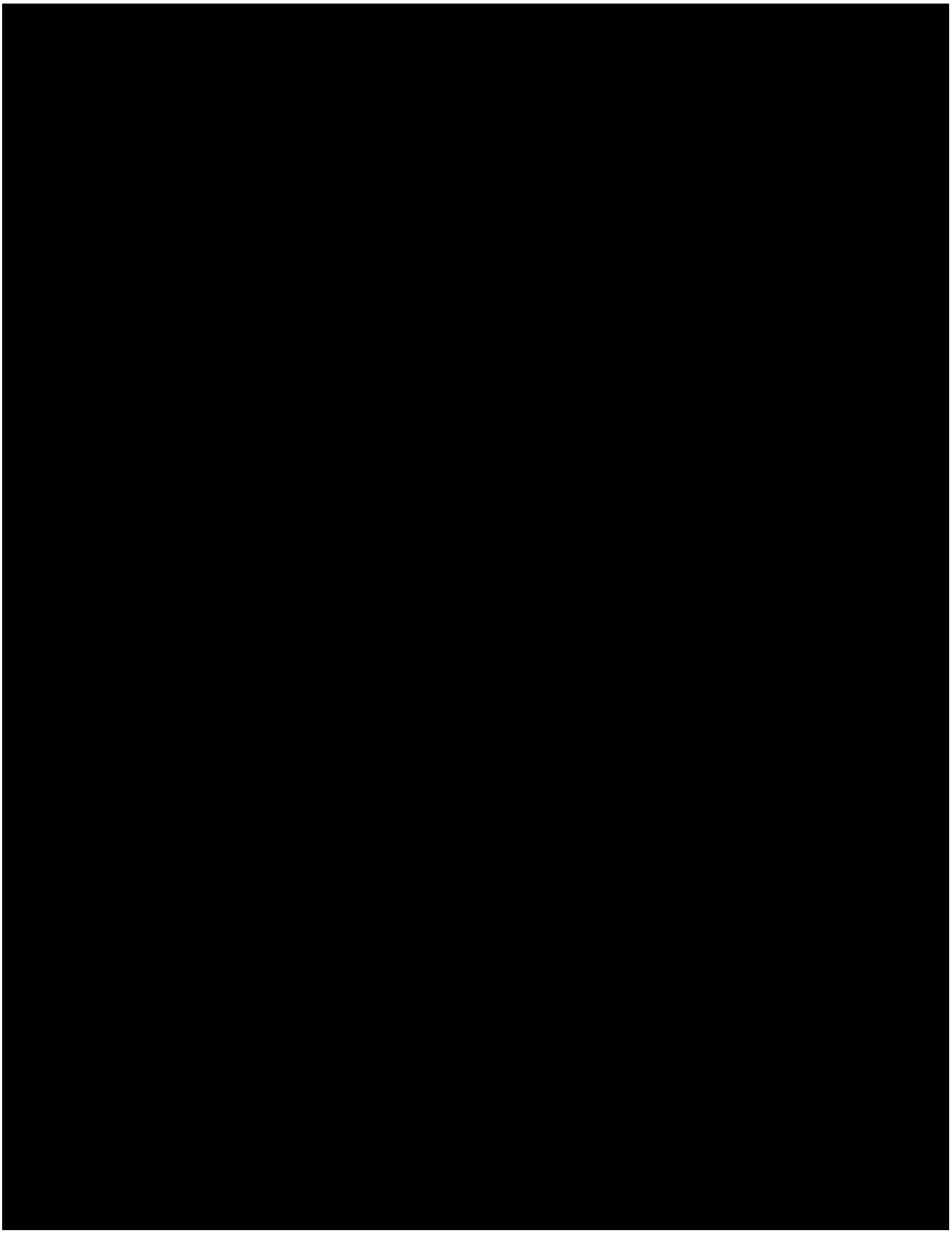

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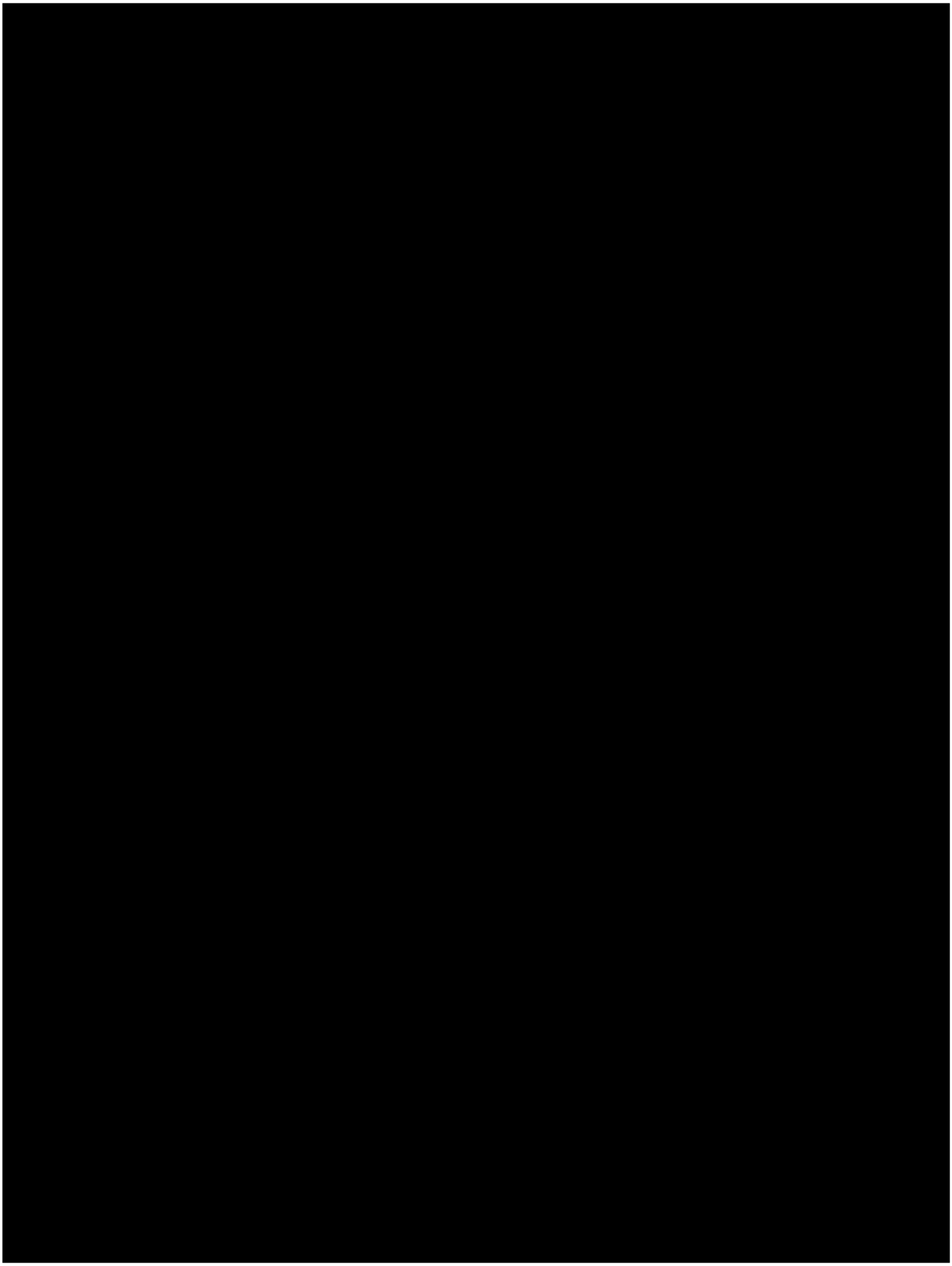
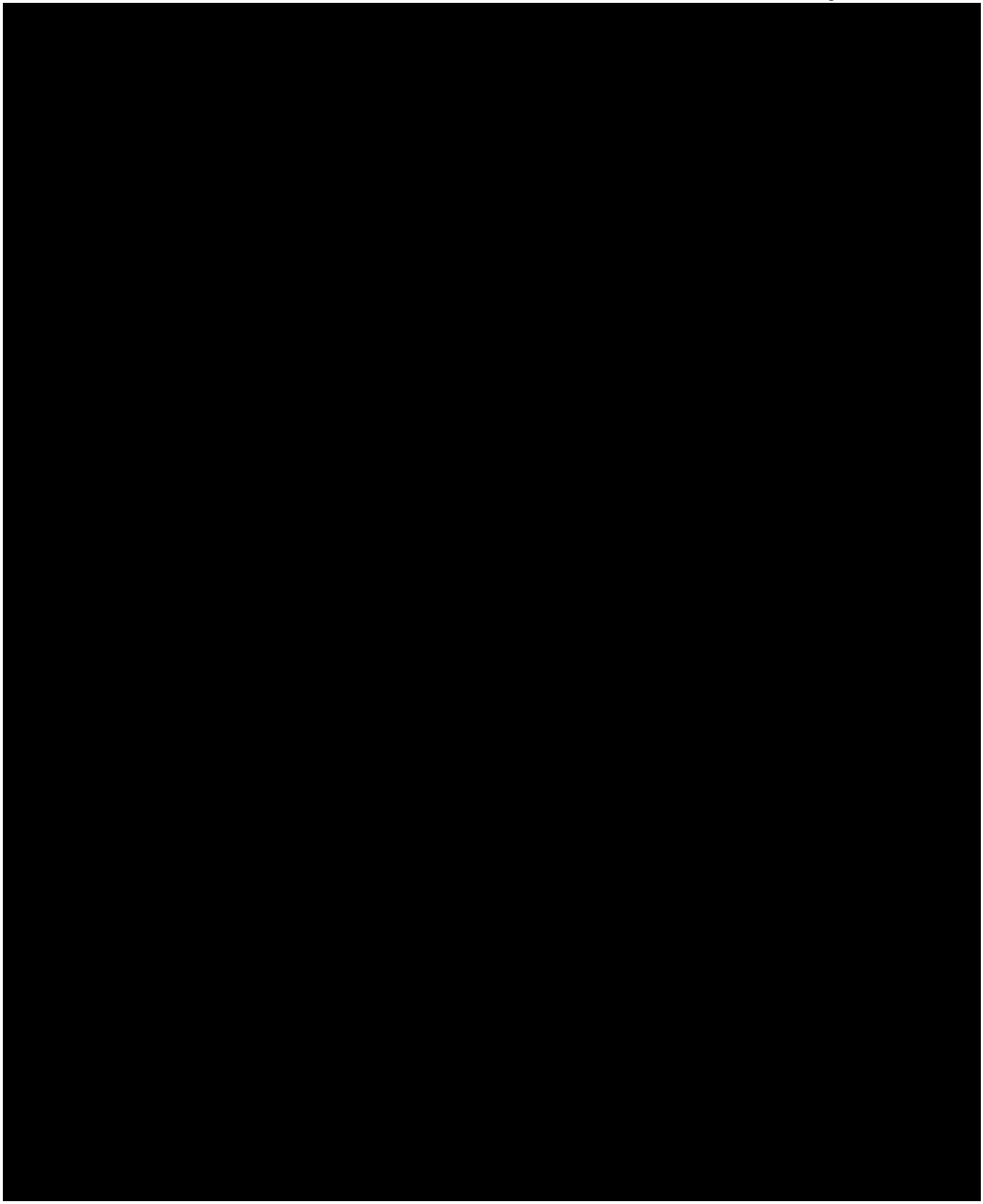




