Alcon A Novartis Division

Title:

Clinical Performance of a Monthly Replacement Silicone Hydrogel Lens

Protocol Number:	CLY935-C004 / NCT03586167
Sponsor Name and Address:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product(s):	LID014341
Investigator Agreement:	I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practice (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements. 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 Sponsor.
Principal Investigator:	

Signature Date

Name:

Address:

SEE Protocol Template, Vision Care version 2.0, approved 09 SEP 2017

1 PROTOCOL SYNOPSIS

Trial Sponsor	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099
Name of Test Product(s)	LID014341
Name of Control Product(s)	CooperVision® BIOFINITY© contact lenses (BIOFINITY)
Title of Trial	Clinical Performance of a Monthly Replacement Silicone Hydrogel Lens
Protocol Number	CLY935-C004
Number of Sites Country	~ 4 US
Planned Duration of Exposure	Test Product: 30 (-4 / +2) days Control Product: 30 (-4 / +2) days
Number of Subjects	Target to complete: 78
	Planned to enroll: ~ 86
Study Population	Volunteer subjects aged 18 or over who are habitual monthly replacement soft 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 8 hours per day. Pregnant or breast-feeding women are not excluded from this study.
Objective(s)	The objective of this study will be to describe the clinical performance of an investigational, coated silicone hydrogel contact lens over 30 days of daily wear.
Endpoints	Primary Effectiveness • Distance VA (logMAR) 

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness • Distance VA (logMAR) • Manifest refraction • BCVA (Snellen 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</td></tr>
<tr><td rowspan="4">Test Product Details</td><td>Primary component/material</td><td>HD13B1 with water gradient coating</td></tr>
<tr><td>LID Number</td><td>LID014341</td></tr>
<tr><td>Manufacturer</td><td>Alcon Laboratories, Inc.</td></tr>
<tr><td>Other</td><td>-1.00D to -6.00D, 0.25D steps</td></tr>
<tr><td rowspan="4">Control Product Details</td><td>Primary component/material</td><td>comfilcon A</td></tr>
<tr><td>Product Name</td><td>BIOFINITY</td></tr>
<tr><td>Manufacturer</td><td>CooperVision</td></tr>
<tr><td>Other</td><td>-1.00D to -6.00D, 0.25D steps</td></tr>
<tr><td>Inclusion Criteria</td><td colspan="2">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 monthly replacement soft contact lenses in both eyes for a minimum of 5 days per week and 8 hours per day during the past 3 months.
4. Manifest cylinder ≤ 0.75D in each eye.
5. BCVA 20/25 or better in each eye.
6. Subject must be willing to stop wearing their habitual contact lenses for the duration of study participation.
7. Able to wear contact lenses within a range of sphere power from -1.00D to -6.00D (0.25D steps) and subject</td></tr>
</table>

	willing and able to wear the study lenses for the full duration of the study. [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. 3. History of refractive surgery or plan to have refractive surgery during the study or irregular cornea in either eye. 4. Ocular or intraocular surgery (excluding placement of punctal plugs) within the previous 12 months or planned during the study. 5. Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher. 6. Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear. 7. Current or history of herpetic keratitis in either eye. 8. Eye injury in either eye within 12 weeks immediately prior to enrollment for this trial. 9. Current or history of intolerance, hypersensitivity, or allergy to any component of the study products. 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. 11. Any use of topical ocular medications and artificial tear or rewetting drops that would require instillation during contact lens wear. 12. The Investigator, his/her staff, family members of the Investigator, family members of the Investigator's staff, or individuals living in the households of the aforementioned persons may not participate in the study.

	13. Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial. 14. Habitual BIOFINITY contact lens wearers.
Associated Materials	Subjects will also be randomized to use OPTI-FREE® REPLENISH® multi-purpose disinfection solution (OFR) or CLEAR CARE® Cleaning & Disinfecting Solution (CC). Lubrication/re-wetting drops will not be permitted during lens wear. However, habitual drop usage is allowed up to 10 minutes prior to lens insertion and any time after lens removal.

