Alcon

Title

Clinical Evaluation of a Silicone Hydrogel Daily Wear Monthly Replacement Contact Lens

Protocol Number:	CLY935-C012 / NCT04422990
Development Stage of Project:	Development
Sponsor Name and Address:	Alcon Research, LLC and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	LID018869

Investigator Agreement:

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

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

Principal Investigator:

Signature Date

Name and professional position:

Address:

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1 GLOSSARY OF TERMS

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

	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 (IP)	Is defined as a preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or control product in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
Malfunction	Failure of a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Randomized Subjects	Any subject who is assigned a randomized treatment.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • 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 serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.* *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 adverse event 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	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
[redacted]	[redacted]
Biofinity contact lens or Biofinity	CooperVision BIOFINITY (comfilcon A) soft contact lenses (LID010221)
CFR	Code of Federal Regulations
CI	Confidence interval
CLCDVA	Contact lens corrected distance visual acuity
CLEAR CARE	CLEAR CARE® Cleaning & Disinfecting Solution
[redacted]	[redacted]
CRF	Case report form
[redacted]	[redacted]
D	Diopter(s)
D/C	Discontinue
[redacted]	[redacted]
eCRF	Electronic case report form
EDC	Electronic data capture
FAS	Full analysis set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
IB	Investigator's brochure
ICF	Informed consent form
[redacted]	[redacted]
IEC	Independent ethics committee
[redacted]	[redacted]
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
[redacted]	[redacted]
LID	Lens identification
logMAR	Logarithm of the minimum angle of resolution
[redacted] contact lens or [redacted]	[redacted] soft contact lenses (LID018869)
[redacted]	[redacted]
N/A	Not applicable
OD	Right eye

Abbreviation	Definition
OS	Left eye
OU	Both eyes
[redacted]	[redacted]
PP	Per protocol analysis set
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SiHy	Silicone hydrogel
SOP	Standard operating procedure
[redacted]	[redacted]
UCDVA	Uncorrected distance visual acuity
US / USA	United States of America
USV	Unscheduled visit
VA	Visual acuity
vs	Versus

3 PROTOCOL SUMMARY

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

Approximately 16 sites in the US will enroll approximately 160 subjects. Subjects will be expected to attend 4 office visits: Screening/Baseline/Dispense, Week 1 Follow-up, Month 1 Follow-up, and Month 3 Follow-up/Exit. The total expected duration of participation for each subject is approximately 3-4 months in this daily wear clinical study. Accounting for both screen failure and dropout rates, approximately 96 subjects will be assigned to wear the test lenses and 48 subjects will be assigned to wear the control lenses, [redacted].

[redacted]

[redacted]

Subjects and the study personnel conducting the study evaluations will be masked to treatment. Subjects who meet the inclusion and exclusion criteria will be randomized to wear either the test contact lenses [redacted] in both eyes or the control contact lenses (Biofinity) in both eyes for 3 months of daily wear exposure.

[redacted]

At the Screening/Baseline/Dispense Visit, study lenses will be dispensed to qualified subjects [redacted]

[redacted] All study lenses will be worn for at least 5 days per week and 8 hours per day in a daily wear modality (eg, will not be worn while sleeping). [redacted]

[redacted]. Regardless of whether the subject is randomized to the test or the control group, CLEAR CARE Cleaning & Disinfecting Solution (CLEAR CARE) must be used for cleaning and disinfection. [redacted]

[redacted]

[redacted]

Investigational product type	Medical Device
Study type	Interventional
Investigational products	Test Product: [redacted] soft contact lens Control Product: Biofinity soft contact lens
Purpose and rationale	The purpose of this clinical study is to evaluate the safety and performance of the investigational [redacted] soft contact lens compared to the commercially available Biofinity soft contact lens, when worn in a daily wear modality, by assessing visual acuity as the primary endpoint.

