Title

DD T2 Daily Disposable Registration Trial

Protocol Number:	CLE383-C005 / NCT03305770
Development Stage of Project:	Development
Sponsor Name and Address:	Alcon Research, Ltd. and its affiliates (“Alcon”) 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	DD T2
Investigator Agreement:	I have read the clinical study described herein, and recognize its confidentiality. I agree to conduct this study in accordance with the ethical principles contained within the Declaration of Helsinki, and the described study in compliance with the protocol, Good Clinical Practice (GCP), ISO 14155, and all applicable regulatory requirements. Additionally, I will comply with all procedures for data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the Study Sponsor.
Principal Investigator:	
	Signature Date
Name and professional position:	
Address:	

[redacted]

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1 GLOSSARY OF TERMS

Names of test product	Throughout this document, Test product will be referred to as DD T2.
Name of Control Product	Alcon DAILIES TOTAL1® (delefilcon A) (DT1)
Adverse Device Effect	AEs related to the use of an investigational medical device (test product) or control product. *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 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.* Requirements for reporting AEs 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.* Requirements for reporting Device Deficiencies in the study can be found in Section 11.
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	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 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 a SAE.
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 SAE.
Serious Adverse Event (SAE)	AE that led to any of the following: • Death. • A serious deterioration in the health of the subject that either resulted in: 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. c. in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a SAE. 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 AEs. 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.* *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.

	Refer to Section 11 for additional SAEs.
Significant Non-Serious Adverse Event	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 11 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.*

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
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CRF	Case report form
CSM	Clinical site manager
CTT	Clinical trial team
D	Diopter(s)
D/C	Discontinue
DD	Daily disposable
DD T2	Daily Disposable T2 Soft Contact Lenses
DT1	DAILIES TOTAL1 Daily Disposable Contact Lenses
DS	Diopters sphere
eCRF	Electronic case report form
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
[redacted]	[redacted]
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
IP	Investigational product
IRB	Institutional review board
IRT	Interactive response technology
ISO	International Organization for Standardization
LCSM	Lead clinical site manager
LID	Lens identification
LogMAR	Logarithm of the minimum angle of resolution
mm	Millimeter
MOP	Manual of procedures
n	Number
N/A	Not applicable
O/R	Over refraction
OU	Both eyes
pt	Point
SAE	Serious adverse event
SADE	Serious adverse device effect

Abbreviation	Definition
SiHy	Silicone hydrogel
SLE	Slit-lamp examination
SOP	Standard operating procedure
US / USA	United States of America
USADE	Unanticipated serious adverse device effect
USAN	United States Adopted Name
USV	Unscheduled visit
VA	Visual acuity
vs	Versus

3 PROTOCOL SUMMARY

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

Approximately 6 sites in the US will enroll approximately 99 subjects. Subjects will be randomized to wear either the test DD T2 lenses in both eyes or the control DT1 lenses in both eyes for 3 months. Approximately 66 subjects will be assigned to wear the test lenses and 33 the control lenses, following the 2:1 subject allocation ratio as recommended by ISO 11980:2012 and the US FDA 510(k) guidance document.

Subjects will be expected to attend 7 office visits: Baseline, Dispense, 1-week follow-up, 2-week follow-up, 1-month follow-up, 2-month follow-up and 3-month follow-up/Exit.

Following randomization at the Baseline visit, study lenses will be trial fit using the fitting set supplied by the Sponsor, and the correct contact lens power for the individual subject will be determined. The Sponsor will send investigational lenses for each subject to the site after receiving an order from the Investigator. Between the Baseline and Dispense visits, subjects will be allowed to wear their habitual lenses. Biomicroscopy will be repeated at the Dispense visit.

