Alcon

Vision Care [redacted] Protocol for CLE383-E002 / NCT04942925

Title: Clinical Comparison of Two Daily Disposable Contact Lenses – Pilot Study 3

Sponsor Name and Address:	Alcon Research, LLC and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product(s):	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, all applicable regulatory authority regulations, and conditions of approval imposed by the reviewing IRB or regulatory authority.
- 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.

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

Principal Investigator:

Signature Date

Name and professional position:

Address:

1 PROTOCOL SYNOPSIS

Trial Sponsor	Alcon 6201 South Freeway Fort Worth, Texas 76134-2099
Name of Test Product(s)	PRECISION1
Name of Control Product(s)	INFUSE
Title of Trial	Clinical Comparison of Two Daily Disposable Contact Lenses – Pilot Study 3
Protocol Number	CLE383-E002
Number of Sites Country	~ 4 US
Clinical Investigation Type	☐ Early Feasibility ☒ Traditional Feasibility ☐ Pivotal (premarket monadic claims) ☐ Postmarket Interventional / Confirmatory ☐ Postmarket Noninterventional / Observational
Planned Duration of Exposure	~ 16 days in total duration (test and control) Test Product: ~ 8 days Control Product: ~ 8 days
Number of Subjects	Target to complete: ~ 52 [redacted] Planned to enroll: ~ 60 [redacted]
Study Population	Volunteer subjects aged 18 or over who are habitual spherical contact lens wearers (excluding current/previous PRECISION1 and INFUSE contact 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 INFUSE contact lenses.
Endpoints	Primary Effectiveness • Distance VA (logMAR) with study contact lenses [redacted] Safety • Adverse Events (AEs) • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness • VA (logMAR distance) with study lenses • VA (logMAR distance) with habitual correction • Manifest refraction (sphere, cylinder, axis) • BCVA (logMAR distance) with manifest refraction [redacted]

<table>
<tr><td></td><td colspan="2">Safety
• AEs
• Biomicroscopy
• Device deficiencies</td></tr>
<tr><td rowspan="2">Study Design</td><td>☒ Prospective
☐ Single group
☒ Parallel group
☒ Crossover
☐ Other</td><td>☐ Single-masked (trial subject)
☐ Single-masked (investigator)
☒ Double-masked
☐ Open-label
☐ Other</td></tr>
<tr><td>☐ Contralateral
☒ Bilateral
☐ Monocular lens wear</td><td>☒ Randomized (stratified by symptomatology):
[redacted]</td></tr>
<tr><td rowspan="4">Test Product Details</td><td>Primary component/material</td><td>Verofilcon A</td></tr>
<tr><td>Product Name</td><td>PRECISION1</td></tr>
<tr><td colspan="2">[redacted]</td></tr>
<tr><td>Manufacturer</td><td>Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, Texas 76134-2099
USA</td></tr>
<tr><td>Rx Power Range</td><td>-1.00 to -6.00 D in 0.25 D steps, as available</td></tr>
<tr><td rowspan="4">Control Details</td><td>Primary component/material</td><td>Kalifilcon A</td></tr>
<tr><td>Product Name</td><td>INFUSE</td></tr>
<tr><td colspan="2">[redacted]</td></tr>
<tr><td>Manufacturer</td><td>Bausch + Lomb
400 Somerset Corporate Blvd.
Bridgewater, NJ 08807
USA</td></tr>
</table>

	Rx Power Range	-1.00 to -6.00 D in 0.25 D steps, as available
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]	
Exclusion Criteria	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. [redacted]	

	[redacted]
	10. Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment.
	[redacted]
	14. Current/previous PRECISION1 and INFUSE contact lens wearers.
	[redacted]
Associated Materials	Lubrication/re-wetting drops will not be permitted.

