Alcon

Title:

Clinical Comparison of 2 Daily Disposable Contact Lenses – Pilot Study 2 NCT04528017

Protocol Number:	CLE383-P004
Sponsor Name and Address:	Alcon Research, LLC and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product(s):	PRECISION1™ (verofilcon A) Soft Contact Lenses (PRECISION1)
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 all applicable regulatory requirements. [redacted]

Principal Investigator:

Signature Date

Name:

Address:

[redacted]

1 PROTOCOL SYNOPSIS

Trial Sponsor	Alcon Research, LLC 6201 South Freeway Fort Worth, Texas 76134-2099
Name of Test Product(s)	PRECISION (verofilcon A) Soft Contact Lenses (PRECISION1)
Name of Control Product(s)	CooperVision® Clariti® 1 day (Clariti 1-Day)
Title of Trial	Clinical Comparison of 2 Daily Disposable Contact Lenses – Pilot Study 2
Protocol Number	CLE383-P004
Number of Sites Country	~ 4 US
Planned Duration of Exposure	~ 16 days total duration (test and control) Test Product: ~ 8 days Control Product: ~ 8 days
Number of Subjects	Target to complete: 52 [redacted]
	Planned to enroll: ~ 72
Study Population	Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous PRECISION1, Clariti 1-Day and DAILIES TOTAL1® lens wearers), have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and at least 10 hours per day. [redacted]
Objective(s)	The primary objective of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to Clariti 1-Day.
Endpoints	Primary Effectiveness • Distance VA (logMAR) with study lenses [redacted]

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness • Distance VA (logMAR) with study lenses [redacted] Safety • AEs • Biomicroscopy

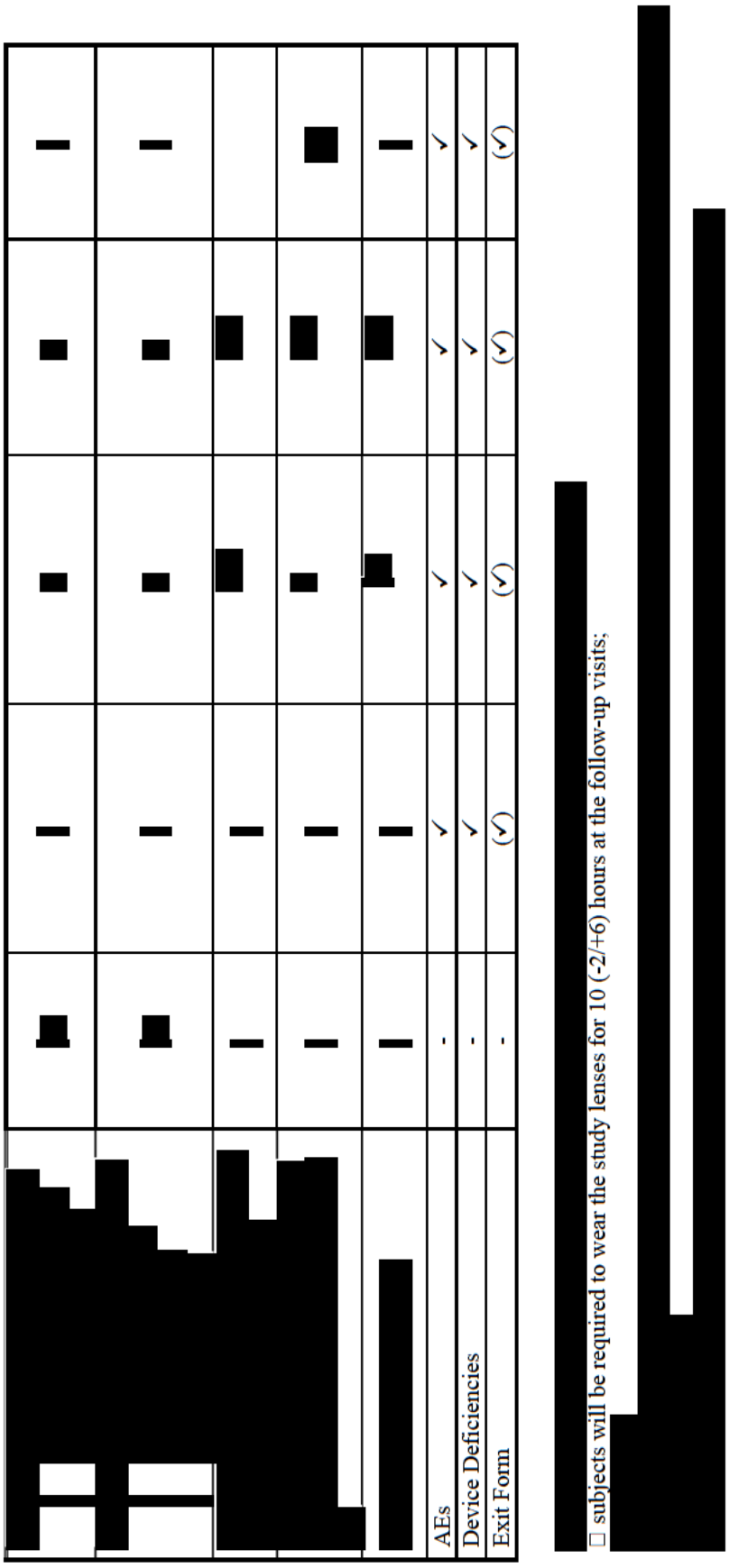
	• Device deficiencies	
Study Design	☒ Prospective	☐ Single-masked (trial subject)
	☐ Single group [redacted]	☐ Single-masked (Investigator)
	☒ Crossover	☒ Double-masked
	☐ Other	☐ Open-label
		☐ Other
	☐ Contralateral	☒ Randomized
	☒ Bilateral	
	☐ Monocular lens wear	
Test Product Details	Primary component/material	Verofilcon A
	Product Name	PRECISION1
	[redacted]	[redacted]
	Manufacturer	Alcon
	[redacted]	[redacted]
Control Product Details	Primary component/material	somofilcon A
	Product Name	Clariti 1-Day
	[redacted]	[redacted]
	Manufacturer	CooperVision
	[redacted]	[redacted]
Inclusion Criteria	1. Subject must be at least 18 years of age. 2. Subject must be able to understand and must sign an ICF that has been approved by an IRB. 3. Successful wear of spherical soft contact lenses in both eyes for a minimum of 5 days per week and 10 hours per day during the past 3 months. [redacted]	