# 5 INTRODUCTION

## 5.1 Rationale and Background

Extended wear contact lenses have been marketed and tested in the United States and Europe since the 1970s. Extended wear contact lenses offer around the clock vision correction to patients without the inconvenience of removal for daily cleaning and disinfection. For successful overnight lens wear, the lenses must not only be safe and effective, but also comfortable over the prescribed wearing period.

New SiHy materials continue to be developed possessing unique material properties and superior oxygen transmissibility over contact lenses made with conventional hydrogel materials. A new lens, known here as the [redacted] contact lens, has been developed in an effort to maintain sustained performance by providing an inherently wettable core material. The new SiHy lens has been designed to provide favorable performance for daily wear and extended wear for up to 6 nights continuous wear with 1-week replacement.

In this clinical trial, the performance of the investigational [redacted] contact lens will be compared to the commercially available Biofinity contact lens in a parallel group design to demonstrate the safety and effectiveness of the [redacted] contact lens when worn for extended wear (up to 6 nights/7 days of continuous wear followed by 1 night of no lens wear, and replaced on a weekly basis) as compared to Biofinity contact lens worn for extended wear (up to 6 nights/7 days of continuous wear followed by 1 night of no lens wear, and replaced on a weekly basis). The intended use of this contact lens is for vision correction. Therefore, the measurement of distance VA is planned as the primary effectiveness variable. [redacted] The recommendations of ISO 11980:2012, FDA (510(k)) Guidance Document for Daily Wear Contact Lenses and variables directly relevant to the evaluation of extended wear soft contact lenses were considered.

## 5.2 Purpose of the Study

The purpose of this clinical trial is to evaluate the safety and performance of the [redacted] contact lens compared to the commercially available Biofinity contact lens, by assessing ocular serious and significant non-serious ADEs as the primary safety variable and distance VA as the primary effectiveness variable.

At the end of the study, a clinical study report will be prepared in accordance with applicable regulatory requirements and standards.

[redacted]

## 5.3 Risks and Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Biofinity contact lenses are approved for extended wear for up to 6 nights/7 days of continuous wear. Further details on any known potential risks and benefits can be found in the package insert.

Material properties and design characteristics of the investigational (not approved by the FDA) [redacted] contact lenses are consistent with successful contact lens wear. To date, supportive results from preclinical tests and documented rationale for applicability of test results, and the previous clinical studies, described in the IB, provide a basis for the anticipated acceptable performance and safety profile of the [redacted] contact lenses for up to 6 continuous nights of extended wear with planned weekly replacement in the upcoming 12-month registration study. This study will evaluate any long term or new risks with the extended wear of [redacted] contact lenses and how these risks compare to a marketed extended wear control lens. A summary of the known and potential risks and benefits associated with [redacted] contact lenses is presented in the IB. The potential harms associated with on-eye exposure to the new lens materials include toxicity response, blurred vision, and ocular discomfort.

Under the conditions of a clinical study, which include compliance with subject selection criteria, oversight by study Investigators, adequate informed consent, subject instructions, scheduled lens wear/replacement, and frequent follow-up visits, risks to study subjects are controlled and minimized. Site personnel will educate subjects on proper hygiene and lens handling, and compliance with the use of contact lenses according to the protocol. Subjects should be instructed not to wear contact lenses while swimming due to increased risk of infection. Site personnel should advise the subjects to remove contact lenses and return for prompt follow-up of symptoms such as ocular discomfort, foreign body sensation, excessive tearing, vision changes, or hyperemia.

Refer to the IB for additional information.

# 6 STUDY OBJECTIVES

## 6.1 Primary Objective(s)

**Table 6–1 Primary Objective(s)**

| Objective(s) | Endpoint(s) |
|---|---|
| Demonstrate safety and effectiveness of the [redacted] contact lens as compared to Biofinity contact lens, when both study lenses are worn for extended wear (up to 6 nights/7 days of continuous wear followed by 1 night of no lens wear) and replaced on a weekly basis. | Primary Safety<br>• Proportion of ocular serious and significant non-serious ADEs<br>Primary Effectiveness<br>• Distance VA (Snellen) |

## 6.2 Secondary Objective(s)

Not Applicable

## 6.3 Exploratory Objective(s)

Not Applicable

## 6.4 Other Safety Objective(s)

**Table 6–2 Other Safety Objective(s)**

| Objective(s) | Endpoint(s) |
|---|---|
| Duty of care and evaluation of safety profile of the investigational products. | AEs<br>Device deficiencies<br>Biomicroscopy findings |

# 7 INVESTIGATIONAL PLAN

## 7.1 Study Design

This will be a prospective, randomized, [redacted] controlled, double-masked, parallel-group, extended wear clinical study.