Table 1-1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	**Visit 1 Screen / Baseline / Dispense**	**Visit 2 1-Week Follow-up** [Day 8 (-1/+2 days) minimum 6 hrs after insertion)]	**Visit 3 2-Week Follow-up** [Day 15 (±2 days)]	**Visit 4 1-Month Follow-up/Exit** [Day 30 (-4/+2 days)]	**Early Exit**	**Unscheduled Visit**
Informed Consent	✓	--	--	--	--	--
Demographics	✓	--	--	--	--	--
Medical History	✓	✓	✓	✓	✓	✓
Concomitant Medications	✓	✓	✓	✓	✓	✓
Inclusion/ Exclusion	✓	--	--	--	--	--
Habitual lens (brand, power) and lens care	✓	--	--	--	--	--
[redacted]						

Procedure/ Assessment	**Visit 1 Screen / Baseline / Dispense**	**Visit 2 1-Week Follow-up** [Day 8 (-1/+2 days) minimum 6 hrs after insertion)]	**Visit 3 2-Week Follow-up** [Day 15 (±2 days)]	**Visit 4 1-Month Follow-up/Exit** [Day 30 (-4/+2 days)]	**Early Exit**	**Unscheduled Visit**
Keratometry readings*	✓	--	--	✓	✓	--
Manifest refraction*	✓	(✓)	(✓)	✓	✓	(✓)
BCVA (OD, OS, Snellen distance with manifest refraction)*	✓	(✓)	(✓)	✓	✓	(✓)
Biomicroscopy	✓	✓	✓	✓	✓	✓
Dispense study lenses	✓	(✓)	(✓)	--	--	(✓)
VA w/ study lenses (OD, OS, logMAR distance), (OU* as necessary) ^	✓	✓	✓	✓	✓	(✓)
[redacted]						

Procedure/ Assessment	**Visit 1 Screen / Baseline / Dispense**	**Visit 2 1-Week Follow-up** [Day 8 (-1/+2 days) minimum 6 hrs after insertion)]	**Visit 3 2-Week Follow-up** [Day 15 (±2 days)]	**Visit 4 1-Month Follow-up/Exit** [Day 30 (-4/+2 days)]	**Early Exit**	**Unscheduled Visit**
[redacted]						
AEs	✓	✓	✓	✓	✓	✓
Device deficiencies	✓	✓	✓	✓	✓	✓
[redacted]						
Exit Form	(✓)	(✓)	(✓)	✓	✓	(✓)

(✓) assessment performed as necessary, eg, decrease of VA by 2 lines or more with investigational product (IP)
***** Source only
^ If subject fitted with monovision, near eye must have distance over-refraction in place to assess VA.

1.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
BIOFINITY	CooperVision BIOFINITY contact lenses
CC	CLEAR CARE Cleaning & Disinfecting Solution
CDMA	Clinical Development and Medical Affairs
CFR	Code of Federal Regulations
D	Diopter
D/C	Discontinue
eCRF	Electronic case report form
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed consent form
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
LID	Lens identification
LogMAR	Logarithm of the minimum angle of resolution
mm	Millimeter
[redacted]	[redacted]
N/A	Not applicable
OD	Right eye
OFR	OPTI-FREE REPLENISH multi-purpose disinfection solution
OS	Left eye
OU	Both eyes
SAE	Serious adverse event
SADE	Serious adverse device effect
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

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3 INTRODUCTION

3.1 Study Rationale and Purpose

This new contact lens in development is intended for the optical correction of refractive ametropia in persons with non-diseased eyes.

The purpose of this study is to obtain on-eye performance data to inform contact lens product development. The primary endpoint was selected to fulfil the primary objective of the study. Procedures for measurement of these endpoints were selected based on common practice for these assessments. The design of this study is justified based upon preclinical and clinical testing, as described within the Investigator's Brochure. BIOFINITY was chosen as the control product because these lenses have the same wear modality.

There are no immediate plans to submit the results of this early clinical development 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.

3.2 Trial Objective

The objective of this study is to describe the clinical performance of an investigational, coated silicone hydrogel contact lens over 30 days of daily wear.