Table 1-1 Schedule of Study Procedures and Assessments

	[redacted]	Visit 1 Screening / Baseline / Fitting [redacted] Lens 1 & Lens 2 Dispense Lens 1 [redacted]	Visit 2 Week 1 Follow–up Lens 1 ‡ / Dispense Lens 2 [redacted]	Visit 3 Week 1 Follow –up Lens 2 ‡ / Exit	Early Exit	Unscheduled Visit
Procedure / Assessment		**Day 0**	**8 (0/+3) days after Visit 1**	**8 (0/+3) days after Visit 2**	**N/A**	**N/A**
[redacted]						
Informed Consent	-	X	-	-	-	-
Demographics	-	X	-	-	-	-
Medical History*	-	X	X	X	X	X
Concomitant Medications*	-	X	X	X	X	X
Inclusion/Exclusion	-	X	-	-	-	-
Habitual lens (brand, power), solution (brand if applicable)*	-	X	-	-	-	-
VA w/habitual correction (OD, OS, logMAR distance)*	-	X	-	X	X	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Manifest refraction*	-	X	(X)	(X)	(X)	(X)
BCVA (OD, OS, logMAR distance with manifest refraction)*	-	X	(X)	(X)	(X)	(X)
Biomicroscopy	-	X	X	X	X	X
VA (logMAR distance) with fitting [redacted] lenses (OD, OS)*		X (with both [redacted] lens types)	-	-	-	-
Lens fitting assessments [redacted] • Lens movement – primary gaze, peripheral gaze (overall fit) • Lens position (Centration)	-	X (with both [redacted] lens types)	-	-	-	-

	[redacted]	**Visit 1 Screening / Baseline / Fitting [redacted] Lens 1 & Lens 2 Dispense Lens 1 [redacted]**	**Visit 2 Week 1 Follow–up Lens 1 ‡ / Dispense Lens 2 [redacted]**	**Visit 3 Week 1 Follow –up Lens 2 ‡ / Exit**	**Early Exit**	**Unscheduled Visit**
Procedure / Assessment		**Day 0**	**8 (0/+3) days after Visit 1**	**8 (0/+3) days after Visit 2**	**N/A**	**N/A**
[redacted]						
• Lens surface (front surface wettability, front surface deposits, back surface deposits).						
Keratometry readings	-	X	-	-	-	-
Randomize	-	X	-	-	-	-
Dispense (provide) study lenses*	-	X	X	-	-	(X)
VA w/ study lenses (OD, OS, logMAR distance)	-	-	X	X	(X)	(X)
[redacted]						

	[redacted]	Visit 1 Screening / Baseline / Fitting [redacted] Lens 1 & Lens 2 Dispense Lens 1 [redacted]	Visit 2 Week 1 Follow–up Lens 1 ‡ / Dispense Lens 2 [redacted]	Visit 3 Week 1 Follow –up Lens 2 ‡ / Exit	Early Exit	Unscheduled Visit
Procedure / Assessment		**Day 0**	**8 (0/+3) days after**	**8 (0/+3) days**	**N/A**	**N/A**
[redacted]						
AEs[α]	-	X	X	X	X	X
Device deficiencies	-	X	X	X	X	X
Exit Form	-	(X)	(X)	X	X	(X)

(X) Assessment performed as necessary, e.g., reduction of VA by 2 lines or more with investigational product (IP)

* Source only

α Comprehensive details of all AEs will be documented in the source records; however, targeted collection will be utilized in the eCRF.

1.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CIP	Clinical investigation plan
Control	INFUSE contact lenses
[redacted]	[redacted]
eCRF	Electronic case report form
EDC	Electronic data capture
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICF	Informed consent form
INFUSE or INFUSE contact lenses	INFUSE (kalifilcon A) Soft Contact Lenses
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
N/A	Not applicable
OD	Right eye
OS	Left eye
PRECISION1 or PRECISION1 contact lenses	PRECISION (verofilcon A) Soft Contact Lenses
SAE	Serious adverse event
SADE	Serious adverse device effect
Test	PRECISION1 contact lenses
US	United States
VA	Visual acuity
[redacted]	[redacted]

2 TABLE OF CONTENTS

List of Tables

List of Figures

3 INTRODUCTION

3.1 Study Rationale and Purpose

PRECISION1 is a new daily disposable silicone hydrogel contact lens with a material that combines high oxygen transmissibility with a low modulus of elasticity.