This clinical trial will engage approximately 45 clinic sites to enroll approximately 812 subjects [redacted]

[redacted]

Sites will be identified and notified prior to study start.

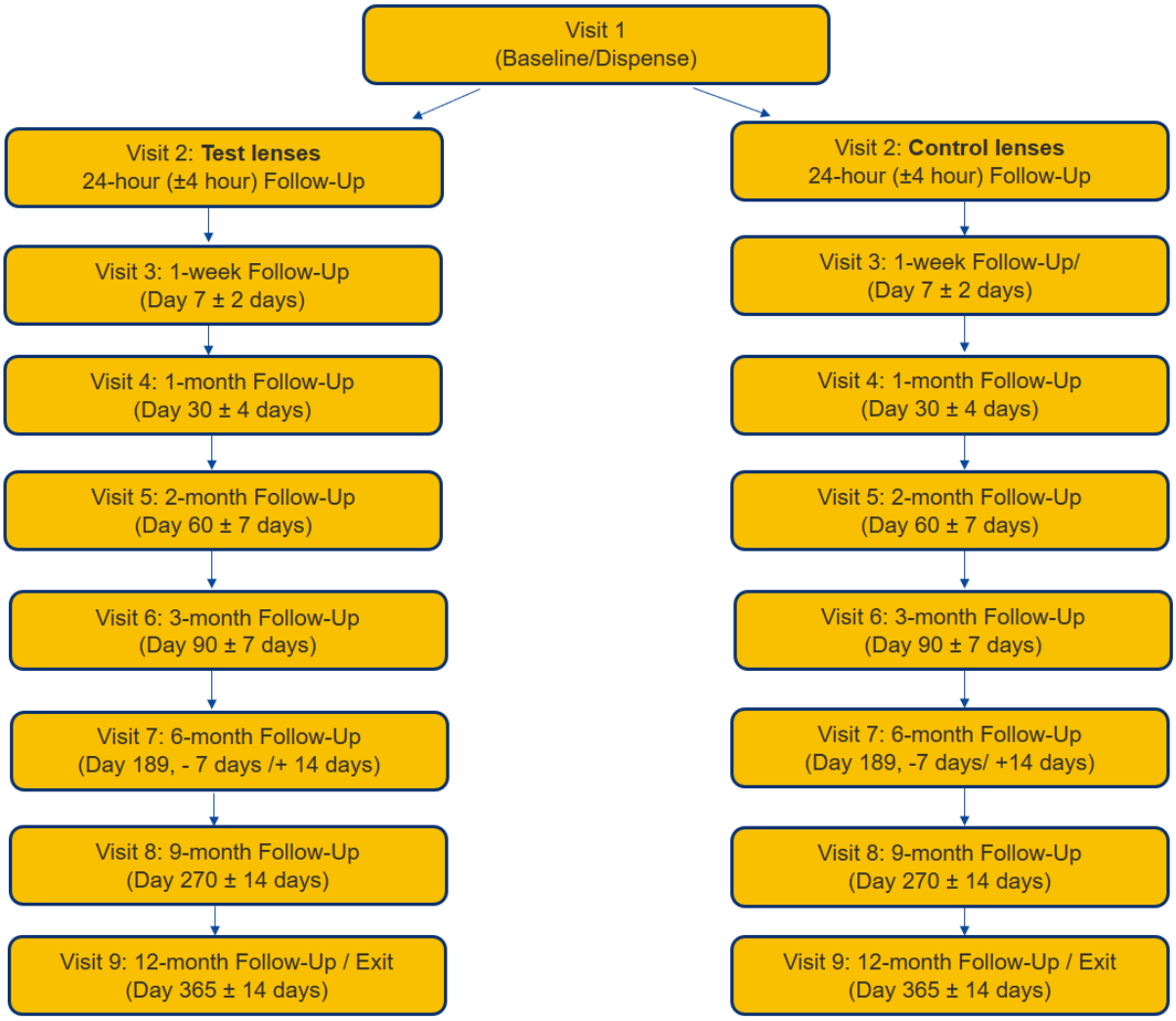
Subjects will be expected to attend 9 office visits: Baseline/Dispense, 24-hour follow-up, 1-week follow-up, 1-month follow-up, 2-month follow-up, 3-month follow-up, 6-month follow up, 9-month follow-up and 12-month follow-up/Exit. The total expected duration of participation for each subject is approximately 12 months in this extended wear study. Subjects will be randomized to wear either the test [redacted] contact lenses in both eyes or the control Biofinity contact lenses in both eyes.

Following randomization, study lenses will be dispensed to the subject. Subjects will be provided with sufficient lens supplies to follow a weekly replacement schedule until the next scheduled visit.

Subjects will wear the lenses while awake and asleep for up to 6 nights/7 days of continuous wear in an extended wear modality. CLEAR CARE and LacriPure (or equivalent) will be permitted if the subject must remove their lens(es) for any reason. Systane will be also permitted but should only be used if necessary and is the only product permitted for use in the eye.

The study outline is provided in Figure 7-1 below:

**Figure 7-1 Flowchart of Study Visits**




## 7.2 Rationale for Study Design

In this clinical trial, the safety and performance of the investigational [redacted] contact lens will be compared to the commercially available Biofinity contact lens in a double-masked, parallel-group design with approximately 12 months of exposure. The study is designed primarily following the recommendations for a new extended wear contact lens material from ISO 11980:2012 and the US FDA 510(k) guidance document for reporting format.

## 7.3 Rationale for Duration of Treatment/Follow-Up

The duration of exposure and follow-up duration are in compliance with the recommended guidance from ISO 11980:2012.

## 7.4 Rationale for Choice of Control Product

Biofinity contact lens was chosen as the control product because this lens is a proper predicate device to compare to [redacted] contact lens with regard to effectiveness and safety. Both [redacted] contact lens and Biofinity contact lens are frequent replacement SiHy lenses and are to be prescribed for extended wear for up to 6 nights/7 days of continuous wear. The Biofinity contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes.

## 7.5 Data Monitoring Committee

Not Applicable

# 8 STUDY POPULATION

The study population consists of adult male or female subjects (aged 18 or over), with non-diseased eyes, who require optical correction for refractive ametropia. The aim is to enroll approximately 812 subjects in approximately 45 US sites, with approximately 18-20 subjects per site. Estimated time needed to recruit subjects for the study is approximately 16 weeks. Competitive enrollment may be implemented across investigative sites should the need arise to help meet the target enrollment objective.

The intended study population consists of volunteer subjects who are frequent replacement daily wear or extended wear soft contact lens wearers, who have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week. Subjects must have regularly worn their habitual lenses for at least **10 hours** per day. Additionally, extended wear lens wearers must have regularly worn their habitual lenses for at least one night per week. [redacted]

[redacted]

[redacted]

## 8.1 Inclusion Criteria

Written informed consent must be obtained before any study specific assessment is performed. Upon signing informed consent, the subject will be considered enrolled in the study.