[redacted]

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: DD T2 soft contact lenses Control Product: DT1 (delefilcon A) soft contact lenses

Purpose and rationale	The purpose of this clinical trial is to evaluate the performance of the investigational DD T2 lens compared to the commercially available DT1 lens, by assessing visual acuity as the primary variable.
Objectives	The primary objective is to demonstrate effectiveness and safety of the DD T2 soft contact lens when worn for daily disposable wear as compared to DT1 soft contact lens.
Endpoints	Primary Effectiveness • Distance VA (Snellen) [redacted] Safety • AEs • Device deficiencies • Biomicroscopy
Assessments	Effectiveness • VA (Snellen distance) with IP • [redacted] • [redacted]

	• [redacted] • [redacted] • [redacted] • [redacted] • [redacted] • [redacted] • [redacted] Safety • AEs • Device deficiencies • Biomicroscopy
Study Design	This will be a prospective, randomized, stratified, controlled, double-masked, parallel-group clinical trial. Subject participation in the study will be approximately 15 weeks with approximately 3 months of exposure to IP.
Subject population	Volunteer subjects aged 18 or over who are soft contact lens wearers, excluding DT1 habitual 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 8 hours per day. Subjects must require contact lenses in a power range from -1.00 to -6.00 DS. [redacted]

Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Successful wear of spherical soft contact lenses for distance correction in both eyes during the past 3 months for a minimum of 5 days per week and 8 hours per day. • Best corrected VA 20/25 or better in each eye.
Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	• Any current or prior wear experience with DT1 lenses. • 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.
Data analysis and sample size justification	In adherence to the reporting format as specified in the ISO and FDA 510(k) guidance documents, effectiveness and safety data will be presented separately based upon subject study status of Completed or Discontinued. [redacted] Sample size is based upon ISO and FDA 510(k) requirements and recommendations of at least 50 subjects in the Test group, in a 2:1 Test to Control ratio.
Key words	DD T2, DT1, daily disposable, registration
Associated materials	Lubrication/re-wetting drops provided by Alcon will be permitted as needed.

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Visit 1, Baseline/ Screening (Day 0)	Visit 2, Dispense study lenses	Visit 3, Week 1 follow-up	Visit 4, Week 2 follow-up	Visit 5, 1-month follow-up	Visit 6, 2-month follow-up	Visit 7, 3-month follow-up/ exit	USV
		Up to 4 days after lens order (Day 1 of lens wear)	7 days (-1/+2 days) from the Dispense visit	15 days (-1/+3 days) from the Dispense visit	30 days (-2 days /+5 days) from the Dispense visit	60 days (-2 days /+5 days) from the Dispense visit	95 days (-2 days /+5 days) from the Dispense visit	
Informed Consent	✓	-	-	-	-	-	-	-
Demographics	✓	-	-	-	-	-	-	-
Medical History	✓	-	-	-	-	-	-	-
Concomitant Medications	✓	✓	✓	✓	✓	✓	✓	(✓)
Inclusion/ Exclusion	✓	-	-	-	-	-	-	-
Habitual lens information (brand / manufacturer, modality, power, wear success)	✓	-	-	-	-	-	-	-
VA w/ habitual correction (Snellen distance)	✓	✓	-	-	-	-	✓	(✓)
[redacted]								
Biomicroscopy	✓	✓	✓	✓	✓	✓	✓	(✓)
[redacted]								
Order subject's study lenses	✓	-	-	-	-	-	-	-
Dispense or provision of study lenses	-	✓	-	-	✓	✓	-	(✓)
VA w/ study lenses (Snellen distance)	✓	✓	✓	✓	✓	✓	✓	(✓)
[redacted]								

Procedure/ Assessment	**Visit 1, Baseline/ Screening (Day 0)**	**Visit 2, Dispense study lenses**	**Visit 3, Week 1 follow-up**	**Visit 4, Week 2 follow-up**	**Visit 5, 1-month follow-up**	**Visit 6, 2-month follow-up**	**Visit 7, 3-month follow-up/ exit**	**USV**
		Up to 4 days after lens order (Day 1 of lens wear)	7 days (-1/+2 days) from the Dispense visit	15 days (-1/+3 days) from the Dispense visit	30 days (-2 days /+5 days) from the Dispense visit	60 days (-2 days /+5 days) from the Dispense visit	95 days (-2 days /+5 days) from the Dispense visit	
[redacted]								
AEs	✓	✓	✓	✓	✓	✓	✓	(✓)
Device deficiencies	✓	✓	✓	✓	✓	✓	✓	(✓)
Exit Form	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)

(✓) assessment performed as necessary, eg, decrease of visual acuity by 2 lines or more with investigational products.
USV = Unscheduled Visit

[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.