PRECISION1 contact lenses are intended for the optical correction of refractive ametropia in persons with non-diseased eyes requiring subjects to wear spectacles for vision correction.

The purpose of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to INFUSE contact lenses [redacted]

3.2 Trial Objective

The primary objective of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to INFUSE contact lenses.

3.3 Risks and Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Material properties and design characteristics of the contact lenses ensure successful contact lens wear.

PRECISION1 and INFUSE contact lenses are not intended for use with a cleaning/disinfecting solution, and the biocompatibility with lens care solutions was not tested and any associated clinical effects are unknown.

A summary of the known potential risks and benefits associated with the study contact lenses can be found in the package insert of both study contact lenses. 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 60 volunteer subjects to be enrolled at approximately 4 sites, with approximately 15 subjects enrolled per site. [redacted]

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 multisite, prospective, randomized, crossover, double-masked, stratified (by symptomatology) study comparing 2 contact lenses. The expected duration of subject participation in the study is up to 24 days, with 3 scheduled visits. The study is expected to be completed in approximately 11 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	EDC/randomization integration system	Lens Name
Sequence 1	[redacted]	PRECISION1/INFUSE
Sequence 2	[redacted]	INFUSE/PRECISION1

4.1 Identity of Study Treatments

DESCRIPTION OF TEST AND CONTROL PRODUCTS		
	Test	Control
[redacted]	[redacted]	[redacted]
Lens	PRECISION1	INFUSE
Material	Verofilcon A	Kalifilcon A
Water Content	51%	55%
Base Curve (mm)	8.3	8.6
Diameter (mm)	14.2	14.2
Rx Power Range	-1.00 to 6.00 D in 0.25 D steps, as available	-1.00 to 6.00 D in 0.25 D steps, as available
Packaging, Labeling, and Supply	• Blister foil pack • Foil label includes at a minimum: - Identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - sponsor information - country of origin. • Provided in ~ 12 lenses per power per carton, identified with the following at a minimum: - a color coded label stating the protocol number [redacted] - power - an investigational use only statement - tracking number. • Lenses should be stored at room temperature. • [redacted] study lenses will be provided by the sponsor before the start of the study	• Blister foil pack • Foil label includes at a minimum: - Identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - sponsor information - country of origin. • Provided in ~ 12 lenses per power per carton, identified with the following at a minimum: - a color coded label stating the protocol number [redacted] - power - an investigational use only statement - tracking number • Lenses should be stored at room temperature. • [redacted] study lenses will be provided by the sponsor before the start of the study
Usage	• Wear:	

	○ Daily Wear ○ Bilateral • Replacement period: Daily Disposable • Exposure: ○ ~16 days total duration (Test and Control) [redacted] • Lens Care: N/A • Both study contact lenses will be used according to their registered/approved indications for use and within the approved wearing schedule and duration.

4.2 Accountability Procedures

Upon receipt of the study lenses, the investigator or delegate will conduct an inventory. Designated unmasked study staff will provide the study lenses to the subjects in accordance with their randomization schedule. Throughout the study, the unmasked 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.

The unmasked delegate should make every effort to collect unused lenses, foils, and supplies from subjects.

It is the investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner.
- 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 (i.e., 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.