Subjects eligible for inclusion in this study must fulfill **all** of the following criteria:

| | |
|---|---|
| 1. | Subject must be at least 18 years of age. |
| 2. | Subject must be able to understand and sign an IRB/IEC approved Informed Consent Form. |
| 3. | Willing to attend all scheduled study visits as required per protocol. |
| 4. | Willing and able to wear assigned study lenses as required per protocol. |
| 5. | Successful wear of spherical daily wear or extended wear soft contact lenses in both eyes during the past 3 months for a minimum of 5 days per week. Habitual daily wear and extended wear subjects must have worn their lenses at least 10 hours per day. Additionally, the extended wear lens wearers must have worn their lenses overnight at least one night per week. |
| 6. | Manifest cylinder ≤ 0.75 D in each eye. |

[redacted]

[redacted]

## 8.2 Exclusion Criteria

Subjects fulfilling **any** of the following criteria are not eligible for participation in this study.

| | |
|---|---|
| 1. | Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator. |
| 2. | Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the Investigator. |
| 3. | History of ocular or intraocular surgery, including refractive surgery and / or irregular cornea; current or previous orthokeratology treatment; or any wear of RGP contact lenses in the past 12 months. |

[redacted]

| | |
|---|---|
| 9. | Daily disposable contact lens wearers. |

[redacted]

| | |
|---|---|
| 11. | Currently pregnant or breast-feeding. |
| 12. | Monovision contact lens wearers. |

[redacted]

## 8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

# 9 TREATMENTS ADMINISTERED

## 9.1 Investigational Product(s)

*Test Product(s):* [redacted] soft contact lenses

*Control Product(s) (If applicable):* Biofinity (comfilcon A) soft contact lenses

**Table 9–1 Test Product**

| | |
|---|---|
| Test Product | [redacted] soft contact lenses ([redacted] contact lens)<br>(LID015385) |
| Manufacturer | Alcon Vision, LLC<br>6201 South Freeway<br>Fort Worth, Texas 76134-2099<br>USA |
| Indication for use and intended purpose in the current study | The intended use of this contact lens is for vision correction. |

| | |
|---|---|
| Product description and parameters available for this study | [redacted]<br>• Water content target: 55% ±2%<br>• Power range:<br>  o -0.50 to -6.00 D (0.25 D steps)<br>  o Additional powers (provisional): -6.50 to -8.00 D (0.50 D steps)<br>  o +0.50 D to +4.00 D (0.25 D/0.50 D steps)<br>• Base curve target: 8.4 (±0.2 mm)<br>• Diameter: 14.2 mm |
| Formulation | Silicone hydrogel. Additional details can be found in the [redacted] extended wear IB. |
| Usage | • Wear:<br>  o Extended Wear<br>  ▪ Up to 6 nights/7 days continuous wear (awake and asleep) and must sleep 1 night without lenses.<br>  o Bilateral<br>• Exposure: ~12 months<br>• Replacement period: Planned replacement each week over the course of the study duration. Subjects will wear a fresh pair of lenses in alignment with weekly planned replacement schedule.<br>  o For planned replacement, lenses will be replaced even if one or both of the lenses have not been used for the full 1-week wearing schedule.<br>• Lens Care: CLEAR CARE, LacriPure (or equivalent), Systane, and OFPM MPDS as needed.<br>• Additional details can be found in the MOP |

| | |
|---|---|
| Number/Amount of product to be provided to the subject | At each study visit, sites will ensure that subjects are given adequate lenses to last until the next planned study visit, allowing for planned and unplanned lens replacements. |
| Packaging description | Blister foil pack |
| Labeling description | • Lens Foil label includes:<br>- identifier<br>- base curve<br>- diameter<br>- manufacturing protocol number<br>- packing solution<br>- power<br>- lot number<br>- expiration date<br>- content statement<br>- investigational device statement<br>- Sponsor information<br>• Provided in boxes of up to 18 lenses per power per box, identified with the following:<br>- a color coded label stating the protocol number<br>- identifier<br>- power<br>- an investigational use only statement<br>- tracking number |
| Storage conditions | Stored at room temperature. |

| | |
|---|---|
| Supply | • Fitting sets and spare lenses will be provided by the Sponsor before the start of the trial to be used during Visit 1.<br>• Study lenses will be provided to the site for each subject as per the Investigator's order form. The site will dispense the study lenses to the subject at Visit 1, and according to the planned lens replacement schedule throughout the study. Refer to the MOP for a detailed description. |

**Table 9–2 Control Product**

| | |
|---|---|
| Control Product(s) | Biofinity (comfilcon A) soft contact lenses (Biofinity contact lens) (LID010221) |
| Manufacturer | CooperVision |
| Indication for Use | The intended use of this contact lens is for vision correction. |
| Product description and parameters available for this study | • Material: comfilcon A<br>• Water content: 48%<br>• Power range:<br>o -0.50 to -6.00 D (0.25 D steps)<br>o Additional powers (provisional): -6.50 to -8.00 D (0.50 D steps)<br>o +0.50 D to +4.00 D (0.25 D/ 0.50 D steps)<br>• Base curve: 8.6 mm<br>• Diameter: 14.0 mm |
| Formulation | Silicone Hydrogel. Additional details can be found in the Biofinity package insert. |
| Usage | • Wear:<br>o Extended Wear –<br>▪ Up to 6 nights/7 days continuous wear (awake and asleep) and must sleep 1 night without lenses. |

| | |
|---|---|
| | ○ Bilateral<br>• Exposure: ~12 months<br>• Replacement period: Planned replacement each week over the course of the study duration. Subjects will wear a fresh pair of lenses in alignment with weekly planned replacement schedule.<br>○ For planned replacement, lenses will be replaced even if one or both of the lenses have not been used for the full 1-week wearing schedule.<br>• Lens Care: CLEAR CARE, LacriPure (or equivalent), Systane, and OFPM MPDS as needed.<br>• Additional details can be found in the MOP |
| Number/Amount of Product to be Provided to the subject | At each study visit, sites will ensure that subjects are given adequate lenses to last until the next planned study visit, allowing for planned and unplanned lens replacements. |
| Packaging description | Blister foil pack. |
| Labeling description | • Lens Foil label includes:<br>- identifier<br>- base curve<br>- diameter<br>- packing solution<br>- power<br>- lot number<br>- expiration date<br>- content statement<br>- investigational device statement<br>- Sponsor information<br>• Provided in boxes of up to 18 lenses per power per box, identified with the following: |

| | |
|---|---|
| | - a color coded label stating the protocol number<br>- identifier<br>- power<br>- an investigational use only statement<br>- tracking number |
| Storage conditions | Stored at room temperature. |
| Supply | • Fitting sets and spare lenses will be provided by the Sponsor before the start of the trial to be used during Visit 1.<br>• Study lenses will be provided to the site for each subject as per the Investigator's order form. The site will dispense the study lenses to the subject at Visit 1, and according to the planned lens replacement schedule throughout the study. Refer to the MOP for a detailed description. |

More information on the test product can be found in the IB; information on the control product can be found in the Package Insert.

## 9.2 Other Medical Device or Medication Specified for Use During the Study

Other than the pre-specified CLEAR CARE, LacriPure (or equivalent), Systane rewetting drops, and OFPM MPDS, no other medical devices or medications are required to be used in conjunction with the treatments during the clinical study.

## 9.3 Treatment Assignment / Randomization

Subjects will be randomized in a 1:1 manner to receive either the [redacted] or Biofinity contact lenses, respectively. [redacted]

Only after signing the ICF, a subject will be assigned a subject number by the electronic data capture system.

A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio [redacted] Subjects will be assigned a treatment arm according to the randomization list

uploaded in the IRT system. The randomization list will be generated and maintained by the Study Sponsor.

At Visit 1, all eligible subjects will be randomized via the EDC/IRT integration system to one of the treatment arms. The Investigator's delegate will access the respective system after confirming that the subject meets all the eligibility criteria. A randomization number will be automatically assigned to the subject according to the subject randomization list but will not be communicated to the site user. The EDC/IRT integration system will inform the site user of the treatment assignment to be dispensed to the subject.

## 9.4 Treatment masking

This study is double-masked, with subjects randomized to use [redacted] or Biofinity contact lenses for the duration of the 12-month treatment period. [redacted]

Masked study personnel must avoid seeking information that may compromise masking. Unmasked study personnel must not disseminate information that is potentially unmasking to any masked personnel. The masked and unmasked site personnel must coordinate all study activities as necessary to protect masking and minimize bias during the study.

In the event of a medical emergency where the knowledge of subject treatment is required, individual Investigator(s) will have the ability to unmask the treatment assignment for a specific subject. If time allows, the appropriate Study Sponsor representative should be

contacted prior to unmasking. Unmasking must be done according to the instructions provided for the study IRT system.