Objective(s)	The primary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in CLCDVA at Week 1 Follow-up. The secondary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in the percentage of subjects achieving CLCDVA 20/20 or better, in each eye, at Week 1 Follow-up.
Endpoint(s)	Primary Effectiveness • Mean contact lens corrected distance visual acuity (CLCDVA, Snellen converted to logMAR) in each eye at Week 1 Follow-up Secondary Effectiveness • Percentage of subjects achieving CLCDVA 20/20 or better in each eye, at Week 1 Follow-up [redacted]

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessment(s)	Effectiveness • VA with study lenses (Snellen distance) [redacted]

	[redacted] Safety • AEs • Biomicroscopy • Device deficiencies
Study Design	This will be a prospective, randomized, [redacted] controlled, double-masked, parallel-group, daily wear clinical study. Subject participation in the study will be approximately 3 – 4 months with approximately 3 months of exposure to study lenses.
Subject population	Volunteer subjects aged 18 or over who are adapted daily wear frequent replacement soft contact lens wearers, excluding Biofinity habitual wearers, have at least 3 months of soft contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and at least 8 hours per day. [redacted]
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Successful wear of spherical daily wear frequent replacement 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 • Manifest cylinder ≤ 0.75 D in each eye

<table>
<tr><td></td><td>

- Best spectacle corrected visual acuity (using manifest refraction) of 20/20 or better in each eye
- [redacted]

</td></tr>
<tr><td>Key exclusion criteria
(See Section 8.2 for a complete list of exclusion criteria)</td><td>

- 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
- Monovision or multifocal contact lens wearers
- Habitually wearing Biofinity lenses

</td></tr>
<tr><td>Data analysis [redacted]</td><td>

To address the primary and secondary effectiveness objectives, data from a pre-determined subset of subjects (see Section 12) from CLY935-C010 will be combined with the current study, and all planned analyses will be performed on this combined set as summarized below:

<table>
<tr><th>Endpoint</th><th>Comparison</th><th>Statistical Method</th></tr>
<tr><td>Primary</td><td></td><td></td></tr>
<tr><td>Mean CLCDVA (Week 1 Follow-up)</td><td>[redacted] vs Biofinity Noninferiority (margin = 0.10 logMAR)</td><td>Mixed effects repeated measures model</td></tr>
<tr><td>Secondary</td><td></td><td></td></tr>
<tr><td>Proportion of subjects with CLCDVA of 20/20 or better in both eyes (Week 1 Follow-up)</td><td>[redacted] vs Biofinity Noninferiority (margin = 0.10)</td><td>Generalized linear mixed model</td></tr>
</table>

[redacted]

No inferential testing will be carried out for safety endpoints.

</td></tr>
</table>

	[redacted]
[redacted]	[redacted] Biofinity, daily wear, [redacted]
Associated materials	CLEAR CARE will be used for daily cleaning and disinfection. [redacted]

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense	Visit 2 Week 1 Follow-up[5]	Visit 3 Month 1 Follow-up[5]	Visit 4 Month 3 Follow-up/Exit[5]	Early Exit	USV
	Day 1	Day 8 [redacted]	Day 30 [redacted]	Day 95 [redacted]		
Informed Consent	X					
Demographics	X					
Medical History	X	X	X	X	X	(X)
Pregnancy	X	X	X	X	X	(X)
Concomitant Medications	X	X	X	X	X	(X)
Inclusion/Exclusion	X					
Habitual lens information (brand/manufacturer, power, modality/wear success, habitual lens care brand)	X					
[redacted]	[redacted]			X	[redacted]	[redacted]
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
Biomicroscopy [redacted]	X	X	X	X	X	(X)
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
[redacted]	[redacted]					
Randomize and record lens power	X					

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense Day 1	Visit 2 Week 1 Follow-up[5] Day 8	Visit 3 Month 1 Follow-up[5] Day 30	Visit 4 Month 3 Follow-up/Exit[5] Day 95	Early Exit	USV
[redacted]	[redacted]					
[redacted]	[redacted]	[redacted]	[redacted]			[redacted]
IP Dispense*	X	(X)	X			(X)
VA w/ study lenses (OD, OS Snellen distance)	X	X	X	X	X	(X)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Printed By:

Print Date:

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense	Visit 2 Week 1 Follow-up[5]	Visit 3 Month 1 Follow-up[5]	Visit 4 Month 3 Follow-up/Exit[5]	Early Exit	USV
	Day 1	Day 8	Day 30	Day 95		
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adverse Events	X	X	X	X	X	(X)
Device deficiencies	X	X	X	X	X	(X)
Exit Form	(X)	(X)	(X)	X	X	(X)

[redacted]

[redacted]

5 INTRODUCTION

[redacted]

In this clinical study, the performance of the investigational [redacted] contact lens will be compared to the commercially available Biofinity contact lens in a parallel group design to demonstrate the safety and effectiveness of the [redacted] contact lens, both to be worn in a daily wear modality and replaced on a monthly basis. The intended use of this contact lens is for vision correction. Therefore, the measurement of distance VA is planned as the primary effectiveness variable. [redacted]

[redacted]

5.2 Purpose of the Study

The purpose of this clinical study is to evaluate the safety and performance of the investigational [redacted] soft contact lens compared to the commercially available Biofinity soft contact lens when worn in a daily wear modality, by assessing VA as the primary variable.