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 lens in development are features consistent with successful contact lens wear.

Based upon non-clinical testing and documented rationale for applicability of test results to the IP, the new contact lens in development is assessed to be non-toxic and biocompatible for on-eye use. Clinical studies involving similar contact lens material coating formulations have been completed.

A summary of the known potential risks and benefits associated with the new contact lens in development can be found in the Investigator's Brochure. 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 the new contact lens in development are anticipated to be similar to other marketed monthly soft contact lenses.

The site personnel will educate subjects on proper hygiene, 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 86 volunteer subjects to be enrolled at approximately 4 sites in the US, with approximately 22 subjects enrolled per site. The study population will consist of subjects with normal eyes who are adapted, existing wearers of soft contact lenses in both eyes.

Subjects must be screened according to the full list of inclusion/exclusion criteria in Section 1 of this protocol.

After informed consent is signed, a separate screening visit is allowed for the following criteria:

- INC01 – Subject must be at least 18 years of age
- EXC13 – Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial

This separate screening visit can take place regardless of whether any other criterion has been verified.

Rescreening of subjects is not allowed in this study.

3.5 Outline of Study

This will be a multi-site, prospective, randomized, subject-masked, study comparing 2 contact lenses. The expected duration of subject participation in the study is approximately 32 days, with 4 scheduled visits. The study is expected to be completed in approximately 2 months.

4 TREATMENTS ADMINISTERED

Subjects will be randomized in a 2:2:1:1 manner to one of the following 4 groups:

1. LID014341 + OFR
2. LID014341 + CC
3. BIOFINITY + OFR
4. BIOFINITY + CC

4.1 Identity of Study Treatments

DESCRIPTION OF TEST AND CONTROL PRODUCTS		
	Test Product	Control Product
LID Number	LID014341	N/A
Lens identified in randomization system as:	LID014341	BIOFINITY
Lens	LID014341	BIOFINITY
Material	HD13B1 with water gradient coating	comfilcon A
Water Content	~54%	48%
Base Curve (mm)	8.0 – 8.9	8.6
Diameter (mm)	14.0 – 14.5	14.0
Rx powers to be available in this study (D)	-1.00D to -6.00D (0.25D steps)	-1.00D to -6.00D (0.25D steps)
Packaging, Labeling, and Supply	• Blister foil pack • Foil label includes at a minimum: - lens identifier - base curve - diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational	• Blister foil pack • Commercial foil • Available in commercial boxes of ~6 lenses per power per box • Lenses should be stored at room temperature.

	device statement - Sponsor information - country of origin • Provided in boxes of ~10 lenses per power, identified with the following at a minimum: - a color coded label stating the protocol number - lens identifier - power - an investigational use only statement - tracking number • Lenses should be stored at room temperature.	
Lens care solutions identified in randomization systems as:	Randomization will also include 2 lens care solutions: • OFR • CC	
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Replacement lenses will not be provided to the subject. In the event a lens needs to be replaced, the subject must return to the site for a replacement lens. Until the replacement lens is obtained, the subject must store the fellow lens in the provided lens care solution and wear their habitual spectacles. • Exposure: At least 8 hours per day, 5 days per week, over a 4-week period.	
Control lens procurement	Each site will procure their own control lenses. [redacted]	
Lens care solution procurement	Alcon will provide lens care solution to each site.	

4.2 Accountability Procedures

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

It is the Investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner
- All used foils and unused supplies are returned by each subject
- All unused products are available for return to the Study Sponsor, as directed
- Any test lenses associated with a device deficiency or with any product-related adverse event [ie, ADE or SADE] are returned to the Study Sponsor for investigation. Refer to Section 7.3 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

[redacted]

5 STUDY PROCEDURES AND ASSESSMENTS

5.1 Visits and Examinations

5.1.1 Visit 1 (Day 1) – Screen/ Baseline/ Dispense

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

2	Obtain demographic information and medical history, including information on all medications used within the past 30 days. Include herbal therapies, vitamins, and all over-the-counter as well as prescription medications.
[redacted]	
6	Obtain keratometry readings, OD, OS.* **Source only.*
7	Perform a manifest refraction.
8	Perform Snellen BCVA with manifest refraction. • OD, OS, distance only *Note: Distance BCVA must be 20/25 or better in each eye for the subject to qualify for the study.*