	7. Subject must be willing to wear contact lenses for at least 16 hours of lens per day. [redacted]
Exclusion Criteria	1. Current/previous PRECISION1, Clariti 1-Day and DAILIES TOTAL1 lens wearers and any monovision & multifocal lens wearers. 2. Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator. [redacted]

[redacted]	[redacted]

Table 1-1 Schedule of Study Procedures and Assessments

Procedure / Assessment	[redacted]	**Visit 1** Screening/Baseline/ Dispense Lens 1 [redacted]	**Visit 2** Week 1 Follow-up Lens 1 □ / Dispense Lens 2	**Visit 3** Week 1 Follow-up Lens 2 □ / Exit	**Unscheduled Visit / Early Exit**
		[redacted]	8 -0/+3 days after Visit 1 [redacted]	8 -0/+3 days after Visit 2	**N/A**
Informed Consent	-	✓	-	-	-
Demographics	-	✓	-	-	-
Medical History	-	✓	✓	✓	✓
Concomitant Medications	-	✓	✓	✓	✓
Inclusion/Exclusion	-	✓	-	-	-
[redacted]					
Biomicroscopy	-	✓	✓	✓	✓
[redacted]					
Randomize	-	✓	-	-	-
Dispense (provide) study lenses	-	✓	✓	-	(✓)
VA (logMAR distance) with study lenses, OD, OS	-	-	✓	✓	-


AEs
Device Deficiencies
Exit Form
☐ subjects will be required to wear the study lenses for 10 (-2/+6) hours at the follow-up visits;

1.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
ASADE	Anticipated Serious Adverse Device Effect
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CIP	Clinical investigational plan
Clariti 1-Day or Clariti 1-Day contact lenses	CooperVision® Clariti® 1 day (Clariti 1-Day)
D	Diopter
D/C	Discontinue
eCRF	Electronic case report form
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed consent form
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
[redacted]	[redacted]
LogMAR	Logarithm of the minimum angle of resolution
mm	Millimeter
MOP	Manual of procedures
[redacted]	[redacted]
N/A	Not applicable
OD	Right eye
OS	Left eye
OU	Both eyes
PRECISION1 or PRECISION1 contact lenses	PRECISION (verofilcon A) Soft Contact Lenses
SADE	Serious adverse device event
SAE	Serious adverse event
US	United States
USADE	Unanticipated serious adverse device effect
V	Visit
VA	Visual acuity
[redacted]	[redacted]

2 TABLE OF CONTENTS

List of Tables

List of Figures

3 INTRODUCTION

3.1 Study Rationale and Purpose

[redacted]

[redacted]

The purpose of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to Clariti 1-Day. [redacted] Clariti 1-Day contact lenses were chosen as the control product because these lenses have the same wear modality.

[redacted]

3.2 Trial Objective

The primary objective of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to Clariti 1-Day.

3.3 Risks and Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. [redacted]

PRECISION1 and Clariti 1-Day contact lenses are for daily wear use under a daily disposable wear modality; further details on any known potential risks and benefits can be found in the package insert.

PRECISION1 and Clariti 1-Day contact lenses are not intended for use with a cleaning/disinfecting solution, and the biocompatibility with lens care solutions and any associated clinical effects are unknown.

A summary of the known potential risks and benefits associated with PRECISION1 can be found in the package insert. Risks are minimized by compliance with the eligibility criteria and study procedures, and through close supervision by a licensed clinician during exposure to the study lenses.