4.1 Amendments

There are no amendments. This is the first version of the protocol.

5 INTRODUCTION

5.1 Rationale and Background

Daily disposable (DD) lenses are worn for a full day, during waking hours, and then discarded after usage. This type of contact lens eliminates the requirement for lens cleaning and disinfection and has been shown to have higher compliance rates with lens replacement schedules compared to other lens wearing modalities (Dumbleton 2009). Silicone hydrogel contact lenses provide superior oxygen transmissibility over contact lenses made with conventional materials.

A new DD SiHy lens, known here as DD T2, has been developed that combines high oxygen transmissibility with a low modulus of elasticity.

In this clinical trial, the performance of the investigational DD T2 lens will be compared to the commercially available DT1 (delefilcon A) lens in a parallel-group design with 3 months of exposure. The intended use of this contact lens is for vision correction. Therefore, the objective measurement of VA is planned as the primary variable for the comparison with the DT1 lens. [redacted] The recommendations of ISO 11980:2012 and FDA (510(k)) Guidance Document for Daily Wear Contact Lenses in regard to variables to assess were considered.

5.2 Purpose of the Study

The purpose of this clinical trial is to evaluate the performance of the investigational DD T2 lens compared to the commercially available DT1 lens, by assessing VA as the primary variable. The study is designed to follow the 2:1 subject allocation ratio as recommended by ISO 11980:2012 and the US FDA 510(k) guidance document. At the end of the study, a clinical study report will be prepared in accordance with applicable regulatory requirements and standards.

There are no immediate plans to submit the results of this study for publication; however, the results may be offered for publication if they are of scientific interest, or if the results relate to a product that is subsequently approved or cleared for marketing.

5.3 Risks and Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Material properties and design characteristics of DD T2 are features consistent with successful contact lens wear. Based upon nonclinical testing and documented rationale for applicability of test results, DD T2 are assessed to be non-toxic and biocompatible for on-eye use.

DT1 lenses are for daily wear use under a DD wear modality; further details on any known potential risks and benefits can be found in the package insert.

DD T2 and DT1 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 DD T2 can be found in the IB. 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 potential harms associated with on-eye exposure to the new lens materials include toxicity response, blurred vision, and ocular discomfort. In general, the risks with DD T2 are anticipated to be similar to other marketed DD soft contact lenses.

There may also be unknown risks with the use of DD T2. Risks to subjects in this clinical study will be minimized by compliance with the eligibility criteria and study procedures, clinical oversight, and monitoring. 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 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

The primary objective is to demonstrate the effectiveness and safety of the DD T2 soft contact lens when worn for daily disposable wear as compared to the DT1 soft contact lens.

6.2 Secondary Objective

Not applicable.

6.4 Safety Objective(s)

Safety endpoints are as follows:

Table 6–2 Safety Objective(s)

Objective(s)	**Endpoint(s)**
To assess duty of care and demonstration of safety.	AEs Device Deficiencies Biomicroscopy