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
10	Determine study lens powers based upon the manifest refraction and habitual lens powers.
11	Review inclusion/exclusion criteria to determine if the subject qualifies to be randomized into the study. If subject qualifies, request randomization. If subject does not qualify, exit the subject from the study as a screen failure.
12	Obtain Randomization of study lens and lens care solution from EDC/IRT integration system.
[redacted]	
14	Based upon the randomized assignment, have the subject insert the appropriate study lenses, being careful to maintain the correct OD and OS lens assignments • *Keep all lidding foils of lenses used during lens fit process for study lens accountability.* • *Follow procedures to maintain masking.*

15	Evaluate the study lenses by performing the following: • logMAR VA with study lenses (OD and OS at distance)* (OU as necessary)^ **Small adjustments can be made in final lenses dispensation. VA w/study lenses must be equivalent to 20/40 OU or better for subject to leave the office. Use the logMAR VA from final study lenses to record in EDC.* *^Record in source only.*
[redacted]	
18	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.*
19	Dispense randomized lens care. Provide the subject with written and verbal instructions on lens wear and care.
20	Schedule Visit 2 to take place 8 -1/ +2 days after Visit 1. Instruct subject on the minimum amount of lens wear time for the day of the follow up visit. [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.*

5.1.2 Visit 2 (Day 8 -1/ +2 Days) – 1-Week Follow-up

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]	
6	Evaluate the study lenses by performing the following: • logMAR VA with study lenses (OD and OS at distance) (OU, as necessary)* * *Record in source only.*
[redacted]	
8	Perform a manifest refraction, if necessary.
9	Perform Snellen BCVA, if necessary. • OD, OS, distance only

10	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
11	Dispense study lenses, if necessary.
[redacted]	
13	Schedule Visit 3 to take place 15 ± 2 days after Visit 1. *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 as well as lens removal on site, if possible. The subject should then be scheduled to return to the clinic for Visit 3 (if possible) or exited from the study.*

5.1.3 Visit 3 (Day 15 ± 2 Days) – 2-Week Follow-up

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]

6	Evaluate the study lenses by performing the following: • logMAR VA with study lenses (OD and OS at distance) (OU, as necessary)* * *Record in source only.*

[redacted]

8	Perform a manifest refraction, if necessary.
9	Perform Snellen BCVA, if necessary. • OD, OS, distance only

10	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
11	Dispense study lenses, if necessary.
[redacted]	
13	Schedule Visit 4 to take place 30 -4/ +2 days after Visit 1. *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 as well as lens removal on site, if possible. The subject should then be scheduled to return to the clinic for Visit 4 (if possible) or exited from the study.*

5.1.4 Visit 4 (Day 30 -4/ +2 Days) – 1-Month Follow-up/ 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]

8	Evaluate the study lenses by performing the following: • logMAR VA with study lenses (OD and OS at distance) (OU, as necessary)* ** Record in source only.*

[redacted]

10	Perform a manifest refraction.
11	Perform Snellen BCVA. • OD, OS, distance only

12	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
13	Obtain keratometry readings, OD, OS.* **Source only.*
[redacted]	
16	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. During all unscheduled visits, the Investigator must conduct the procedures according to Table 1-1: Schedule 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 case history source documents.

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

5.3 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after signing the informed consent, including screen failures. Subjects may discontinue from the study at any time for any reason. Subjects may also be discontinued from the study at any time if, in the opinion of the Investigator, their continued participation poses a risk to their health. Discontinued subjects will not be replaced (ie, their subject numbers will not be re-assigned/re-used).

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

Any subject who exits early from the study (excluding screen failures) must undergo all procedures outlined at Visit 4, as applicable.

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

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

5.4 Clinical Study Termination

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

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

- The Study Sponsor must:
    - Immediately notify the Investigator(s) and subsequently provide instructions for study termination.
    - Inform the Investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension, as applicable.