The 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 sleeping or swimming. The site personnel will also 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.

3.4 Subject Population

The study population includes approximately 72 volunteer subjects to be enrolled at approximately 4 sites, with approximately 18 subjects enrolled per site. The study population will consist of subjects with normal eyes (other than the need for optical correction for myopia and astigmatism),

Subjects must be screened according to the full list of inclusion/exclusion criteria in Section 1 of this protocol. Rescreening of subjects is not allowed in this study.

3.5 Outline of Study

This will be a multi-site, prospective, randomized, crossover, double-masked, study comparing 2 contact lenses. The expected duration of subject participation in the study is up to 22 days, with 3 scheduled visits. The study is expected to be completed in approximately 7 weeks.

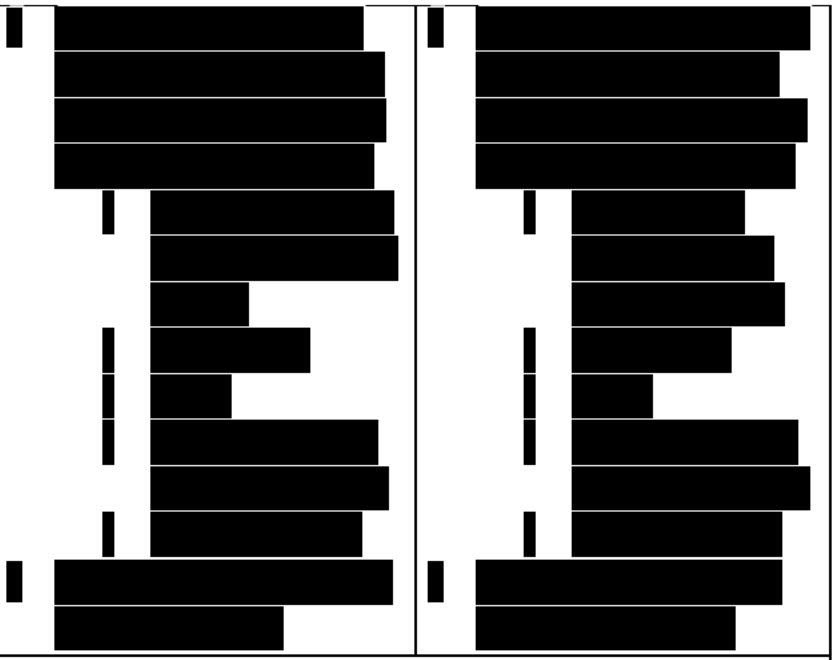
4 TREATMENTS ADMINISTERED

Subjects will be [redacted] randomized in a 1:1 manner to receive treatment (lens) in a crossover sequence: Test product then Control product, or Control product the Test product, respectively.

Sequence 1: PRECISION1 → Clariti 1-Day
Sequence 2: Clariti 1-Day → PRECISION1

4.1 Identity of Study Treatments

DESCRIPTION OF TEST AND CONTROL PRODUCTS		
	Test	Control
[redacted]	[redacted]	[redacted]
Lens	PRECISION1	Clariti 1-Day
Material	verofilcon A	somofilcon A
Water Content	51%	56%
Base Curve (mm)	8.3	8.6
Diameter (mm)	14.2	14.1
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

	
Usage	• Wear: ○ Daily Wear ○ Bilateral • Replacement period: Daily Disposable • Exposure: ○ 16 days total duration (test and control) ▪ Test Product: 8 (-0/+3) days ▪ Control Product: 8 (-0/+3) days • Lens Care: N/A

4.2 Accountability Procedures

Upon receipt of the study lenses, the Investigator or delegate will conduct an inventory. Designated study staff will provide the study lenses to the subjects in accordance with their randomization schedule. Throughout the study, the Investigator or delegate must maintain records of study treatment dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation.

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 adverse event [ie, ADE or SADE] are returned to the Study Sponsor for investigation. Refer to Section 7.3 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

4.3 Worn Lens Collection, Storage and Return

Worn lenses are to be discarded and do not need to be returned to Sponsor, unless in cases of AE or Device Deficiency. Refer to MOP for return instructions.

5 STUDY PROCEDURES AND ASSESSMENTS

5.1 Visits and Examinations

[redacted]

5.1.2 Visit 1 (Day 0) – Screening/Baseline/Dispense Lens 1

1	Explain the purpose and nature of the study, and have the subject read, sign, and date the IRB-approved informed consent document. Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the informed consent document. Provide a photocopy of the signed document to the subject and place the original signed document in the subject's chart. After signing the ICF, a subject will be assigned a subject number by the EDC system. A signed informed consent document defines the point of enrollment.
2	Obtain demographic information and medical history, 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.
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]	[redacted]
6	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining • Conjunctival staining • Palpebral conjunctival observations • Corneal epithelial edema • Corneal stromal edema • Corneal vascularization • Conjunctival compression/indention • Chemosis • Corneal infiltrates • Other findings
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
11	Review inclusion/exclusion criteria to determine if the subject qualifies to be randomized into the study. If subject qualifies, request randomization. If subject does not qualify, exit the subject from the study as a screen failure.
12	Based upon the randomized treatment sequence assignment, dispense (provide) the appropriate study lenses (Lens 1). • *Subjects should be instructed to discontinue habitual lens wear after the screening visit* • *Subjects should be instructed to insert dispensed study lenses after approximately 12 hours of spectacle wear or no lens wear following Visit 1*
[redacted]	[redacted]
14	Provide the subject with verbal instructions on lens wear.