7 INVESTIGATIONAL PLAN

7.1 Study Design

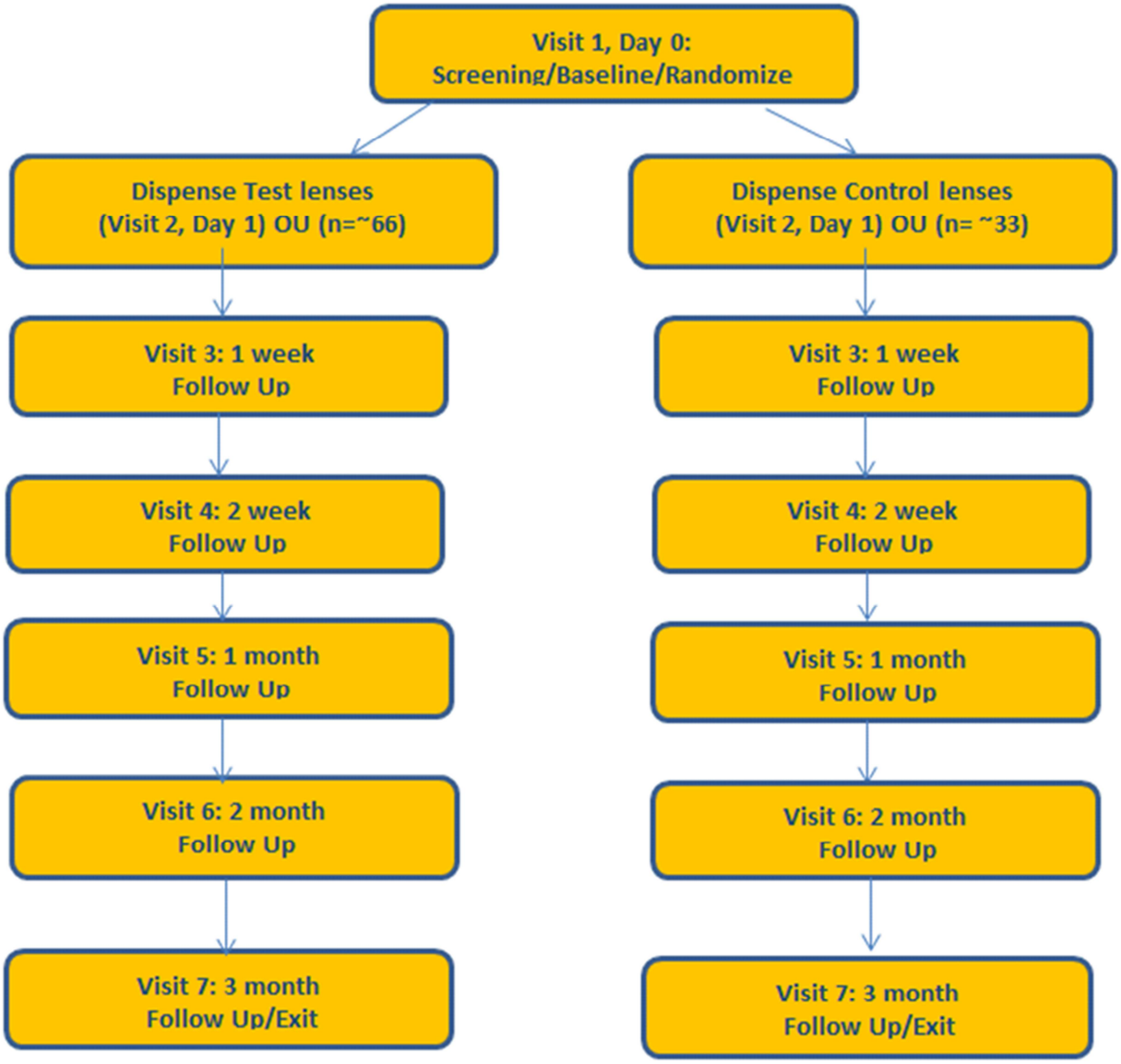
This will be a prospective, randomized, [redacted] controlled, double-masked, parallel-group clinical trial.

Approximately 6 sites in the US will enroll approximately 99 subjects and with approximately 15-18 subjects per site. Subjects will be randomized to wear either the test DD T2 lenses in both eyes or the control DT1 lenses in both eyes.

Subjects will be expected to attend 7 office visits. The total expected duration of the subject's participation is approximately 3 months.