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

[redacted]

5.3 Risks and Benefits

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

In the US, Biofinity contact lenses have approved indications for use for both daily wear and extended wear for up to 6 continuous nights. Further details on any known potential risks and benefits can be found in the product package insert.

A summary of the known potential risks and benefits associated with [redacted] contact lenses can be found in the IB. [redacted]

[redacted]

[redacted].

Refer to the IB for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
Demonstrate noninferiority of [redacted] compared to Biofinity in CLCDVA at Week 1 Follow-up.	Mean CLCDVA in each eye at Week 1 Follow-up.

6.2 Secondary Objective(s)

Table 6–2 Secondary Objective(s)

Objective(s)	Endpoint(s)
Demonstrate noninferiority of [redacted] compared to Biofinity in the percentage of subjects achieving CLCDVA 20/20 or better in each eye, at Week 1 Follow-up.	Percentage of subjects achieving CLCDVA 20/20 or better in each eye at Week 1 Follow-up.

[redacted]

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

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

7 INVESTIGATIONAL PLAN

7.1 Study Design

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

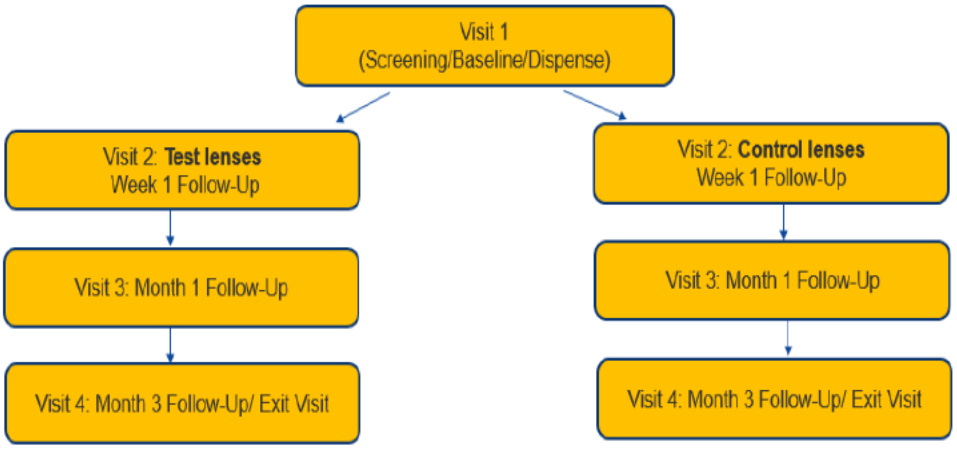
This clinical study will engage approximately 16 clinic sites to enroll approximately 160 subjects with approximately 10 - 15 subjects per site.

Subjects will be expected to attend 4 office visits: Screening/Baseline/Dispense, Week 1 Follow-up, Month 1 Follow-up, and Month 3 Follow up/Exit. The total expected duration of participation for each subject is approximately 3-4 months with approximately 3 months of exposure to study lenses in this daily wear study. Subjects will be randomized to wear either the test [redacted] contact lenses in both eyes or the control Biofinity contact lenses in both eyes.

Following randomization, study lenses will be dispensed to the subject. [redacted]

Subjects will wear the lenses while awake in a daily wear modality. CLEAR CARE will be used for daily cleaning and disinfection. [redacted]

Figure 7-1 Flowchart of Study Visits



[redacted]

7.4 Rationale for Choice of Control Product

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

[redacted]

8 STUDY POPULATION

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

The intended study population consists of volunteer subjects who are frequent replacement daily wear soft contact lens wearers, excluding Biofinity 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 8 hours per day.

[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. At least 18 years of age.
2. Able to understand and sign an IRB/IEC approved Informed Consent form.
3. Willing and able to attend all scheduled study visits as required per protocol.
4. Successful wear of frequent replacement spherical daily wear 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.
5. Manifest cylinder ≤ 0.75 D in each eye.

6. Best spectacle corrected (using manifest refraction) VA 20/20 or better in each eye.

[redacted]

8.2 Exclusion Criteria

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

[redacted]

[redacted]

12. Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment.