## 9.5 Accountability Procedures

Upon receipt of the IPs, the Investigator or delegate must conduct an inventory. During the study, unmasked designated study staff must provide the IPs to the subjects in accordance with their randomization assignment. Throughout the study, the unmasked designated study staff must maintain records of IP dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. All IPs sent to the Investigator must be accounted for by Study Sponsor personnel, and in no case be used in an unauthorized situation.

It is the Investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner
- All used foils and unused supplies are returned by each subject
- All unused products are available for return to the Study Sponsor, as directed
- Any study lenses associated with a device deficiency or with any product-related AE (ie, ADE or SADE) are returned to the Study Sponsor for investigation, unless otherwise directed by the Sponsor. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.
- Every effort should be made to return opened and unopened investigational lenses from those subjects lost to follow-up.
- All supplies are to be retrieved from the subject at the final visit. If a subject misses the final visit, all efforts MUST be made to reschedule the final visit provided it is scheduled within the visit window.

The Investigator is responsible for proper disposition of all unused IPs at the conclusion of the study, according to the instructions provided in the MOP.

## 9.6 Changes to concomitant medications, treatments/ procedures

After the subject is enrolled into the study, the Investigator must instruct the subject to notify the study site about:

- Any new medications
- Alterations in dose or dose schedules for current medications,
- Any medical procedure or hospitalization that occurred or is planned
- Any non-drug therapies (including physical therapy and blood transfusions).

The Investigator must document this information in the subject's case history source documents.

# 10 STUDY PROCEDURES AND ASSESSMENTS

Subjects will be expected to attend 9 office visits, as shown in Table 10-1.

**Table 10–1 Study Visits**

| Visit # | Visit Type | Visit Day | Visit Window |
|---|---|---|---|
| **Visit 1** | Baseline/Dispense | Day 1 | N/A |
| **Visit 2** | 24-Hour Follow-Up Visit | Day 2 | Hours 20–28 |
| **Visit 3** | 1-Week Follow-Up Visit | Day 7 | Days 5–9 |
| **Visit 4** | 1-Month Follow-Up Visit | Day 30 | Days 26–34 |
| **Visit 5** | 2-Month Follow-Up Visit | Day 60 | Days 53–67 |
| **Visit 6** | 3-Month Follow-Up Visit | Day 90 | Days 83–97 |
| **Visit 7** | 6-Month Follow-Up Visit | Day 189 | Days 182–203 |
| **Visit 8** | 9-Month Follow-Up Visit | Day 270 | Days 256–284 |
| **Visit 9** | 12-Month Follow-Up / Exit Visit | Day 365 | Days 351–379 |

Unscheduled Visits and Early Termination Visits are allowed, if necessary.

At the Baseline/Dispense Visit, study lenses will be trial fit using the fitting sets supplied by the Sponsor, and the correct contact lens power for the individual subject will be determined. Sites will be provided with adequate lens supply to dispense the first pair of study lenses during Visit 1.

The Sponsor will send study lenses for each subject to the site after receiving an order from the Investigator. The Investigator will complete the order forms as and when needed to provide a consistent stream of lens supply for each subject enrolled in this clinical study.

At the Baseline/Dispense Visit, study lenses will be dispensed to the subject. All subjects will wear the study lenses in an extended wear modality, while awake and asleep for up to 6 nights/7 days of continuous wear with one night of no lens wear. This wearing schedule will be repeated throughout the course of the trial. The wearing schedule assignment for either test or control lens should be preserved as much as possible unless there are safety reasons that necessitate a modification to the wearing schedule assignment.

Subjects assigned to wearing [redacted] or Biofinity contact lenses will insert a new pair of study lenses each week and discard them at the end of the week. Problem lenses (if any) will not be discarded but collected by the subject and returned to the investigational site. [redacted] VA will be measured at all visits, and any decrease of 2 or more lines from the Baseline/Dispense Visit to any follow-up visit should be explained by the Investigator. Keratometry will be performed at the Baseline/Dispense, 6-Month, and Exit Visits, and manifest refraction will be performed at the Baseline/Dispense and Exit Visits.

## 10.1 Informed Consent and Screening

The Investigator or delegate must explain the purpose and nature of the study, and have the subject read, sign, and date the IRB/IEC-approved informed consent document. The subject must sign the ICF BEFORE any study-specific procedures or assessments can be performed, including study-specific screening procedures. Additionally, the individual obtaining consent from the subject and a witness, if applicable, must sign and date the informed consent document.

The Investigator or delegate must provide a copy of the signed document to the subject and place the original signed document in the subject's chart, or provide documentation as required by local regulations.

## 10.2 Description of Study Procedures and Assessments

Detailed descriptions of assessments and procedures are provided in the MOP. The Investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified site personnel.

### 10.2.1 Demographics

Obtain demographic information including age, race, ethnicity, and sex.

### 10.2.2 Medical History

Collect medical history information, including information on all medications used within the past 30 days. Include herbal therapies, vitamins, and all over-the-counter as well as prescription medications. Throughout the subject's participation, obtain information on any changes in medical health and/or the use of concomitant medications.

### 10.2.3 Investigational Product compliance

Review subject compliance with the IP usage and adjunct product usage and collect all used and unused study IPs and other products that were dispensed.

### 10.2.4 Adverse Event Collection: Safety Assessment

Assess and record any AEs that are observed or reported, including those associated with changes in concomitant medication dosing since the previous visit.

### 10.2.5 Slit-Lamp Biomicroscopy: Safety Assessment

Slit-lamp examination of the cornea, iris/anterior chamber and lens must be performed in both eyes before instillation of any diagnostic eye drops.

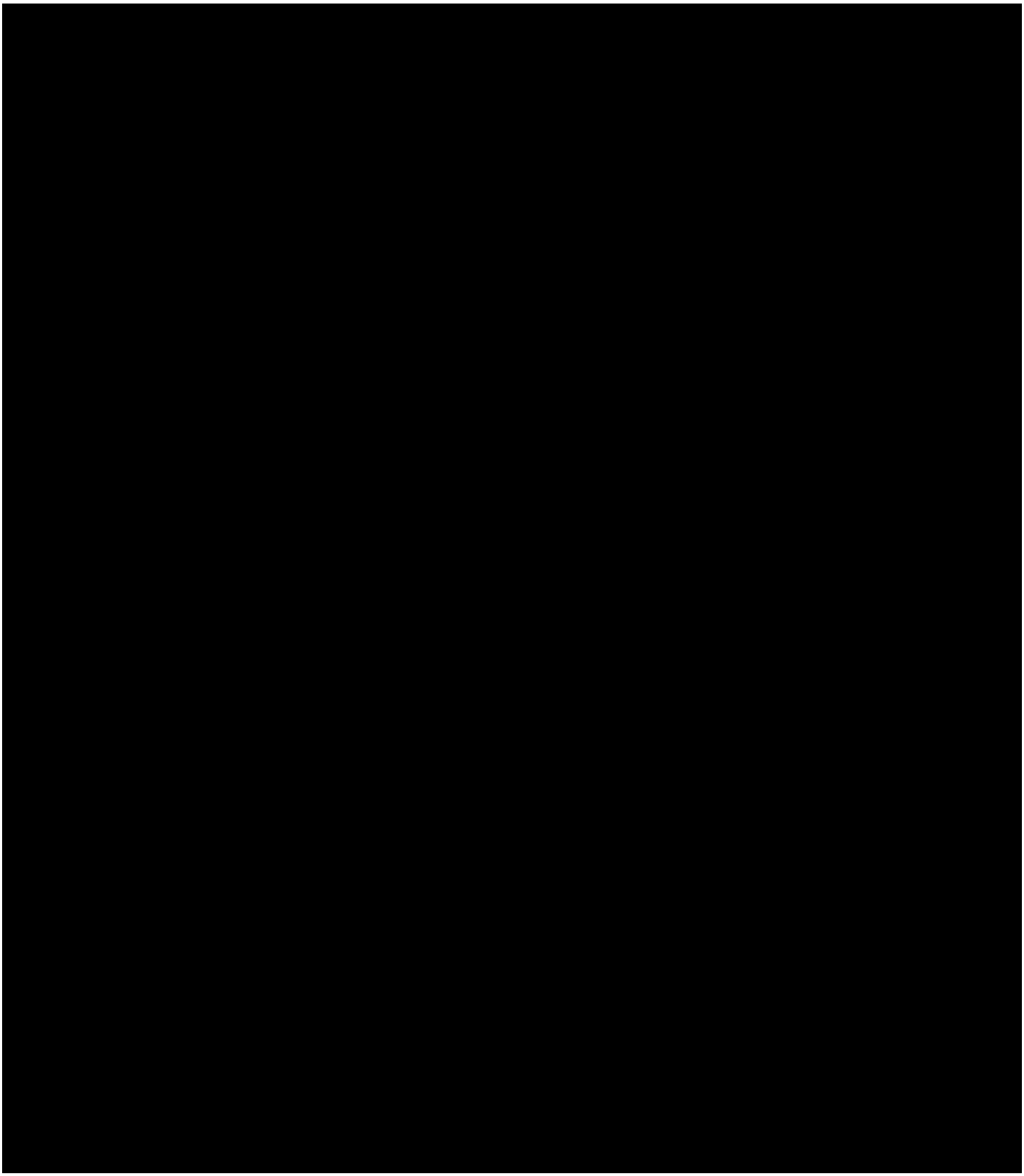
### 10.2.6 Device Deficiencies: Safety Assessment