The study is expected to take approximately 4 months for completion. 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 performance of the investigational DD T2 lens will be compared to the commercially available DT1 (delefilcon A) lens in a double-masked, parallel-group design with approximately 3 months of exposure. The study is designed following the recommendations for registration from ISO 11980:2012 and the US FDA 510(k) guidance document.

7.3 Rationale for Duration of Treatment/Follow-Up

The duration of exposure as well as the schedule of follow-up visits follow the recommended guidance from ISO 11980:2012 and the US FDA 510(k) guidance document.

7.4 Rationale for Choice of Control Product

DT1 contact lenses were chosen as the control product because this lens is a proper predicate device to compare to DD T2 in regards to effectiveness and safety. Both DD T2 and DT1 are silicone hydrogel lenses and are to be prescribed for single use, daily disposable wear. The DT1 spherical soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes. The lenses are not intended to be cleaned or disinfected and should be discarded after a single use.

7.5 Data Monitoring Committee

Not applicable.

8 STUDY POPULATION

The study population consists of adult male and female subjects (aged 18 or over), with non-diseased eyes, who require optical correction for refractive ametropia. [redacted]

The intended study population consists of volunteer subjects aged 18 or over who are soft contact lens wearers, excluding DT1 habitual wearers, who 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 8 hours per day. Subjects must require contact lenses in a power range from -1.00 to -6.00 DS. [redacted]

8.1 Inclusion Criteria

Written informed consent must be obtained before any study specific assessment is performed. Upon signing informed consent, the subject is 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 and must be able to understand and sign an IRB/IEC approved informed consent form.

2.	Willing and able to attend all scheduled study visits as required per protocol.
3.	Successful wear of spherical soft contact lenses for distance correction in both eyes during the past 3 months for a minimum of 5 days per week and 8 hours per day.
4.	Manifest cylinder ≤ 0.75 D in each eye.
5.	Best spectacle corrected visual acuity 20/25 or better in each eye.

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.
4.	Biomicroscopy findings at baseline that are moderate (grade 3) or higher and/or corneal vascularization that is mild (grade 2) or higher.
5.	Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear.
6.	Current or history of herpetic keratitis in either eye.
7.	Eye injury in either eye within 12 weeks immediately prior to enrollment for this trial.
8.	Any current or prior wear experience with DT1 lenses.
9.	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
10.	History of intolerance or hypersensitivity to any component of the study lenses.
11.	Enrollment of site staff or family/household members of the site staff who are listed

	on the study personnel log as having a role in the execution of this study.
12.	Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product: DD T2 daily disposable soft contact lenses

Control Product: DT1 (delefilcon A) daily disposable soft contact lenses

Table 9–1 Test Product

Test Product	DD T2 daily disposable soft contact lenses (LID 006841)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 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	• Material: [redacted] • Water content: 51% • Power range: -1.00 D to -6.00 D, 0.25 D steps • Base curve (mm): 8.3 • Diameter (mm): 14.2 • Additional details can be found in the IB.
Formulation	Silicone Hydrogel. Additional details can be found in the IB for DD T2.
Usage	• Wear: o Daily Wear

	○ Bilateral • Replacement period: Daily Disposable • Exposure: At least ~8 hours per day and at least ~5 days per week over a 3 month exposure period. • Lens Care: N/A • Additional details can be found in the MOP
Number/Amount of product to be provided to the subject	A carton containing ~40 lenses (per eye) will be provided to the subject at the following study visits: • Visit 2 (Dispense) • Visit 5 (1 month follow-up) • Visit 6 (2 month follow-up)
Packaging description	Blister foil pack
Labeling description	• Lens Foil label includes: - material name or identifier - base curve - diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information • Provided in boxes of ~40 lenses per power per box, identified with the following: - a color coded label stating the protocol number - material identifier - power - an investigational use only statement - tracking number
Storage conditions	Stored at room temperature.
Supply	• Fitting sets will be provided by the Sponsor before the start of the trial to be used during Visit 1.

	• 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 2 and provide monthly supplies at Visit 5 and 6.