[redacted]

14. Monovision or multifocal contact lens wearers.

[redacted]

18. Any habitual wear of Biofinity lenses.

[redacted]

[redacted]

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

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

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

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

Table 9–1 Test Product

Test Product	[redacted] soft contact lenses ([redacted] contact lens) (LID018869)
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.

[redacted]

[redacted]

Usage	• Wear: ○ Daily Wear ▪ During waking hours only. [redacted] ○ Bilateral • Exposure: At least ~8 hours per day and ~5 days per week over a ~3-month exposure period. [redacted] • Lens Care: CLEAR CARE (mandatory), [redacted] • [redacted]
[redacted]	[redacted]
Packaging description	Blister foil pack

[redacted]

[redacted]

Storage conditions	Stored at room temperature.

[redacted]

Table 9–2 Control Product

Control Product(s)	Biofinity (comfilcon A) soft contact lenses (Biofinity contact lens) (LID010221)
Manufacturer	CooperVision
Indication for Use	The intended use of this contact lens is for vision correction.
Product description and parameters available for this study	• Material: comfilcon A • Water content: 48% [redacted] • Base curve: 8.6 mm • Diameter: 14.0 mm
Formulation	Silicone Hydrogel. Additional details can be found in the Biofinity package insert.
Usage	• Wear: o Daily Wear ▪ During waking hours only. [redacted] o Bilateral • Exposure: At least ~8 hours per day and ~5 days per week over a ~3-month exposure period. [redacted]

	• Lens Care: CLEAR CARE (mandatory), [redacted] • [redacted]
Number/Amount of Product to be Provided to the subject	At each study visit, sites will ensure that subjects are given adequate lenses to last until the next planned study visit, allowing for planned and unplanned lens replacements.
Packaging description	Blister foil pack.
[redacted]	
Storage conditions	Stored at room temperature.

[redacted]

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

[redacted]

9.3 Treatment Assignment/Randomization

Subjects will be randomized in a 2:1 manner to receive either the [redacted] or Biofinity contact lenses, respectively. [redacted]

[redacted]

[redacted]

At Visit 1, all eligible subjects will be randomized [redacted] to one of the treatment arms. [redacted]

9.4 Treatment masking

This study is double-masked, with subjects randomized to use [redacted] or Biofinity contact lenses for the duration of the 3-month treatment period. [redacted]

[redacted]

[redacted]

[redacted]

9.5 Accountability Procedures

[redacted]

It is the Investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner
- [redacted]
- 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. [redacted]

The Investigator is responsible for proper disposition of all unused IPs at the conclusion of the study. [redacted]

9.6 Changes to concomitant medications, treatments/ procedures

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

- Any new medications
- Alterations in dose or dose schedules for current medications,
- Any medical procedure or hospitalization that occurred or is planned

- Any non-drug therapies (including physical therapy and blood transfusions).

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

10 STUDY PROCEDURES AND ASSESSMENTS

Subjects will be expected to attend 4 office visits, as shown below.

Visit #	**Visit Type**	**Visit Day**	[redacted]
Visit 1	Screening/Baseline/Dispense	Day 1	[redacted]
Visit 2	Week 1 Follow-up Visit	Day 8	[redacted]
Visit 3	Month 1 Follow-up Visit	Day 30	[redacted]
Visit 4	Month 3 Follow-up/Exit Visit	Day 95	[redacted]

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

[redacted]

[redacted]

At the Screening/Baseline/Dispense Visit, study lenses will be dispensed to the subject. All subjects will wear the study lenses in a daily wear modality, only during waking hours.

[redacted]

[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

[redacted].

10.2.1 Demographics

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

10.2.2 Medical History and Concomitant Medications

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 [redacted]

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. Requirements for reporting AEs in the study can be found in Section 11.

10.2.5 Slit-Lamp Biomicroscopy: Safety Assessment

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

Slit-lamp examination of the tear film stability will also be performed at each visit.

10.2.6 Device Deficiencies: Safety Assessment

Assess and record any device deficiencies that are reported or observed since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11.

[redacted]

- VA with habitual correction

[redacted]

- Perform biomicroscopy (assessments with or without lenses, as applicable)

[redacted]

10.5 Discontinued Subjects

10.5.1 Screen Failures

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

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

Subject numbers must not be re-used.