Assess and record any device deficiencies that are reported or observed, including those associated with changes in concomitant medication dosing since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11.

## 10.3 Additional Study Assessments: Effectiveness and Safety Assessment

The following are additional study assessments. Refer to the MOP for further details.

- Distance VA with study lenses (Snellen)
- Distance VA with habitual correction (Snellen)
- Manifest refraction
- [redacted]
- Keratometry



## 10.4 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visits, this visit must be documented as an Unscheduled Visit. During all unscheduled visits, the Investigator must conduct the following procedures:

- Collect AE information, as applicable
- Record changes in medical condition or concomitant medication
- Collect device deficiency information, as applicable
- Assess and record VAs
- Perform biomicroscopy (assessments with or without lenses, as applicable)

[redacted]

- Collect symptoms, problems, and complaints

[redacted]

The Investigator may perform additional procedures for proper diagnosis and treatment of the subject according to Table 3-1. The Investigator must document this information in the subject's case history source documents.

If, during an Unscheduled Visit, the subject is to discontinue IP or is discontinuing from the study, the Investigator must conduct Exit procedures according to Table 3-1, as possible.

## 10.5 Discontinued Subjects

### 10.5.1 Screen Failures

Screen failures are subjects who were excluded from the study after signing the informed consent, not meeting the inclusion/exclusion criteria, and prior to randomization to product/dispense of study product.

The Investigator must document the reason for screen failure in the subject's case history source documents.

Subject numbers must not be re-used.

### 10.5.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the Investigator after signing the informed consent.

Subject numbers of discontinued subjects must not be re-used.

Subjects may discontinue from study or study treatment at any time for any reason. Subjects may also be discontinued from study treatment at any time if, in the opinion of the Investigator, continued treatment poses a risk to their health.

Subjects missing consecutive follow-up visits will be evaluated to determine if discontinuation may be necessary.

For subjects discontinuing from the study, the Investigator must complete all Exit procedures according to Table 3-1, if the subject is willing and able, and if in the opinion of the Investigator it is safe for the subject to do so.

The Investigator must document the reason for study or treatment discontinuation in the subject's case history source documents.

To ensure the safety of all subjects who discontinue early, Investigators must assess each subject and, if necessary, advise them of any therapies and/or medical procedures that may be needed to maintain their health.

### 10.5.3 Schedule of Procedures and Assessments for Subjects Discontinued from Investigational Product

Other than screen failures, if a subject discontinues from the study, the subject should undergo an Early Exit Visit. Refer to Table 3-1.

## 10.6 Clinical Study Termination

The Study Sponsor reserves the right to close the investigational site or terminate the study in its entirety at any time.

If the clinical study is prematurely terminated or suspended by the Study Sponsor:

- The Study Sponsor must:
    - Immediately notify the Investigator(s) and subsequently provide instructions for study termination.

- Inform the Investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension.

- The Investigator must:
  - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
  - Provide subjects with recommendations for post-study treatment options as needed.

The Investigator may terminate the site's participation in the study for reasonable cause.

### 10.6.1 Follow-up of subjects after study participation has ended

Following this study, the subject will return to their eye care professional for their routine eye care.

# 11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

## 11.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test article). Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

**Figure 11–1 Categorization of All Adverse Events**

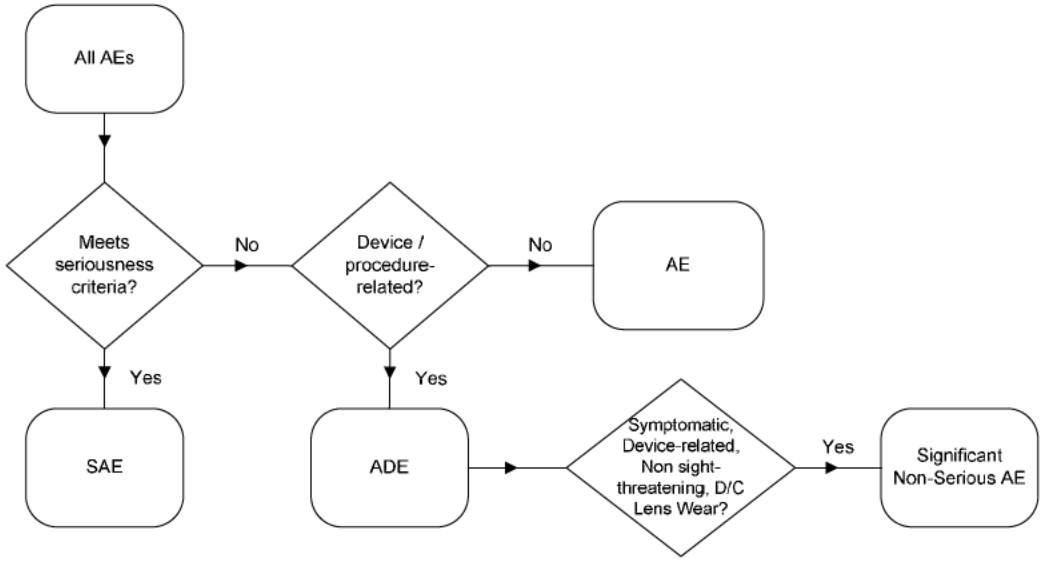
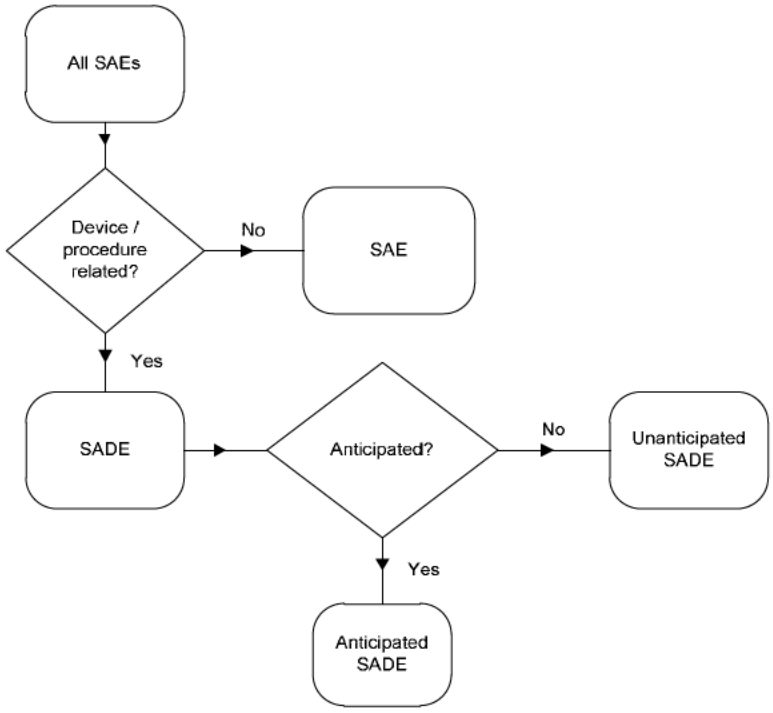


