Title

A Prospective, Randomized, Controlled, Multi-Center Clinical Investigation of the AcrySof IQ Vivity Extended Vision IOL vs. TECNIS Symfony and AT LARA Extended Depth of Focus IOLs

Protocol Number:	ILI875-P001 / NCT04098367
Development Stage of Project:	Postmarket
Sponsor Name and Address:	Alcon Laboratories (Australia) Pty, Ltd. and its affiliates ("Alcon") Suite 1, Level 7, 15 Talavera Road Macquarie Park NSW 2113 Australia
Test Product:	AcrySof™ IQ Vivity™ Extended Vision IOL Model DFT015

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	AcrySof™IQ Vivity™ Extended Vision IOL, Model DFT015; throughout this document, test product will be referred to as VIVITY.
Name of Control Products	• TECNIS Symfony® Extended Range of Vision IOL Model ZXR00; throughout this document this control product will be referred to as SYMFONY. • AT LARA® extended depth of focus IOL Model 829MP; throughout this document this control product will be referred to as AT LARA. *Note: Model number of device may be different if a pre-loaded delivery system is used. It should be verified by site staff that the IOL contained within matches the models listed above.*
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). [redacted] 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	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.

Postmarketing/Post-authorization study	Any study conducted within the conditions laid down in product labelling and other conditions laid down for the marketing of the product or under normal conditions of use. A postmarketing study falls either within the definitions of an interventional or a non-interventional study and may also fall within the definition of a post-approval study.
Product Complaints	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling, or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
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), or any ocular secondary surgical intervention excluding posterior capsulotomy". *e.* any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect. *Note: Refer to Section 11 for additional SAEs listing.*
Serious Public Health Threat	Any event type which results in imminent risk of death, serious deterioration in state of health, or serious illness that requires prompt remedial action. This would include: Events that are of significant and unexpected nature such that they become alarming as a potential public health hazard, eg,

	human immunodeficiency virus (HIV) or Creutzfeldt-Jacob Disease (CJD).
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
AAS	All-implanted analysis set
[redacted]	[redacted]
ACD	Anterior chamber depth
ADE	Adverse device effect
AE	Adverse event
AL	Axial length
ANSI	American National Standards Institute
AT LARA	AT LARA extended depth of focus IOL Model 829MP
[redacted]	[redacted]
BCDVA	Best corrected distance visual acuity
[redacted]	[redacted]
CI	Coordinating Investigator
CJD	Creutzfeldt-Jacob Disease
cm	Centimeter
CRF	Case report form
CTN	Clinical Trial Notification
D	Diopter
[redacted]	[redacted]
DFU	Directions for use
eCRF	Electronic case report form
EDC	Electronic data capture
EDF	Extended depth of focus
EN	European Standard
FDA	US Food and Drug Administration
FLACS	Femtosecond laser-assisted cataract surgery
GCP	Good Clinical Practice
GPCMS	Global Product Complaint System
HIV	Human immunodeficiency virus
IEC	Independent ethics committee
ICF	Informed consent form
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IOL	Intraocular lens
[redacted]	[redacted]
IOP	Intraocular pressure
IP	Investigational product
IRB	Institutional review board
IRT	Interactive response technology