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

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

6 ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum, as well as confidence intervals where applicable. Categorical variables will be summarized with counts and percentages from each category. Any deviation 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 the code for masked treatment 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 lens evaluated in this study. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed.

6.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the Safety Analysis Set. Baseline data pertaining to habitual lens (lens brand, power, lens care brand, [redacted]) will be summarized on the Safety Analysis Set as well.

6.4 Effectiveness Analyses

This study defines one primary endpoint [redacted]. The Safety Analysis Set will serve as the primary set for all effectiveness analyses.

6.4.1 Primary Effectiveness

The primary objective of this study is to describe the clinical performance of an investigational, coated silicone hydrogel contact lens over 30 days of wear. The primary endpoint is distance VA with study lenses, collected in logMAR scale, 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 as well as a two-sided 95% confidence interval for the mean of each study lens 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 for the primary analysis.

6.7 Multiplicity

No multiplicity adjustment needs to be considered for the effectiveness endpoints since no formal hypothesis testing will be conducted.

6.8 Safety Analysis

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

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. AEs leading to study discontinuation, significant non-serious AEs, and SAEs will be identified. Individual subject listings will be provided, as necessary.

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

Each biomicroscopy parameter will be tabulated by its grade. For each biomicroscopy parameter, counts and percentages of eyes that experience an increase of ≥ 2 grades from baseline (Visit 1) to any subsequent visit will be presented. A supportive listing will be generated which will include all biomicroscopy data from all visits for these eyes experiencing the increase.

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

No inferential testing will be done for safety analysis.

6.9 Interim Analyses

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

6.10 Sample Size Justification

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

7 ADVERSE EVENTS AND DEVICE DEFICIENCIES

Terms and Definitions

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.*
Adverse Device Effect (ADE)	AE 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.*

Anticipated Serious Adverse Device Effect (ASADE)	Serious ADE which by its nature, incidence, severity or outcome has been identified in the risk management file.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.*
Malfunction	Failure of a medical device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling of the device. The intended performance of the device refers to the intended use for which the device is labeled or marketed.
Non-serious Adverse Event	AE that does not meet the criteria for an SAE.
Serious Adverse Event (SAE)	AE that led to any of the following: • Death. • A serious deterioration in the health of the subject 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 an 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 adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.*

	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 7.1 for additional SAEs.*
Serious Adverse Device Effect (SADE)	ADE that has resulted in any of the consequences characteristic of an SAE.
Significant Non-Serious Adverse Event	A significant non-serious AE is a symptomatic, device-related, non-sight threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 7.1 for additional Significant Non-Serious AEs.*
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk management file.
Use Error	Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. *Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.*

7.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test *product*).

Figure 7–1 Categorization of All AEs

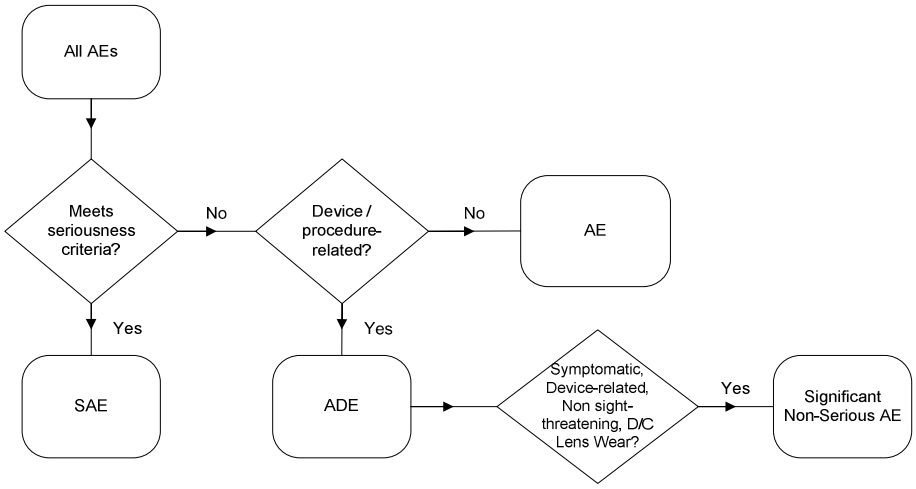
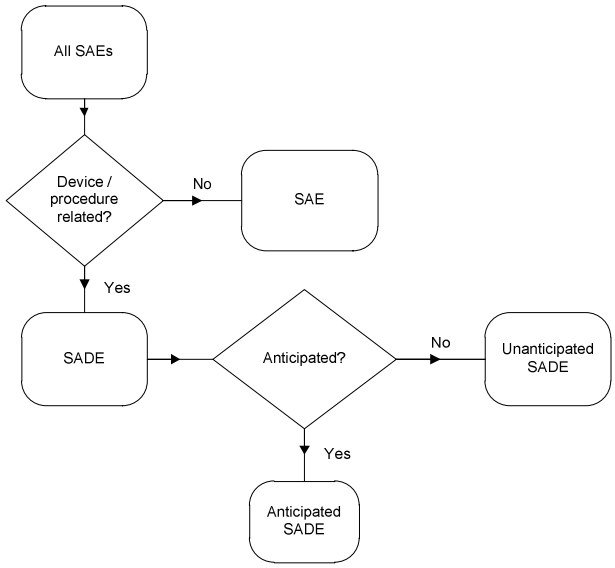