**Figure 11–2 Categorization of All Serious Adverse Events**




***Serious Adverse Events***

In addition to reporting all AEs (serious and non-serious) meeting the definitions, the Investigator must report any occurrence of the following as an SAE:

- An ocular infection including a presumed infectious ulcer with any of the following characteristics*:
    - Central or paracentral location
    - Penetration of Bowman's membrane
    - Infiltrates > 2 mm diameter
    - Iritis
    - Increase in intraocular pressure
    - Culture positive for microorganisms
    - Increasing size or severity at subsequent visits
- Any central or paracentral corneal event (such as neovascularization) that results in permanent opacification
- Hypopyon

- Hyphema
- Neovascularization within the central 6 mm of the cornea
- Permanent vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting ≥ 50% of corneal surface area

*NOTE: Culture samples (from the subject's eyes, lenses, etc) must be taken at investigator's discretion [*as described in the MOP; and documented in the narrative section(s) of the corresponding ADE-SAE eCRF*], for any suspected ocular infection, including infiltrates with overlying epithelial defect.

***Significant Non-Serious Adverse Events***

A significant non-serious AE is a device-related, non-sight threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. In addition, the Investigator must report any occurrence of the following as a Significant Non-Serious Adverse Event:

- Peripheral non-progressive non-infectious ulcers
- All symptomatic corneal infiltrative events
- Corneal staining score greater than or equal to Grade 3 (Refer to MOP for grading scales)
- Temporary vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that persists for 2 or more weeks
- Neovascularization score greater than or equal to Grade 2 (Refer to MOP for grading scales)

*The above events are based upon the categories provided in ISO 11980 and the US FDA Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses.*

***Device Deficiencies***

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with subject harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category listed in the

Device Deficiency eCRF for the identified or suspect device deficiency and report any subject harm separately. Examples of device deficiencies include the following:

- Failure to meet product specifications (eg, incorrect lens power/diameter/base curve/color)
- Lens cloudy
- Lens surface/edge defect
- Torn lens during handling/in pack
- Packaging deficit (eg, mislabeled product)
- Suspect product contamination
- Lack of performance

## 11.2 Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions:

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

Changes in *any protocol-specific parameters and/or questionnaires* evaluated during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in *a protocol-specific parameter or questionnaire response* that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

## 11.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (ie, before informed consent is signed) are not considered AEs in the study and should be recorded in the Medical History section of the eCRF.

In addition, temporary lens awareness or visual changes during the fitting process are not considered AEs if the Investigator assesses that the symptom(s) can reasonably resolve within the anticipated adaptation period.

- ADEs or SAEs are documented on the *Serious Adverse Event and Adverse Device Effect* eCRF within 24 hours of the Investigator's or site's awareness.
- Device deficiencies are documented on the *Device Deficiency* eCRF within 24 hours of the Investigator's or site's awareness.
- A printed copy of the completed *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* eCRF must be included with product returns.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death, etc, if applicable, in narrative section of the *Serious Adverse Event and Adverse Device Effect* eCRF.

*Note:* Should the EDC system become non-operational, the site must complete the appropriate paper *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* Form. The completed form is emailed to the Study Sponsor at [redacted] according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Additionally, any AEs and device deficiencies for non-study marketed devices/products (ie, CLEAR CARE Cleaning and Disinfecting Solution, LacriPure (or equivalent), and Systane preservative-free eye drops) will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives may be contacted for any protocol related question; their contact information is provided in the MOP that accompanies this protocol.

Further, depending upon the nature of the AE or device deficiency being reported, the Study Sponsor may request copies of applicable portions of the subject's medical records. The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

**Intensity and Causality Assessments**

Where appropriate, the Investigator must assess the intensity (severity) of the AE based upon medical judgment with consideration of any subjective symptom(s), as defined below:

***Intensity (Severity)***

| | |
|---|---|
| Mild | An AE is mild if the subject is aware of but can easily tolerate the sign or symptom. |
| Moderate | An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities. |
| Severe | An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities. |

For every AE in the study, the Investigator must assess the causality (Related or Not Related to the medical device or study procedure). An assessment of causality will also be performed by Study Sponsor utilizing the same definitions, as shown below:

***Causality***

| | |
|---|---|
| Related | An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure. |
| Not Related | An AE classified as not related may either be definitely unrelated or simply unlikely to be related (ie, there are other more likely causes for the AE). |

The Study Sponsor will assess the AEs and may upgrade the Investigator's assessment of seriousness and/or causality. The Study Sponsor will notify the Investigator of any AEs that are upgraded from non-serious to serious or from unrelated to related.

Additionally, the Study Sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect, including anticipated adverse events that occur in unanticipated severity or frequency. The results of this evaluation will be reported to the FDA, the IRB, and participating Investigators within 10 working days upon receiving notification of the effect.

## 11.4 Return product analysis

Investigational product associated with device deficiencies and/or product related AEs [ie, ADE or SADE] will be returned for investigation as detailed in the MOP.

## 11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study. If the treatment code needs to be broken in the interest of subject safety, the Investigator is encouraged to contact an appropriate Study Sponsor representative prior to unmasking the information if there is sufficient time. Dependent upon the individual circumstances (ie, medical emergency), the code may be broken prior to contact with the Study Sponsor. The Study Sponsor must be informed of all cases in which the code was broken and of the circumstances involved. Additionally, the Study Sponsor may be required to unmask the information in order to fulfill expedited regulatory requirements.

## 11.6 Follow-Up of Subjects with Adverse Events

The Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

The Investigator should provide the Study Sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ongoing at time of subject exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (ie, database lock).

Any additional data received up to 3 months after subject discontinuation or exit must be documented and available upon the Study Sponsor’s request. All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device’s manufacturer as per local requirements, as applicable.

The Investigator should also report complaints on non-Alcon products directly to the manufacturer as per the manufacturer’s instructions or local regulatory requirements.

## 11.7 Pregnancy in the Clinical Study

Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case-by-case basis. Should a woman become pregnant during study participation, the pregnancy will be documented on the Medical History eCRF.

# 12 ANALYSIS PLAN

Any deviations to the analysis plan will be updated during the course of the study as part of a protocol amendment or will be detailed in the clinical study report.

All analyses will be conducted according to the applicable statistical analysis plan.

## 12.1 Subject Evaluability

Final subject evaluability must be determined prior to breaking the code for masked treatment (lens) assignment and locking the database, based upon the Deviations and Evaluability Plan.

## 12.2 Analysis Sets

Five analysis sets will be defined:

a) All Enrolled – all subjects signing the informed consent form

b) Enrolled Dispensed – subjects/eyes from All Enrolled that have been exposed to study lenses [redacted]

c) Enrolled Not Dispensed – subjects/eyes from All Enrolled that have not been exposed to study lenses [redacted]

d) Completed – Enrolled Dispensed subjects/eyes completing the study

e) Discontinued – Enrolled Dispensed subjects/eyes not completing the study

## 12.3 Demographic and Baseline Characteristics

Demographic information, recent lens-wearing experience (including wear modality and wear success), and habitual lens information will be presented by lens group and overall for the All Enrolled analysis set.

Baseline data will be summarized by lens group, for Completed and Discontinued analysis sets separately, as applicable.