10.5.2 Discontinuations

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

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

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

[redacted]

10.6 Clinical Study Termination

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

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

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

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

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

10.6.1 Follow-up of subjects after study participation has ended

Study visits are not a substitute for routine eye care. 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 AEs

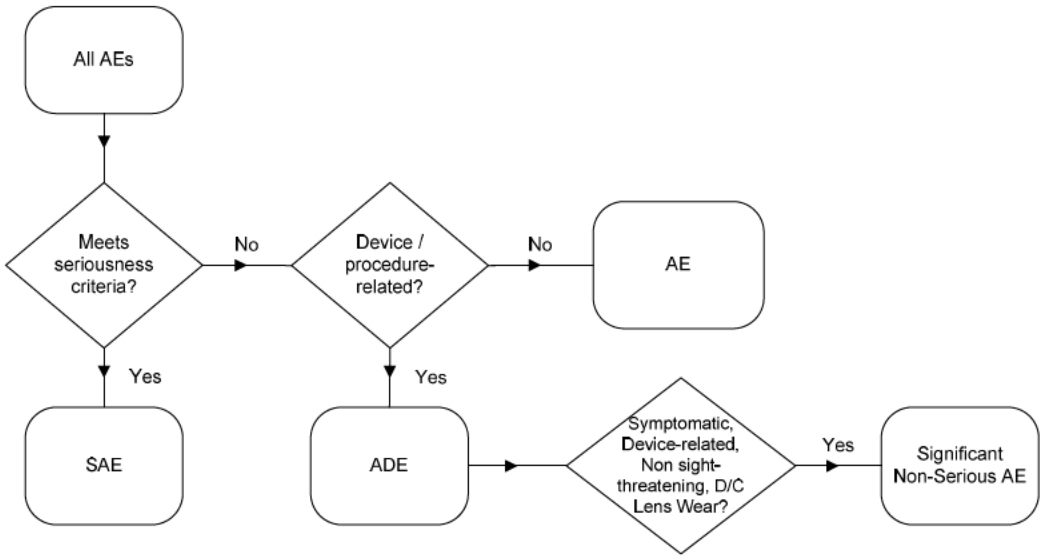
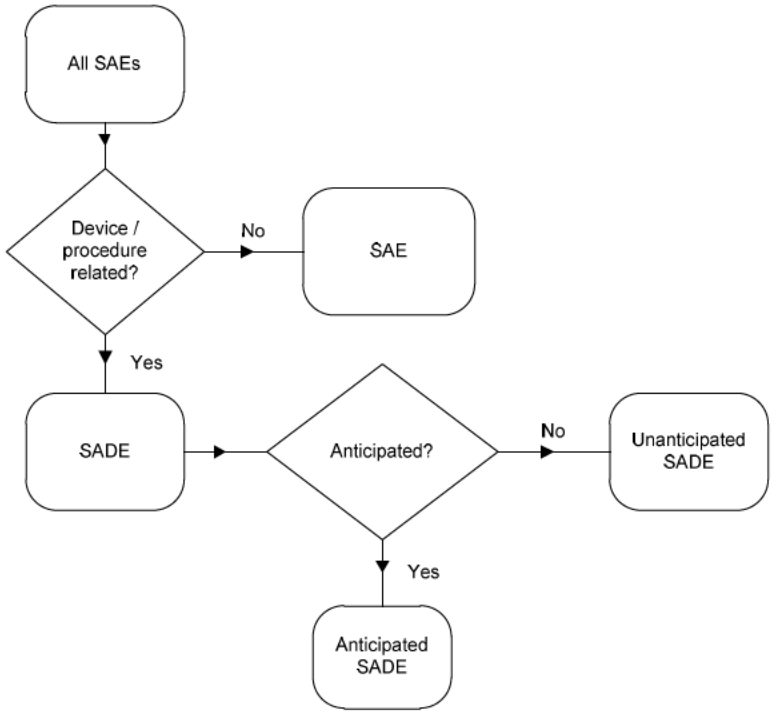


Figure 11–2 Categorization of All SAE



SAEs

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 AE

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 [redacted]
- 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 [redacted]

[redacted]

Device Deficiencies

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

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

11.2 Monitoring for AEs

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?"

[redacted]

11.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. [redacted]

[redacted]

For each recorded event, the ADEs and SAEs documentation must include: date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the Investigator must document all device deficiencies reported or observed with test and control products on the Device Deficiency eCRF.

- 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.

[redacted]

[redacted]

[redacted]

[redacted]

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).