[redacted]

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. Source only.
3	Perform VA logMAR with habitual correction. Source only. • OD, OS, distance only, spectacles or contact lenses.
4	Record habitual lens information (brand, power) and solution (brand if applicable). Source only.
[redacted]	[redacted]
6	Perform a manifest refraction. Source only.
7	Perform BCVA logMAR with manifest refraction. Source only. • OD, OS, distance only *Note: Distance BCVA must be 0.10 logMAR or better in each eye for the subject to qualify for the study.*
8	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
9	Determine study lens powers based upon the manifest refraction and habitual lens powers.
10	Perform VA logMAR with both [redacted] lens types. Source only. OD, OS, distance only.
11	Perform the following assessments with both [redacted] lens types*. Source only. • Lens fit evaluation (movement and position). • Lens surface (front surface wettability, front surface deposits, back surface deposits). **Any abnormal findings or findings of interest during the lens assessment should be captured with slit lamp photography or video.*
12	Obtain keratometry readings OD, OS.
13	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.
14	Based upon the randomized treatment sequence assignment, dispense (provide) the appropriate study lenses (Lens 1).

[redacted]

[redacted]

17	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.*
18	Schedule Visit 2 to take place 8 (0/+3) days after Visit 1.
[redacted]	
	*Note: If for some reason a subject is unable to wear a study lens **for the duration of this visit window**, instruct the subject to return to the site for an Unscheduled Visit, including, if possible, lens removal on site. The subject should then be scheduled to return to the clinic for Visit 2 (if possible) or exited from the study.*

5.1.3 Visit 2 [8 (0/+3 days) after Visit 1] – 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.
[redacted]	

4	Perform VA logMAR with study lenses. • OD, OS, distance only.
[redacted]	
6	Remove study lenses.
7	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
8	Perform Manifest Refraction and BCVA logMAR distance with manifest refraction if there is a decrease of VA with study lenses by 2 lines or more versus VA with fitting lenses from Screening. Source only.
9	Collect the worn study lenses (Lens 1) from Visit 2 for storage and return [redacted] See MOP for details.
10	Dispense (provide) the study lenses (Lens 2).

[redacted]

[redacted]

13	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.*
14	Schedule Visit 3 to take place 8 (0/+3) days after Visit 2.

[redacted]

5.1.4 Visit 3 [8 days (0/+3 Days) after Visit 2] – 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).

[redacted]

[redacted]

4	Perform VA logMAR with study lenses. • OD, OS, distance only.
[redacted]	
7	Remove study lenses.
8	Perform BCVA logMAR distance with manifest refraction if there is a decrease of VA by 2 lines or more with study lenses. Source only.
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]	
11	Perform VA logMAR with habitual correction. Source only. • OD, OS, distance only, spectacles or habitual contact lenses *Note: If this VA with habitual correction shows a decrease of 2 lines or more versus Visit 1 baseline VA with habitual correction, then BCVA with MR is required to*

	confirm a potential loss in VA for AE reporting requirements (see Section 7).
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 all procedures specified in Table 1-1Schedule of Study Procedures and Assessments.

The investigator may perform additional procedures for proper diagnosis and treatment of the subject. The investigator must document this information in the subject's source documents.

If during an Unscheduled Visit the subject is discontinuing from the study, the investigator must refer to Section 5.3 Discontinued Subjects.

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 (i.e., their subject numbers will not be reassigned/reused).

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 poststudy 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 frequencies 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, [redacted] For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding lens sequence.

Subjects who are lost to follow-up and their exposure to dispensed study lenses is unknown will be included in the safety analysis data set. The visit date for Dispense (Lens 1 or Lens 2) [redacted] will be used as the first exposure date for the respective Lens.

6.3 Demographic and Baseline Characteristics

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

6.4 Effectiveness Analyses

This study defines 1 primary [redacted] effectiveness endpoint. 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 INFUSE contact lenses. 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.

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 (frequencies and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. AEs leading to study discontinuation, significant nonserious 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 applicable biomicroscopy parameter, frequencies and percentages of eyes that experience an increase of ≥ 2 grades from baseline (last assessment prior to study lens exposure in each crossover period) 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 within the same period 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]

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 and whether anticipated or unanticipated. *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 events related to the use of investigational medical devices or comparator.*
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device or comparator. *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.*
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 an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan (CIP), or investigator's brochure (IB).

Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
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: • 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, i.e., 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, congenital abnormality, or birth defect including physical or mental impairment. *Note: Planned hospitalization for a preexisting condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.* *Refer to Section7.1 for additional SAEs.*
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.*
Use Error	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. *Note:* *a) Use error includes the inability of the user to complete a task.* *b) Use errors can result from a mismatch between the characteristics of the user, user interface, task, or use environment.* *c) Users might be aware or unaware that a use error has occurred.* *d) An unexpected physiological response of the patient is not by itself considered a use error.* *e) A malfunction of a medical device that causes an unexpected result is not considered 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 (test *product*). Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 7–1 Categorization of All AEs

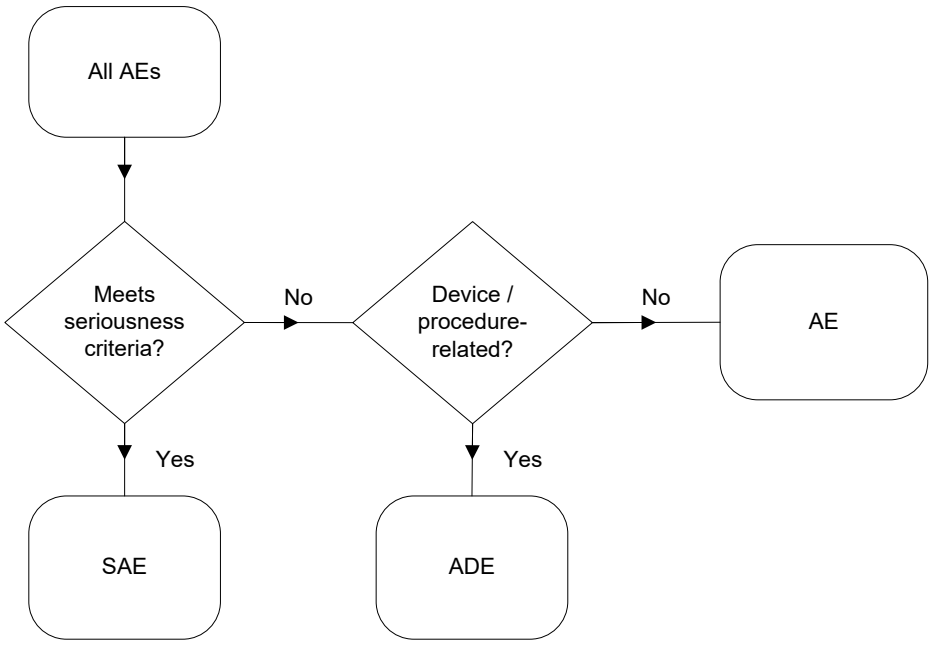
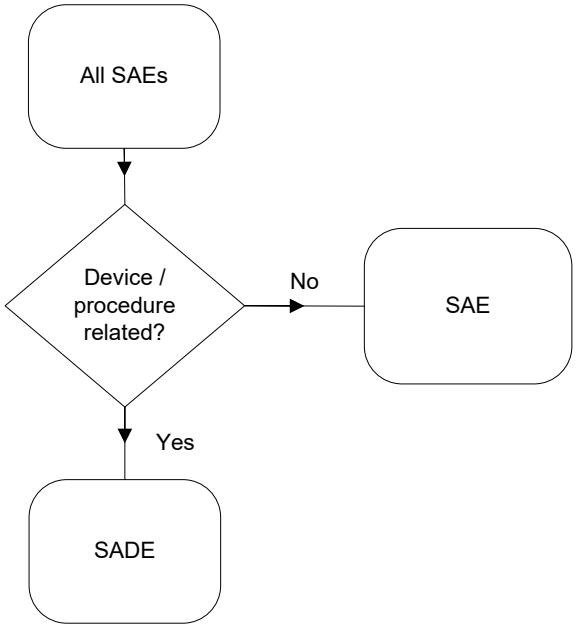


Figure 7–2 Categorization of All Serious Adverse Events



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 (i.e., 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 (e.g., incorrect lens power/diameter/base curve/color)
- Lens cloudy
- Lens surface/edge defect
- Torn lens during handling/in pack
- Packaging deficit (e.g., mislabeled product)
- 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?"