## 12.4 Effectiveness Analyses

For the primary [redacted] endpoint, separate summaries will be prepared, when applicable, for the Completed and the Discontinued analysis sets as follows:

- Completed Control (eyes/subjects)
- Completed Test (eyes/subjects)

- Discontinued Control (eyes/subjects)
- Discontinued Test (eyes/subjects)

No inferential testing will be performed on effectiveness endpoints, and format of the reporting tables will reference FDA's 510(k) guidance document (Clinical Appendix C, Summary of Reporting Tables) as well as the ISO guidance as specified in section A.3 (Reporting of results) of ISO 11980:2012.

### 12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary effectiveness endpoint is distance VA with study lenses, collected in Snellen, for each eye. Conversion will be made to the logMAR scale.

#### 12.4.1.1 Statistical Hypotheses

No hypothesis testing on the primary effectiveness endpoint is planned.

#### 12.4.1.2 Analysis Methods

Summary statistics will be provided. [redacted]

[redacted]

[redacted]

[redacted]

## 12.6 Safety Analyses

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. Descriptive summaries (counts and percentages) and listings will be presented. Individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to IP.

### 12.6.1 Analysis of Primary Safety Endpoint(s)

The primary safety endpoint is the proportion of ocular serious and significant non-serious ADEs, calculated as the number of eyes reporting at least one treatment-emergent device-related ocular serious ADE or treatment-emergent device-related ocular significant non-serious ADE.

#### 12.6.1.1 Statistical Hypotheses

The null and alternative hypotheses for the primary analysis are:

$H_0$: $P_T - P_C \geq 0.05$
$H_a$: $P_T - P_C < 0.05$

where $P_T$ and $P_C$ denote the proportion of eyes reporting ocular serious and significant non-serious ADEs with [redacted] and Biofinity contact lenses, respectively.

#### 12.6.1.2 Analysis Methods

A generalized linear model, with a logit link function, accounting for within-subject correlation will be fit. A one-sided 95% upper confidence limit (UCL) will be calculated for the difference in proportions between treatments ([redacted] contact lens minus Biofinity contact lens), and the null hypothesis will be rejected if UCL < 0.05.

### 12.6.2 Analysis of Other Safety Endpoints

Other safety endpoints include:

- AE (non-serious, non-significant)
- Biomicroscopy findings
- Device deficiencies

#### 12.6.2.1 Statistical Hypotheses

No hypothesis testing on the other safety endpoints is planned.

#### 12.6.2.2 Analysis Methods

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms, for Completed and Discontinued analysis sets. A listing containing details of the AEs will also be provided.

Each biomicroscopy parameter will be tabulated by its grade, on Completed and Discontinued analysis sets. Frequency for each device deficiency category will be presented and a supporting listing will be provided.

## 12.7 Interim Analyses and Reporting

There are no plans to conduct an interim analysis and no criteria by which the study would be terminated early based upon statistical determination.

## 12.8 Sample Size Justification

Sample size calculation was based on extended wear clinical studies from three PMA studies [redacted] and one 52-week extended wear study [redacted] that evaluated 5 currently marketed silicone hydrogel contact lenses. The weighted average, based on sample size, on the proportion of ocular serious and significant non-serious ADEs obtained from these five contact lenses was 0.045. Therefore, assuming that the expected difference between test and control is 0 and that the control proportion is 0.045, a sample size of 213 per group will provide 80% power to reject the null hypothesis of inferiority in test compared to control, with a noninferiority margin of 0.05 (5%).

Taking into consideration the exposure duration of 12 months, approximately 568 subjects will be randomized (284 test and 284 control) to compensate for approximately 25% drop-out rate.

# 13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

## 13.1 Subject Confidentiality

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the Investigator must keep an enrollment log with

confidential identifying information that corresponds to the subject numbers and initials of each study participant. At the end of the clinical study, the Study Sponsor will collect a copy of the enrollment log ***without any identifying subject information***. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

The Study Sponsor may release anonymized study data to external researchers for purposes of future research directly related to the study objectives, or future research that is beyond the scope of the current study objectives. The Informed Consent Form explains this to study subjects. Anonymization means that all identifiable information will be removed from the dataset and all links to the subjects in the study will be removed. Anonymization of the data will maintain confidentiality of the subjects who participate in the study so that they cannot be identified by external researchers. The anonymized data set will contain records from all of the subjects in the current study, but the anonymization process might change the data set in some ways, so external researchers will be informed that they might not be able to duplicate some of the results from this study.

## 13.2 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the CRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the Study Sponsor and are independent of study site staff.

If electronic records are maintained, the method of verification must be determined in advance of starting the study.

At a minimum, source documents include the following information for each subject:

- Subject identification (name, sex, race/ethnicity)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of study parameters, as required by the protocol
- IP accountability records

- Documentation of AEs and other safety parameters (if applicable)
- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation, if applicable

It is required that the author of an entry in the source documents be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the CRF are consistent with the original source data.

Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The Principal Investigator is responsible for reviewing and certifying that the CRFs are accurate and complete. The only subject identifiers recorded on the CRFs will be subject number, and subject demographic information.

## 13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, additional data clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's CRF.

## 13.4 Sponsor and Monitoring Responsibilities

The Study Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals according to the study monitoring plan. The clinical investigation will be monitored to ensure that the rights and well-being of the subjects are protected, the reported data are accurate, complete, and verifiable from the source documents, and the study is conducted in compliance with the current approved protocol (and amendments[s], if applicable), with current GCP, and with applicable regulatory requirements.

The site may not screen subjects or perform the informed consent process on any subject until it receives a notification from an appropriate Study Sponsor representative that the site may commence conducting study activities. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone, written and fax correspondence. Close-out visits will take place after the last visit of the last subject at the site.

A Coordinating Investigator may be identified by the Study Sponsor to review and endorse the final study report. In cases where a Coordinating Investigator is engaged, the Study Sponsor will select the Coordinating Investigator based upon their experience, qualifications, active study participation, and their willingness and availability to take on this role.

## 13.5 Regulatory Documentation and Records Retention

The Investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the Study Sponsor and the Investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is to be kept separately.

Additionally, the Investigator must keep study records and source documents consistent with the terms of the clinical study agreement with the Study Sponsor. If the Investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records, then the Study Sponsor must be notified and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations.

## 13.6 Quality Assurance and Quality Control

The Study Sponsor will secure agreement from all involved parties to ensure direct access to all study related sites, source data and documents, and reports for the purpose of monitoring and auditing by the Study Sponsor, and inspection by domestic and foreign regulatory authorities. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Agreements made by the Study Sponsor with the Investigator/Institution and any other parties involved in the clinical study will be provided in writing as part of the protocol or as a separate agreement.

# 14 ETHICS

This clinical study must be conducted in accordance with the ethical principles contained within:

- The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.
- SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.
- Notifications and timelines for reporting protocol deviations should be based upon applicable Ethics Committee requirements

The Investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The Investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. Deviations from this protocol, regulatory requirements, and/or GCP must be recorded and reported to the Sponsor prior to database lock. If needed, corrective and preventive action should be identified, implemented, and documented within the study records. Use of waivers to deviate from the clinical protocol is prohibited.

Before clinical study initiation, this protocol, the informed consent form, any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IRB/IEC. The Investigator must provide documentation of the IRB/IEC approval to the Study Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. Any Investigator who practices and intends to see study subjects at a hospital or university may require secondary review and approval by an IRB belonging to that institution. A copy of local or secondary IRB approvals should be provided to the Study Sponsor. The IRB/IEC must be provided with a copy of the IB, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. At the end of the study, the Investigator must notify the IRB/IEC about the study's completion. The IRB/IEC also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the IRB/IEC on the progress of the study at intervals stipulated by the IRB/IEC.

Voluntary informed consent must be obtained in writing from every subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or their delegate, must explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told

that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

# 15 REFERENCES

## 15.1 References applicable for all clinical studies

- ISO 11980:2012 Ophthalmic optics - Contact lenses and contact lens care products - Guidance for clinical investigations
- ISO 14155:2011 Clinical investigation of medical devices for human subjects - Good clinical practice

### 15.1.1 US references applicable for clinical studies

- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 812 - Investigational Device Exemptions
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators
- The California Bill of Rights

[redacted]

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