15	Assess and record any AEs and device deficiencies reported or observed during the study visit. *Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent including those that screen fail.*
16	Schedule Visit 2 to take place 8 (-0/+3) days after Visit 1. • *Subjects should be instructed to bring their spectacles to Visit 2.* *Note: subjects are required to wear the study lenses for 10 (-2/+6) hours at the follow-up visits.*
	[redacted]

5.1.3 Visit 2 [Day 8 (-0/+3 Days)] – Week 1 Follow-up Lens 1/Dispense Lens 2

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any device deficiencies or AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit.
3	Review subject compliance with lens wear.
[redacted]	[redacted]
5	Perform logMAR VA with study lenses. • OD, OS, distance only.
6	Perform BCVA if there is a decrease of VA by 2 lines or more with study lenses. Source only.
[redacted]	[redacted]
[redacted]	[redacted]

9	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining • Conjunctival staining • Palpebral conjunctival observations • Corneal epithelial edema • Corneal stromal edema • Corneal vascularization • Conjunctival compression/indention • Chemosis • Corneal infiltrates • Other findings
[redacted]	[redacted]
11	Dispense (provide) the study lenses (Lens 2). [redacted]
[redacted]	[redacted]
13	Provide the subject with verbal instructions on lens wear.
14	Assess and record any AEs and device deficiencies reported or observed during the study visit. *Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent including those that screen fail.*
15	Schedule Visit 3 to take place 8 (-0/+3) days after Visit 2. • *Subjects should be instructed to bring their spectacles to Visit 3.* *Note: subjects are required to wear the study lenses for 10 (-2/+6) hours at the follow-up visits.*
	[redacted]

5.1.4 Visit 3 [Day 8 (-0/+3 Days)] – Week 1 Follow-up Lens 2/Exit

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any device deficiencies or AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit(s).
3	Review subject compliance with lens wear and adjunct product usage.
[redacted]	[redacted]
5	Perform logMAR VA with study lenses. • OD, OS, distance only.
6	Perform BCVA if there is a decrease of VA by 2 lines or more with study lenses. Source only.
[redacted]	[redacted]
[redacted]	[redacted]
9	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining • Conjunctival staining • Palpebral conjunctival observations • Corneal epithelial edema • Corneal stromal edema • Corneal vascularization • Conjunctival compression/indention • Chemosis • Corneal infiltrates • Other findings
[redacted]	[redacted]

[redacted]	[redacted]
12	Assess and record any AEs and device deficiencies reported or observed during the study visit. *Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent including those that screen fail.*
13	Exit the subject from the study.

5.2 Unscheduled Visits

Any visit that occurs between regularly scheduled visits is an Unscheduled Visit. If a subject requires an Unscheduled Visit, he/she must be advised to return to the office wearing the study lenses, if at all possible (unless he/she is experiencing a sign or symptom [as indicated in Section 3.3 Risks and Benefits]). During all unscheduled visits, the Investigator must conduct the following procedures:

- Collect AE and Device Deficiency information
- Assess and record changes in medical condition or concomitant medication
- Assess and record VAs
- Perform biomicroscopy (assessments with or without lenses, as possible)

In addition, all procedures for Unscheduled Visit/Early Exit should be completed (as possible). The Investigator may perform additional procedures for proper diagnosis and treatment of the subject. The Investigator must document this information in the subject's case history source documents.

If during an Unscheduled Visit the subject is discontinuing the study lenses or discontinuing from the study, the Investigator must conduct Exit procedures according to Table 1-1: Schedule of Study Procedures and Assessments, as possible.

5.3 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after signing the informed consent, including screen failures. Subjects may discontinue from the study at any time for any reason. Subjects may also be discontinued from the study at any time if, in

the opinion of the Investigator, their continued participation poses a risk to their health. Discontinued subjects will not be replaced (ie, their subject numbers will not be re-assigned/re-used).

Should a subject exhibit any clinically relevant signs, symptoms, or other clinical observations that possibly could be associated with suspected sensitivity or intolerance to one of the study treatments, the Investigator must document those observations on an AE Form.

Any subject who exits early from the study (excluding screen failures) must undergo all Exit procedures according to Table 1-1: Schedule of Study Procedures and Assessments.

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.

5.4 Clinical Study Termination

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

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

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

6 ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with counts and percentages from each category.

Any deviations to this 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.