Table 9–2 Control Product

Control Product	DAILIES TOTAL1 (LID 006961)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for Use	The intended use of this contact lens is for vision correction.
Product description and parameters available for this study	• Material: delefilcon A • Water content: 33% • Power range: -1.00 D to -6.00 D, 0.25 D steps • Base curve (mm): 8.5 • Diameter (mm): 14.1
Formulation	Silicone Hydrogel. Additional details can be found in the DT1 package insert.
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Daily Disposable • Exposure: At least ~8 hours per day and at least ~5 days per week over a 3 month exposure period. • Lens Care: N/A • Additional details can be found in the MOP
Number/Amount of Product to be Provided to the subject	A carton containing ~40 lenses (per eye) will be provided to the subject at the following study visits: • Visit 2 (Dispense) • Visit 5 (1 month follow-up) • Visit 6 (2 month follow-up)

Packaging description	Control product packaging is identical to Test product, see Table 9-1 for details.
Labeling description	• Lens Foil label includes: - material name or identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information • Provided in boxes of ~40 lenses per power per box, identified with the following: - a color coded label stating the protocol number - material identifier - power - an investigational use only statement
Storage conditions	Stored at room temperature.
Supply	• Fitting sets will be provided by the Sponsor before the start of the trial to be used during Visit 1. • 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 2 and provide monthly supplies at Visit 5 and 6.

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

During the clinical study Sponsor provided rewetting drops may be used, if necessary.

9.3 Treatment Assignment / Randomization

Subjects will be randomized in a 2:1 ratio to receive either DD T2 or DT1 soft 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 treatment according to the randomization list uploaded in the iMedidata BALANCE 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 or 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 DD T2 or DT1 soft contact lenses for the duration of the 3-month treatment period.

Table 9–3 Unmasked Individuals Associated with the Study

Unmasked Individual	Extent of Unmasking	Rationale
Unmasked Study Coordinator(s)	The Unmasked Study Coordinator(s) will manage IP inventory, as well as IP administration. This individual will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP. The unmasked coordinator will also assist with device	The Unmasked Study Coordinator(s) will be unmasked to allow for processing of IP shipment, storage, and dispensing, as well as accountability for all IP.

Unmasked Individual	Extent of Unmasking	Rationale
	deficiency and adverse event reporting.	
LCSM	The LCSM will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP. This individual assists with masked and unmasked data reviews.	The LCSM will be unmasked to allow for oversight of the CSM, in conjunction with all IP accountability tasks.
CSM	CSM will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP accountability. This individual monitors unmasked and masked study data.	The CSM will be unmasked to allow for performance of IP accountability, management of device deficiencies and related AE lens returns, and any other IP related tasks.
Unmasked Data Manager(s)	The Unmasked Data Manager(s) will have access to restricted fields in RAVE that would contain unmasking data.	The Unmasked Data Manager(s) will be unmasked to allow for review of all restricted data.
IRT Manager	The IRT manager will be unmasked to allow for system programming, testing, and to allow for technical oversight of the system.	The IRT manager is unmasked to all aspects of the trial for system development purposes.
Randomization Specialist	The Randomization Specialist will be unmasked to allow for generation of the randomization list and uploading of that list into the IRT system.	Generates and therefore has full knowledge of treatment codes but otherwise is operationally not associated with the CTT or any decision-making aspects related to clinical trial design, execution, or reporting.

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.

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, an individual Investigator will have the ability to unmask the treatment assignment for a specific subject after contacting an appropriate Study Sponsor representative if time allows. 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 Investigator or delegate 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.

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

Changes in concomitant treatments after Visit 1 are not allowed unless needed for the proper medical care and treatment of the subject for a specific medical condition.