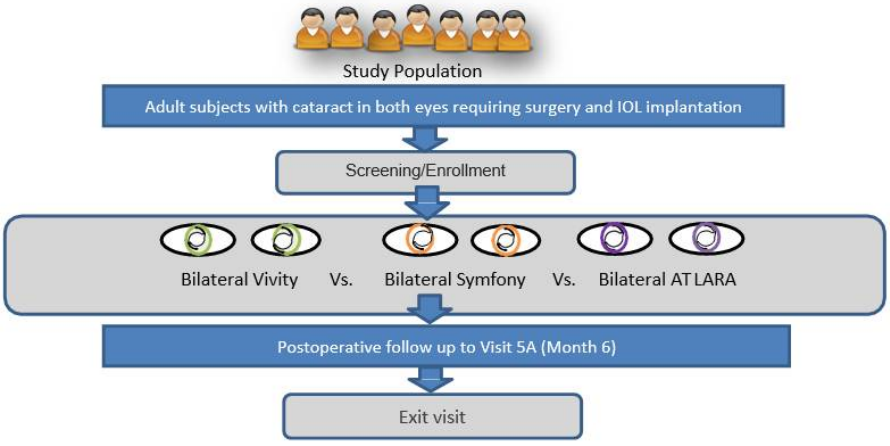
Abbreviation	Definition
ISO	International Organization for Standardization
LASIK	Laser-assisted in situ keratomileusis
[redacted]	[redacted]
m	Meter
mm	Millimeter
[redacted]	[redacted]
MTF	Modulation transfer function
N	Number of subjects
N/A	Not applicable
OD	Right eye
OS	Left eye
OVD	Ophthalmic viscosurgical device
PCO	Posterior capsular opacification
QUVID	Questionnaire for Visual Disturbances
RD	Retinal detachment
SADE	Serious adverse device effect
SAE	Serious adverse event
SN	Serial number
SOP	Standard operating procedures
SPH	Sphere
SSI	Secondary surgical intervention
SYMFONY	TECNIS Symfony Extended Range of Vision IOL Model ZXR00
[redacted]	[redacted]
US	United States
UV	Ultraviolet
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: ACRYSOF IQ VIVITY Extended Vision IOL **Model DFT015** Control Product: • TECNIS SYMFONY Extended Range of Vision IOL **Model ZXR00** • AT LARA extended depth of focus IOL **Model 829MP** *Note: Model number of device may be different if a pre-loaded delivery system is used. It should be verified by site staff that the IOL contained within matches the models listed above.*
Purpose and rationale	To compare the visual disturbance profile of ACRYSOF VIVITY Extended Vision IOL Model DFT015 with those of diffractive extended depth of focus IOLs.
Objective(s)	Primary: To demonstrate superiority of VIVITY over SYMFONY or over AT LARA for the proportion of subjects responding "not bothered at all" by halos on the QUVID questionnaire (Q2.3) at 3 months post-op Secondary: • To demonstrate superiority of VIVITY over SYMFONY or over AT LARA for the proportion of subjects responding "not bothered at all" by glare on the QUVID questionnaire (Q3.3) at 3 months post-op • To demonstrate superiority of VIVITY over SYMFONY or over AT LARA for the proportion of subjects responding "not bothered at all" by starbursts on the QUVID questionnaire (Q1.3) at 3 months post-op [redacted]

	Safety: • To assess safety parameters out to 6 months post-op
Endpoint(s)	Primary Effectiveness: • % of subjects not bothered at all by halos as assessed by QUVID Secondary Effectiveness • % of subjects not bothered at all by glare as assessed by QUVID • % of subjects not bothered at all by starbursts as assessed by QUVID [redacted] Safety: • Adverse events including SSIs • Device deficiencies

	• IOP (clinically significant change) • Slit-lamp exam findings • Dilated fundus exam findings • IOL observations • IOL tilt/decentration • Subjective PCO assessment • Posterior capsulotomy • Intraoperative surgical problems • Other procedures at surgery (combined and/or additional)
Assessment(s)	Effectiveness: • QUVID subject questionnaire to assess visual disturbances [redacted]

	Other Assessments: • [redacted] • Subjective manifest refraction • Biometry Safety: • Adverse events (including SSIs) • Device deficiencies • Surgical Problems/Other procedures at surgery • IOP • Slit-lamp exam • Dilated fundus exam • IOL Observations, IOL Position Change (tilt/decentration) • Subjective PCO assessment, Posterior Capsulotomy
Study design	Prospective, randomized, controlled, subject and assessor-masked, three-arm, parallel group, bilateral implant, 6-month follow-up trial of VIVITY vs. SYMFONY and AT LARA IOLs. 

Masking	☐ None ☒ Observer-Masked (Examiner conducting primary and secondary effectiveness assessments [redacted] ☒ Subject-Masked ☐ Double-Masked
Subject population	Adults (22 years and older) with cataract in both eyes requiring surgery with implantation of an intraocular lens in the capsular bag. Planned number of subjects enrolled/consented: 218 Planned number of randomized/treated/implanted subjects: 198 Planned number of evaluable completed subjects: 180 • 60 Bilateral VIVITY • 60 Bilateral SYMFONY • 60 Bilateral AT LARA
Key inclusion criteria	See Section 8.1 for a complete list of inclusion criteria
Key exclusion criteria	See Sections 8.2 and 8.3 for a complete list of exclusion criteria
Data analysis	In general, descriptive statistics will be generated using mean and two-sided 95% confidence interval, standard deviation, median, minimum, and maximum for quantitative variables and frequency and percentage for qualitative variables. Between-group comparisons for primary and secondary endpoint comparison will be conducted between the test product and each of the two comparators independently using a two sample test of proportions. [redacted].