6.1 Subject Evaluability

The final subject evaluability will be determined prior to breaking of the code for masked treatment (lens) sequence assignment and locking the database, based on the Deviations and Evaluability Plan.

6.2 Analysis Data Sets

6.2.1 Safety Analysis Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. As such, the safety analysis set will include all subjects/eyes exposed to any study lenses evaluated in this study. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding lens sequence.

6.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the Safety Analysis Set.

6.4 Effectiveness Analyses

The Safety Analysis Set will be used for all effectiveness analyses.

6.4.1 Primary Effectiveness

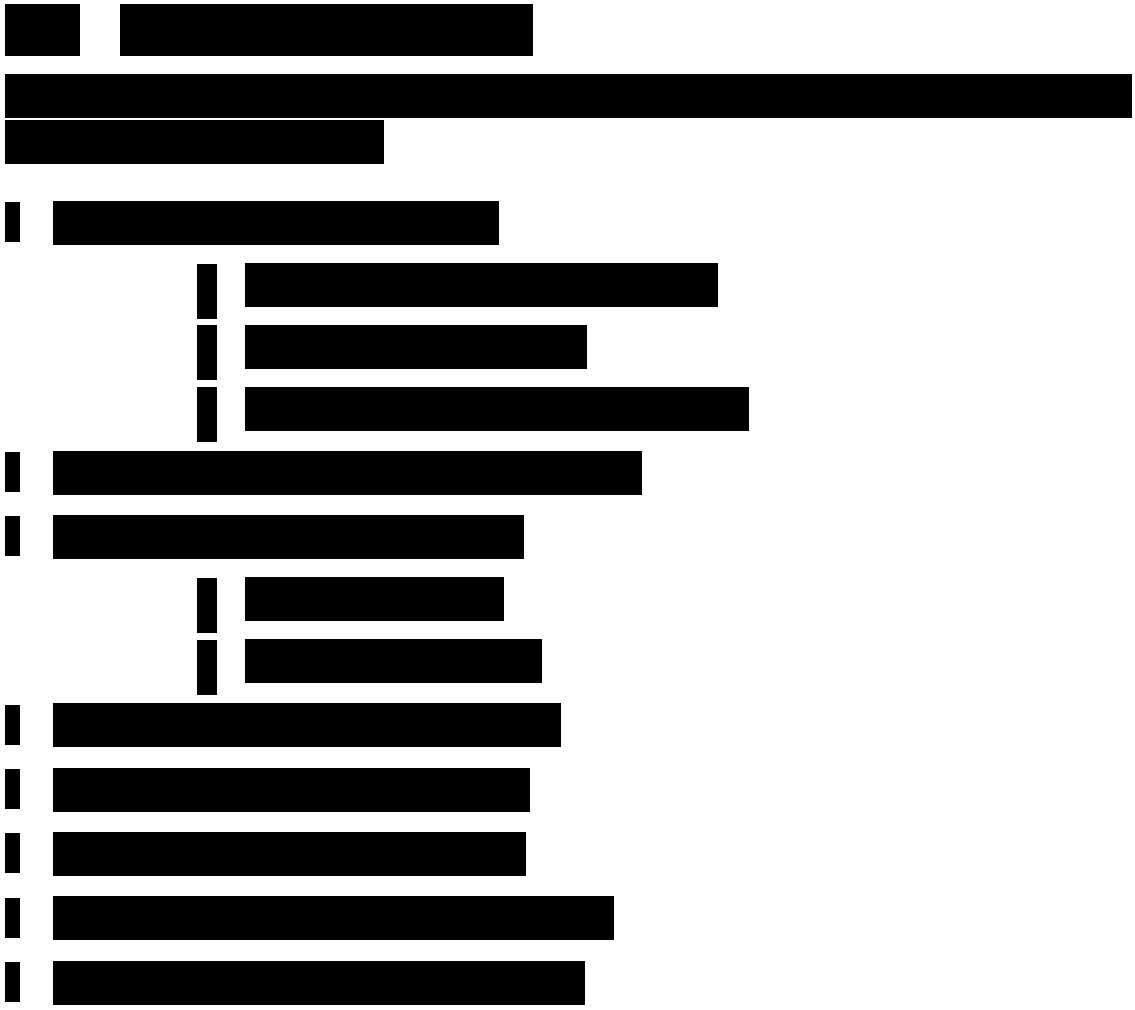
The primary objective of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to Clariti 1-Day. The primary endpoint is distance VA with study lenses, collected in logMAR, for each eye.

6.4.1.1 Statistical Hypotheses

No inferences are to be made on the primary effectiveness endpoint; therefore, no hypotheses are formulated.

6.4.1.2 Analysis Methods

Descriptive statistics will be provided.



[redacted]

6.6 Handling of Missing Data

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out.

[redacted]

6.8 Safety Analysis

The safety endpoints for this study are AEs, biomicroscopy findings, and device deficiencies.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. AEs leading to study discontinuation, significant non-serious AEs, and SAEs will be identified. Individual subject listings will be provided, as necessary.

Individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to study lenses.

Each biomicroscopy parameter will be tabulated by its grade. For each biomicroscopy parameter, counts and percentages of eyes that experience an increase of ≥ 2 grades from baseline (last assessment prior to study lens exposure) to any subsequent visit within the same period will be presented. A supportive listing will be generated which will include all biomicroscopy data from all visits for these eyes experiencing the increase.

Two listings (prior to exposure of study lenses and treatment-emergent) of device deficiencies, as recorded on the Device Deficiency Form, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

[redacted]

[redacted]

[redacted].

6.10 Sample Size Justification

No formal sample size calculation is provided given the descriptive and pilot nature of the study.

7 ADVERSE EVENTS AND DEVICE DEFICIENCIES

Terms and Definitions

Adverse Event (AE)	Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device or comparator. *Note: For subjects, this definition includes events related to the investigational medical device, comparator, or the procedures involved. For users or other persons, this definition is restricted to the use of investigational medical devices.*
Adverse Device Effect (ADE)	AE related to the use of an investigational medical device or comparator.. *Note: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the investigational medical devices or comparator.*
Anticipated Serious Adverse Device Effect (ASADE)	Serious ADE 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, usability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequacy in the*

	information supplied by the manufacturer including labelling related to the investigational medical device or the comparator..
Malfunction	Failure of a medical device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling of the device. The intended performance of the device refers to the intended use for which the device is labeled or marketed.
Non-serious Adverse Event	AE that does not meet the criteria for an SAE.
Serious Adverse Event (SAE)	AE that led to any of the following: • Death. • A serious deterioration in the health of the subject users or other persons as defined by one or more of the following: : a) a life-threatening illness or injury. *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.* b) any potentially sight-threatening event or permanent impairment to a body structure or a body function including chronic diseases. c) in-patient hospitalization or prolonged hospitalization. d) a medical or surgical intervention to prevent a) or b). e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect. *Note: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.* *Refer to Section 7.1 for additional SAEs.*
Serious Adverse Device Effect (SADE)	ADE that has resulted in any of the consequences characteristic of an SAE.

Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons *Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.*
Significant Non-Serious Adverse Event	A significant non-serious AE is a symptomatic, device-related, non-sight threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 7.1 for additional Significant Non-Serious AEs.*
Unanticipated Serious Adverse Device Effect (USADE)	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.*

7.1 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 or comparator. Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 7–1 Categorization of All AEs

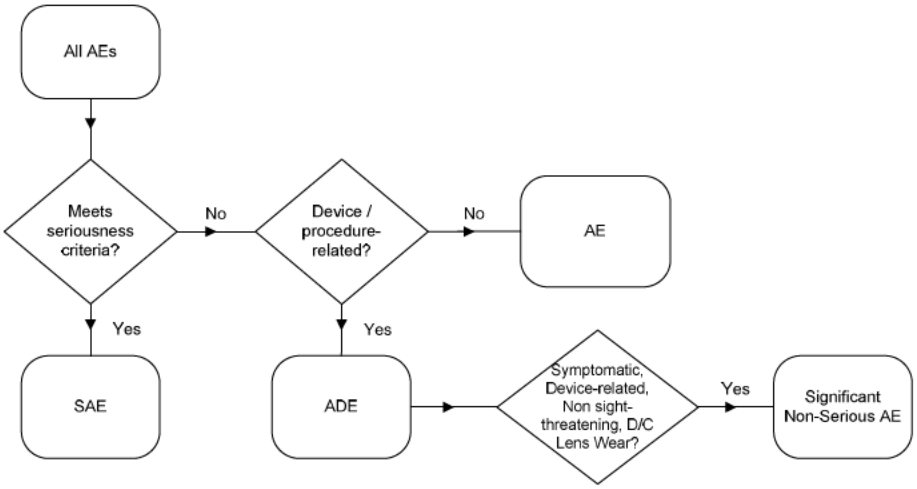
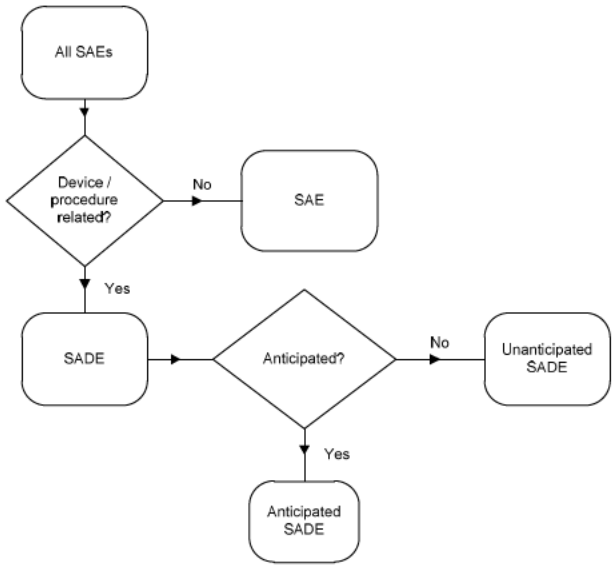


Figure 7-2 Categorization of All Serious Adverse Events



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

Significant Non-Serious Adverse Events

A significant non-serious AE is a symptomatic, 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 AE:

- 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 the ISO 11980 and the US FDA Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses and Contact Lens Care Products.