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 7 office visits, as shown in Table 10-1:

Table 10-1 Study Visits

Visit	[redacted]
Visit 1: Baseline/Screening (Day 0)	
Visit 2: Dispense study lenses (Day 1)	
Visit 3: Week 1 follow-up	
Visit 4: Week 2 follow-up	
Visit 5: 1-month follow-up	
Visit 6: 2-month follow-up	
Visit 7: 3-month follow-up/exit	

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

At the Baseline visit, study lenses will be trial fit using the fitting set supplied by the Sponsor, and the correct contact lens power for the individual subject will be determined. The Sponsor will send investigational lenses for each subject to the site after receiving an order from the Investigator. Between the Baseline and Dispense visits, subjects will be allowed to wear their habitual lenses. Biomicroscopy will be repeated at the Dispense visit.

[redacted]

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, have the individual obtaining consent from the subject and a witness, if applicable, 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

SLE 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.

10.2.7 Additional Study Assessments: Effectiveness and Safety Assessments

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

- VA (Snellen distance) with IP

10.3 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)

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 IP or discontinuing from the study, the Investigator must conduct Exit procedures according to Table 3-1 Schedule of Study Procedures and Assessments, as possible.

10.4 Discontinued Subjects

10.4.1 Screen Failures

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.

10.4.2 Discontinuations

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

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.

For subjects discontinuing from the study, the Investigator must complete all Exit procedures according to Table 3-1, Schedule of Study Procedures and Assessments, 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.

10.4.3 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 Schedule of Study Procedures and Assessments.

10.5 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.

10.5.1 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

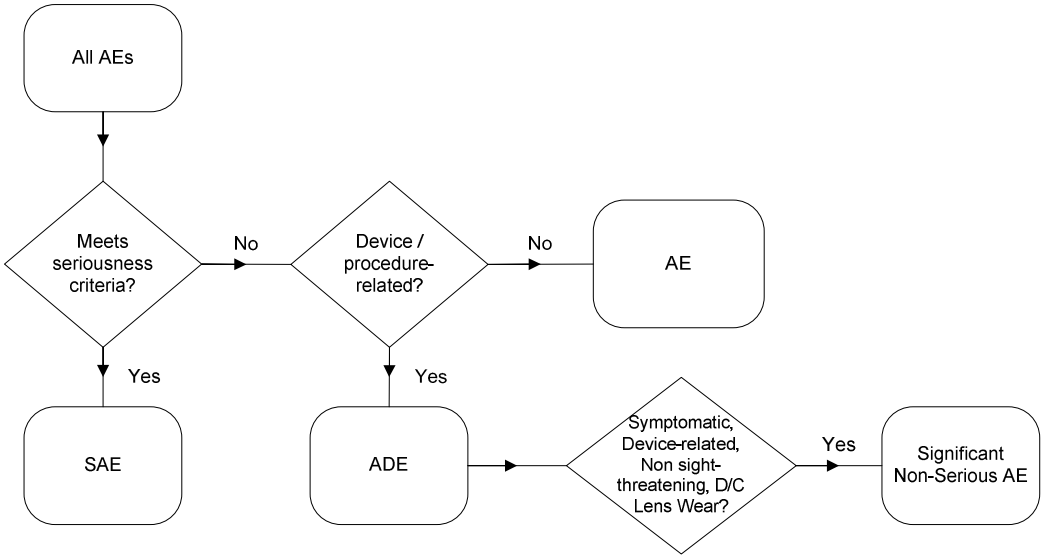
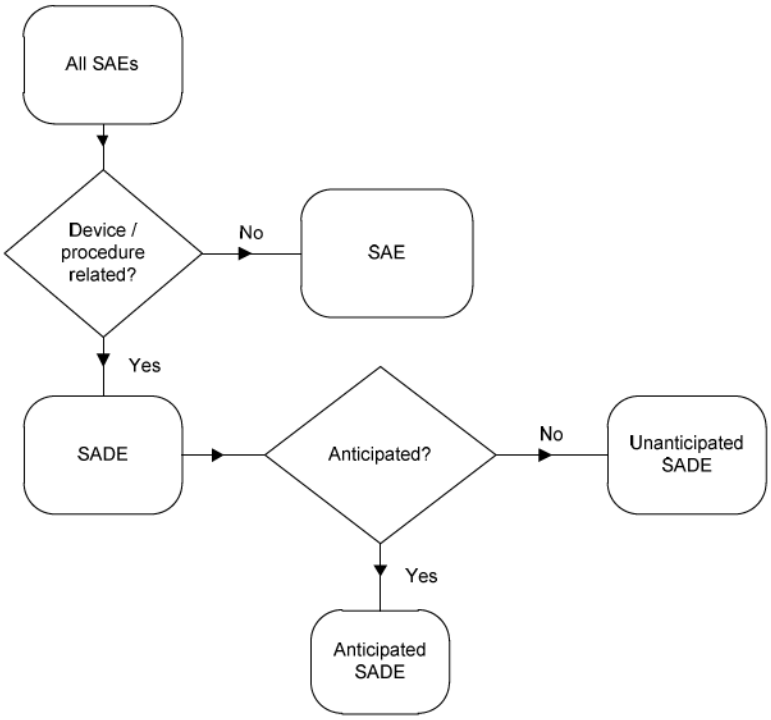