In addition, 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.

7.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any preexisting medical conditions or signs/symptoms present in a subject prior to the start of the study (i.e., 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.

For each recorded event, the ADEs and SAEs documentation must include: date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the investigator must document all device deficiencies reported or observed with test and control products on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the study sponsor immediately as follows

- All SAEs must be reported immediately (within 24 hours) of the investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reported within 10 calendar days 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 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 nonoperational, 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.

Study sponsor representatives may be contacted for any protocol-related question and their contact information is provided in the Manual of Procedures 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 (i.e., 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 nonserious to serious or from unrelated to related.

7.4 Return product analysis (if applicable)

Study Sponsor representatives and their contact information are provided in the MOP that accompanies this protocol.

Alcon products associated with device deficiencies and/or product related AEs should be returned and must include the Complaint #, which will be provided by study sponsor after the case is entered in the study sponsor's Global Product Complaint Management System (GPCMS).

7.5 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 (i.e., database lock).

Any additional data received up to 1 month 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 and should be communicated to the medical device's manufacturer as per local requirements.

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

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. Pregnancy should be included in the Pregnancy eCRF in EDC when a pregnant woman enters the study or if a woman becomes pregnant during the study. Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case–by-case basis.

8 CONFIDENTIALITY, BIAS, AND MASKING

8.1 Subject Confidentiality and Methods Used to Minimize Bias

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. All documents submitted to the sponsor will identify the subjects

exclusively by number and demographic information. No other personally identifying information should be transmitted to the sponsor.

This study is double-masked with subjects randomized to use PRECISION1 or INFUSE for the duration of one-week treatment period and then crossover and use the other study product for one-week treatment period.

The subjects, investigators, and sponsor personnel (other than site monitors, Clinical Operations Lead, person responsible for generating the randomization schedule, and unmasked clinical data managers) involved in reporting, obtaining, and/or reviewing the clinical evaluations will be masked to the identity of the contact lens being administered. This level of masking will be maintained throughout the conduct of the study. Unmasking will occur only after all planned study data have been validated, and the database locked. 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 trial.

8.2 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study. If unmasking is required in the interest of subject safety, the investigator is encouraged to contact an appropriate study sponsor to obtain unmasking information. Additionally, the study sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting

9 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

9.1 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 eCRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Study 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 should 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 eCRF are consistent with the original source data.

Only designated individuals may complete the eCRFs. The eCRFs will be submitted at regular intervals following the clinical study visit schedule. It is expected that all data reported will have corresponding entries in the source documents. The principal investigator is responsible for reviewing and certifying that the eCRFs are accurate and complete. The only subject identifiers recorded on the eCRFs will be subject number and subject demographic information.

9.2 Data Review and Clarifications

Upon completion of the eCRFs, a targeted review of the eCRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. 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 eCRFs.

9.3 Regulatory Documentation and Records Retention

The investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the sponsor and the investigator's files will be reviewed as part of the ongoing study monitoring. Financial disclosure is not subject to regulatory inspection and should be kept separately.

Additionally, the investigator must keep study records and source documents until the sponsor provides written approval for their destruction. If the investigator retires, relocates, or

for any other reason withdraws from responsibility of keeping the study records, the sponsor must be notified and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations (generally 2 years after discontinuing clinical development or after the last marketing approval).

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 inserts, 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.

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]

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

[redacted]

Signature Page for V-CLN-0010709 v2.0

Signature Page for V-CLN-0010709 v2.0