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 patient 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 patient 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, tampered seal, leaking bottle/container)
- Suspect product contamination
- Lack of performance

7.2 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 shown below and report as applicable:

- “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?”

[redacted]

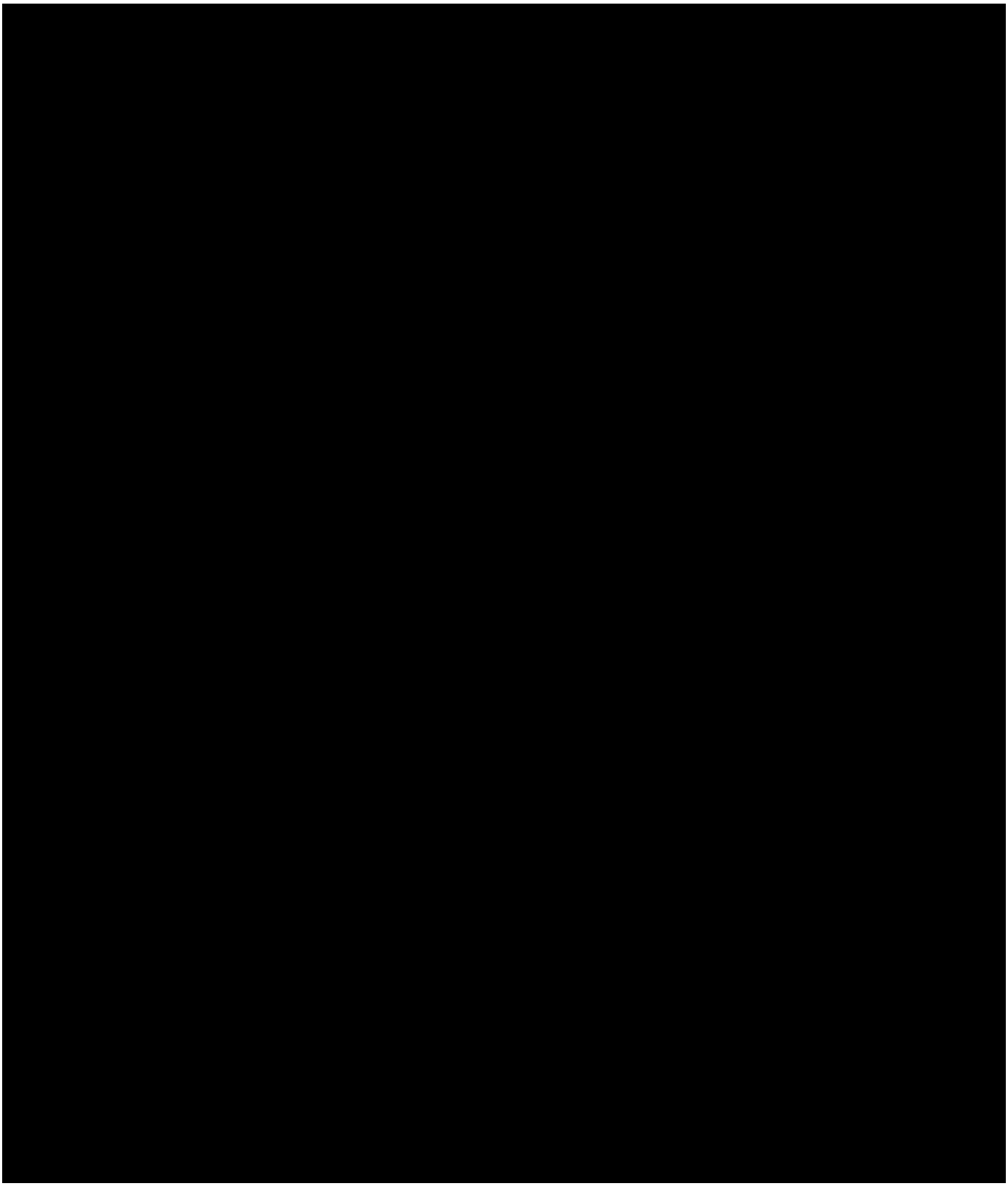
[redacted]