[redacted]

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study. [redacted]

11.6 Follow-Up of Subjects with AEs

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.

[redacted]

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. [redacted]

12 ANALYSIS PLAN

Data from a subset of subjects in the CLY935-C010 study will be combined with data from this study. This combined set will serve as the basis for all planned analyses for the primary and secondary effectiveness objectives. Subjects in CLY935-C010 will be included in the combined set only if they satisfy the following criterion:

- BCVA of 20/20 or better in each eye at the Screening/Baseline/Dispense Visit

[redacted]

[redacted]

[redacted].

12.1 Subject Evaluability

Final subject evaluability must be determined prior to breaking the code for masked treatment (lens) assignment and locking the database, [redacted]

12.2 Analysis Sets

12.2.1 Safety Analysis Set

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

12.2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study, [redacted], and who have at least one post-baseline (post-Dispense) CLCDVA.

12.2.3 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that have met any of the critical deviation or evaluability criteria identified in the DEP.

12.3 Demographic and Baseline Characteristics

Demographic information, recent lens-wearing experience (including wear modality and wear success), and habitual lens information will be presented by lens group and overall. Counts and percentages will be presented for categorical variables such as sex, age group, race, an ethnicity. Number of observations, mean, SD, median, minimum, and maximum will be presented for continuous variables such as age.

12.4 Effectiveness Analyses

This study defines 1 primary, 1 secondary, [redacted]

[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in mean CLCDVA at Week 1 Follow-up.

The primary endpoint is the mean CLCDVA at Week 1 Follow-up. The corresponding assessment is collected with study lenses, in Snellen, for each eye. Conversion will be made to the logMAR scale.

12.4.1.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.10 (in logMAR scale) for noninferiority:

$$H_0: \mu_{(T)} - \mu_{(C)} \geq 0.10$$
$$H_a: \mu_{(T)} - \mu_{(C)} < 0.10$$

where $\mu_{(T)}$ and $\mu_{(C)}$ denote the Week 1 Follow-up mean CLCDVA for [redacted] and Biofinity contact lenses, respectively, on the logMAR scale.

12.4.1.2 Analysis Methods

A mixed effects repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, visit (Dispense, Week 1 Follow-up, Month 1 Follow-up, and Month 3 Follow-up), and lens-by-visit interaction as fixed effects, [redacted] Within-subject correlation due to eye will also be accounted for in the model. Lens difference ([redacted] minus Biofinity) and the corresponding two-sided 95% CI will be computed for 1-Week Follow-up. Noninferiority in CLCDVA will be declared if the upper confidence limit is less than 0.10.

12.4.2 Analysis of Secondary Effectiveness Endpoints

The secondary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in the percentage of subjects achieving distance VA 20/20 or better, in each eye, at Week 1 Follow-up.

The corresponding endpoint is the percentage (proportion) of subjects with CLCDVA of 20/20 or better, measured monocularly, in both OD and OS at Week 1 Follow-up.

12.4.2.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.10 (10%) for noninferiority.

H_0: $P_{(T)} - P_{(C)} \leq -0.10$
H_a: $P_{(T)} - P_{(C)} > -0.10$

where $P_{(T)}$ and $P_{(C)}$ denote the proportion of subjects attaining at least 20/20 in CLCDVA at Week 1 Follow-up in each eye (OD and OS) for [redacted] and Biofinity contact lenses, respectively.

12.4.2.2 Analysis Methods

A binary variable will be defined for each subject to indicate whether the CLCDVA at Week 1 Follow-up is no worse than 20/20 in both OD and OS, and the corresponding proportion will be computed for each lens using the number of subjects as the denominator. [redacted]. From the two-sided 95% CI on the lens difference ([redacted] minus Biofinity),

noninferiority in proportion of subjects achieving 20/20 or better in CLCDVA in both eyes will be declared if the lower confidence limit is greater than -0.10.

[redacted]

[redacted]

12.6 Safety Analyses

The safety endpoints are:

- AEs
- Biomicroscopy Findings
- Device Deficiencies

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.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. Descriptive summaries (counts and percentages) 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 IP.

[redacted]

Two listings for device deficiencies, prior to exposure of study contact lenses and treatment-emergent, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

[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. [redacted]

[redacted]

[redacted]

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.

[redacted]

[redacted]

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. [redacted]

[redacted]

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

[redacted]

- [redacted]
- [redacted]
- [redacted]

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. [redacted]

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. [redacted]

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.

[redacted]

[redacted]

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