Figure 7-2 Categorization of All Serious Adverse Events



Specific Events Relevant to this Protocol

Serious Adverse Events

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

- An ocular infection including a presumed infectious ulcer with any of the following characteristics:
    - Central or paracentral location
    - Penetration of Bowman's membrane
    - Infiltrates > 2 mm diameter
    - Iritis
    - Increase in intraocular pressure
    - Culture positive for microorganisms
    - Increasing size or severity at subsequent visits
- Any central or paracentral corneal event (such as neovascularization) that results in permanent opacification
- Hypopyon
- Hyphema
- Neovascularization within the central 6 mm of the cornea
- Permanent vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting ≥ 50% of corneal surface area

Significant Non-Serious Adverse Events

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

- Peripheral non-progressive non-infectious ulcers
- All symptomatic corneal infiltrative events
- Corneal staining score greater than or equal to Grade 3
- 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

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

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category listed in the Device Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. Examples of device deficiencies include the following:

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

7.2 Monitoring for Adverse Events

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

- “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?”

Additionally, 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 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 msus.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 (ie, OPTI-FREE REPLENISH multi-purpose disinfection solution, and CLEAR CARE Cleaning & Disinfecting Solution) 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.

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.

7.4 Return product analysis

Alcon test products associated with device deficiencies and/or product related AEs should be returned and must include a copy of the corresponding AE or Device Deficiency eCRF. These products should be returned to the Sponsor at the end of the study, unless instructed otherwise by the Sponsor.

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 (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.

The Investigator should also report complaints on non-Alcon products (ie, BIOFINITY contact lenses) 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 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.

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. At the end of the clinical study, the Sponsor will collect a copy of the

enrollment log without any identifying subject information. 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 subject masked with subjects randomized to use LID014341 or Biofinity and OPTI-FREE REPLENISH multi-purpose disinfection solution or CLEAR CARE Cleaning & Disinfecting Solution for the duration of the 4-week treatment period. The Sponsor personnel (other than site monitors, lead clinical site manager, CDMA Project 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. 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 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 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 reporting requirements.

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 Investigator’s Brochure and Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB. At the end of the study, the Investigator must notify the IRB about the study’s completion. The

IRB also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the IRB on the progress of the study at intervals stipulated by the IRB.

Voluntary informed consent must be obtained from every subject 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.

11 PROTOCOL AMENDMENT HISTORY

Version	Brief Description and Rationale
1	Initial Version of this document

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

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
06/16/2018 14:14:21	[redacted]	CDMA Project Lead
06/18/2018 18:10:20	[redacted]	Management of Affected Area Approval
06/18/2018 19:40:46	[redacted]	Global Device Medical Safety
06/19/2018 01:59:30	[redacted]	biostatistics
06/19/2018 03:04:00	[redacted]	Clinical Manager