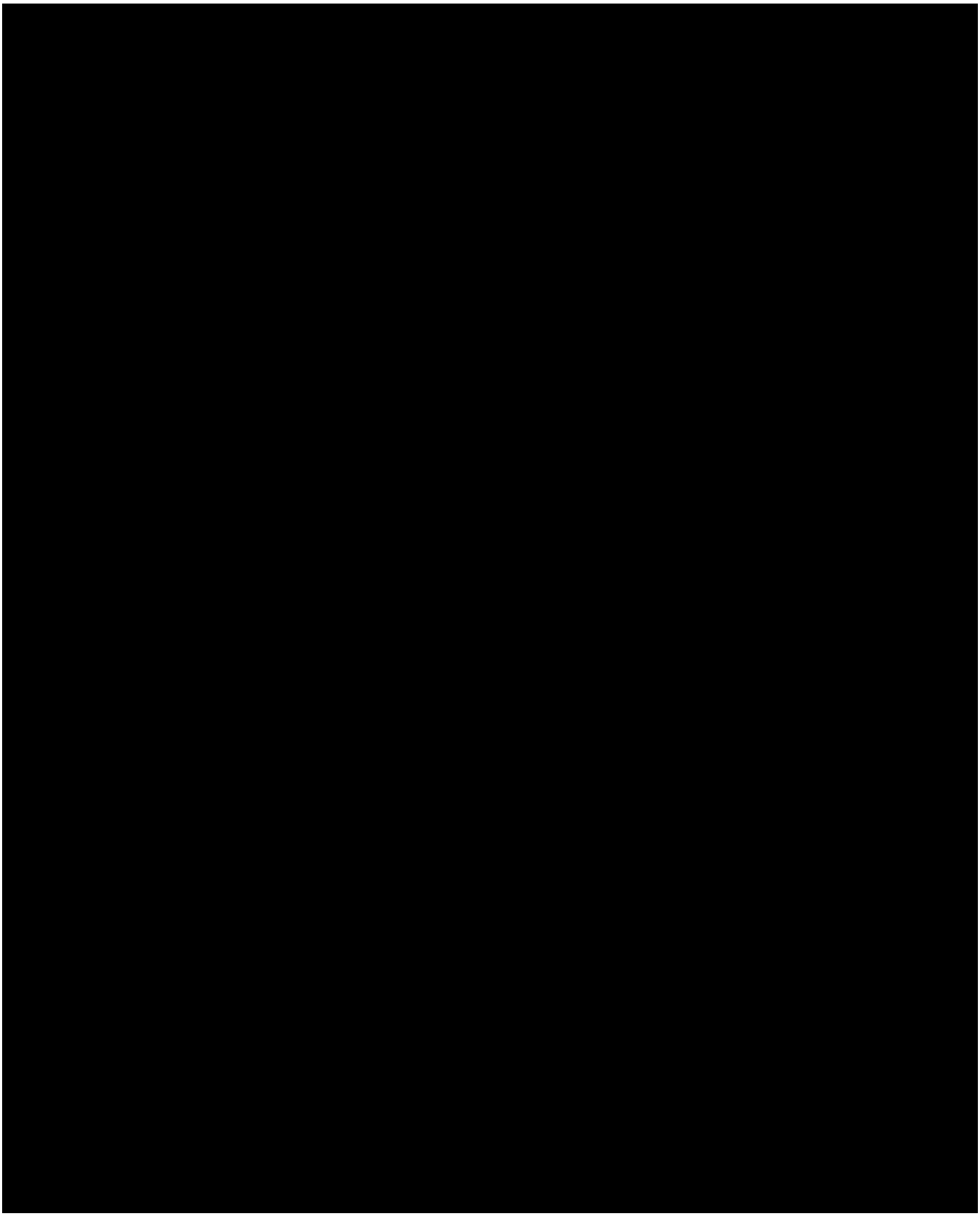
[redacted]

[redacted]

7.6 Pregnancy in the Clinical Study

Women of childbearing potential or women who are pregnant at the time of study entry are not excluded from participation. [redacted]





[redacted]

10 ETHICS AND COMPLIANCE

This trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the referenced directives, regulations, guidelines, and/or standards.

10.1 Compliance

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.

10.2 Institutional Review Board (IRB)

This trial requires IRB approval prior to initiation. This protocol, subject informed consent, and subsequent amendments will be reviewed and approved by an IRB.

Before clinical study initiation, this protocol, the ICF (and assent form, if applicable), any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IRB. The Investigator must provide documentation of the IRB approval to the Study Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), ICF, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. The IRB must be provided with a copy of the Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB. At the end of the study, the Investigator must notify the IRB about the study's completion. The IRB also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the IRB on the progress of the study at intervals stipulated by the IRB.

Voluntary informed consent must be obtained from every subject (and/or legal representative, as applicable) prior to the initiation of any screening or other study-related procedures. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or 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, 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 and must provide a duplicate copy to each subject according to local regulations. Following this study, the subject will return to their eye care professional for their routine eye care and contact lenses.

12 REFERENCES

12.1 References applicable for all clinical trials

- 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

12.1.1 US references applicable for clinical trials

- 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

12.2 References for this clinical trial

Young G, Chalmers RL, Napier L, Hunt C, Kern J. Characterizing contact lens-related dryness symptoms in a cross-section of UK softlens wearers. Contact Lens Anterior Eye 2011;34:64–70.

[redacted]