Figure 11-2 Categorization of All Serious Adverse Events



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

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) [Grading scale is based upon ISO 11980:2012 unless specified differently in MOP]
- 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) [Grading scale is based upon ISO 11980:2012 unless specified differently in MOP]

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.

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)
- 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 FTW.medical_safety@alcon.com according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for non-study marketed devices/products 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 and 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.

11.4 Return product analysis

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).

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 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 (following the postmarket vigilance procedures) 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.

11.7 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 Medical History section of the eCRF 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.

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 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 who have been exposed to study lenses

c) Enrolled Not Dispensed – subjects/eyes from All Enrolled who have not been exposed to study lenses

d) Completed – Enrolled Dispensed subjects completing the study

e) Discontinued – Enrolled Dispensed who did not complete the study

12.3 Demographic and Baseline Characteristics

Demographic information, [redacted] and habitual lens information will be presented by lens group and overall for the All Enrolled set.

[redacted]

12.4 Effectiveness Analyses

For each of the primary [redacted] effectiveness endpoints, separate summary tables will be prepared for the Completed and the Discontinued sets as follows:

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

[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint

The primary objective of this study is to demonstrate the effectiveness and safety of DD T2 compared to DT1.

The primary endpoint is VA with study lenses, collected by eye.

12.4.1.1 Statistical Hypotheses

No hypothesis testing of the primary effectiveness endpoint is planned.

12.4.1.2 Analysis Methods

Summary statistics will be provided.

Additionally, the following will be presented:

- Shift table comparing VA at dispense vs subsequent visits
- Frequency and percent for VA of 20/30 or better, final VA within 1 line of Dispense, final VA worse than 1 line of Dispense
- Listing for VA changes from Dispense of 2 or more lines during the study

[redacted]

[redacted]

12.5 Handling of Missing Data

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

Incidence and reasons for discontinuation by lens group will be tabulated at each visit and overall.

12.6 Safety Analyses

The safety endpoints are:

- AEs
- Device Deficiencies
- Biomicroscopy

There are no safety hypotheses planned in this study. The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of AE as well as the other listed parameters.

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 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 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.

[redacted]

[redacted]

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 Code of Federal 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. 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.

The Study Sponsor assures that the key design elements of this protocol will be registered on www.clinicaltrials.gov as required by current regulations and, if applicable, other public databases as required by local country regulations. In addition, results of this study will be made publicly available on www.clinicaltrials.gov regardless of outcome as required by current regulations and, if applicable, in other public databases as required by local country regulations.

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

15.2 References for this clinical study

- Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses
- 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
- Dumbleton K, Woods C, Jones L, Fonn D, Sarwer D. Patient and Practitioner Compliance with Silicone Hydrogel and Daily Disposable Lens Replacement in the United States. *Eye Contact Lens*. 2009:35(4):164-171.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
08/23/2017 17:36:08	[redacted]	[redacted]
08/23/2017 17:49:11	[redacted]	[redacted]
08/24/2017 13:43:11	[redacted]	[redacted]