Sample size justification	Approximately 218 subjects will be enrolled to achieve 180 subjects who complete the study. [redacted]
Key words	• Cataracts • Intraocular lens • IOL • Extended depth of focus • Presbyopia • Australia • New Zealand • Visual disturbances
[redacted]	[redacted]

Table 3–1 Schedule of Study Procedures and Assessments

Visit	Visit 0	Visit 00	Visit 1	Visit 2	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A[1]	Visit 5A	Unscheduled visit
Eye	Both Eyes	1st Eye	1st Eye	1st Eye	2nd Eye	2nd Eye	2nd Eye	Both Eyes	Both Eyes	Both Eyes	N/A
Day Number	Day -28 to 0	Day 0	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 7-21 Post Visit 00	Day 1-2 Post Visit 00A	Day 7-14 Post Visit 00A	Day 30-60 Post Visit 00A	Day 70-100 Post Visit 00A	Day 120-180 Post Visit 00A	N/A
General Assessments and Procedures											
Informed Consent	X										
Demographics	X										
Medical History	X										
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X
Inclusion/Exclusion	X										
Urine Pregnancy Test[2]	X										
Ophthalmic Assessments											
Questionnaires											
• QUVID (for visual disturbance)	X							X	X	X	
• [redacted]	[redacted]							[redacted]	[redacted]		
[redacted]								[redacted]	[redacted]		

Visit	Visit 0	Visit 00	Visit 1	Visit 2	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A[1]	Visit 5A	Unscheduled visit
Eye	Both Eyes	1st Eye	1st Eye	1st Eye	2nd Eye	2nd Eye	2nd Eye	Both Eyes	Both Eyes	Both Eyes	N/A
Day Number	Day -28 to 0	Day 0	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 7-21 Post Visit 00	Day 1-2 Post Visit 00A	Day 7-14 Post Visit 00A	Day 30-60 Post Visit 00A	Day 70-100 Post Visit 00A	Day 120-180 Post Visit 00A	N/A
[redacted]	[redacted]							[redacted]	[redacted]		
Biometry (collect all available measurements including ACD, AL, keratometry, corneal thickness, crystalline lens thickness, white-to-white)	X[3]								X		
Manifest Refraction	X			X			X	X	X	X	(✓)
[redacted]											
[redacted]									[redacted]		
[redacted]	[redacted]			[redacted]			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]									[redacted]		
[redacted]											
[redacted]									[redacted]		
[redacted]									[redacted]		

Visit	Visit 0	Visit 00	Visit 1	Visit 2	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A[1]	Visit 5A	Unscheduled visit
Eye	Both Eyes	1st Eye	1st Eye	1st Eye	2nd Eye	2nd Eye	2nd Eye	Both Eyes	Both Eyes	Both Eyes	N/A
Day Number	Day -28 to 0	Day 0	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 7-21 Post Visit 00	Day 1-2 Post Visit 00A	Day 7-14 Post Visit 00A	Day 30-60 Post Visit 00A	Day 70-100 Post Visit 00A	Day 120-180 Post Visit 00A	N/A
[redacted]											
[redacted]									[redacted]		
[redacted]									[redacted]		
[redacted]									[redacted]		
[redacted]									[redacted]		
[redacted]									[redacted]		
[redacted]										[redacted]	
Slit-lamp Examination											
• Observations	X[3]		U	U		U	U	U	U	U	U(✓)
• IOL Position change (tilt/decentration)			U	U		U	U	U	U	U	U(✓)
IOP	X[3]		X	X		X	X	X	X	X	(✓)

Printed By:

Print Date:

Visit	Visit 0	Visit 00	Visit 1	Visit 2	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A[1]	Visit 5A	Unscheduled visit
Eye	**Both Eyes**	**1st Eye**	**1st Eye**	**1st Eye**	**2nd Eye**	**2nd Eye**	**2nd Eye**	**Both Eyes**	**Both Eyes**	**Both Eyes**	**N/A**
Day Number	**Day -28 to 0**	**Day 0**	**Day 1-2** Post Visit 00	**Day 7-14** Post Visit 00	**Day 7-21** Post Visit 00	**Day 1-2** Post Visit 00A	**Day 7-14** Post Visit 00A	**Day 30-60** Post Visit 00A	**Day 70-100** Post Visit 00A	**Day 120-180** Post Visit 00A	**N/A**
Dilated Fundus Examination	X[3]										U(✓)
Surgical Procedures & Assessments											
Determination of 1st Operative Eye	X										
IOL Power Calculations (all 3 IOLs, for both eyes)	X										
[redacted]	[redacted]										
Randomization		U									
Treatment		U			U						
IOL Information (Power, Model, SN)		U			U						
Problems During Surgery		U			U						

Visit	Visit 0	Visit 00	Visit 1	Visit 2	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A[1]	Visit 5A	Unscheduled visit
Eye	Both Eyes	1st Eye	1st Eye	1st Eye	2nd Eye	2nd Eye	2nd Eye	Both Eyes	Both Eyes	Both Eyes	N/A
Day Number	Day -28 to 0	Day 0	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 7-21 Post Visit 00	Day 1-2 Post Visit 00A	Day 7-14 Post Visit 00A	Day 30-60 Post Visit 00A	Day 70-100 Post Visit 00A	Day 120-180 Post Visit 00A	N/A
Other Surgical Procedures		U			U						
PCO and Posterior Capsulotomy			U	U		U	U	U	U	U	U(✓)
Adverse Events & Device Deficiencies											
AEs[5]	X	X	X	X	X	X	X	X	X	X	X
Device Deficiencies		X	X	X	X	X	X	X	X	X	X
Other											
Exit Form	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	X	(✓)

[redacted]

(✓) assessment performed as necessary

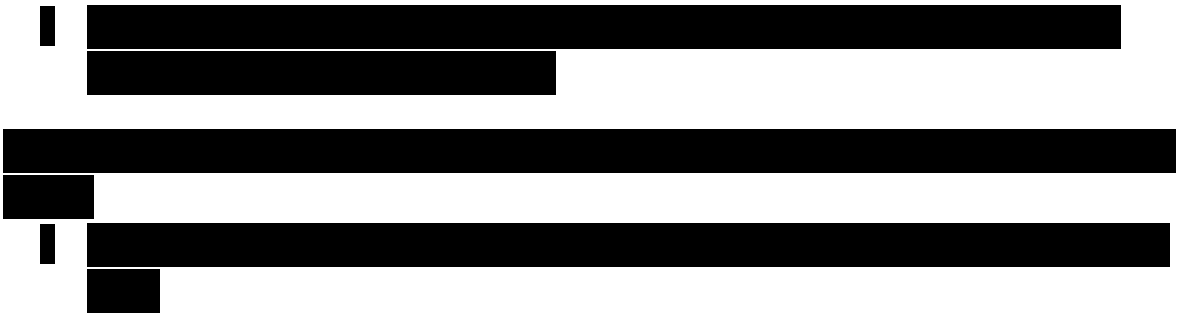
[redacted]

5. Collected from time of consent onward.

4 PROTOCOL AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments must be created by the Study Sponsor and must be approved by the IRB/IEC and global and regional Health Authorities, as applicable, prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all subjects currently enrolled in the study must sign the approved, revised informed consent (re-consent), as required by the IRB/IEC.



5 INTRODUCTION

5.1 Rationale and Background

Depth of focus is the amount of image displacement behind a lens that does not degrade the perceived image quality or in other words, the tolerance of the eye to retinal defocus (Wang 2006). Larger depth of focus allows sharp images of closer objects. A young, healthy human eye allows objects proximal to optical infinity to be in focus due to the accommodative power change; where as a pseudophakic eye with no accommodation must rely on the optical system's depth of focus to achieve a desired range of vision. While subjects implanted with a monofocal IOL with negligible residual refractive error can experience good distance vision, quality of vision at intermediate and near is often insufficient to support activities of daily living without the use of spectacles. Premium IOL solutions, such as diffractive multifocal IOLs, can provide good intermediate and/or near vision, but can also result in complaints of visual disturbances. In view of this, there exists a medical need to provide functional vision at intermediate and near distances, while maintaining good distance vision and a visual disturbance profile similar to that of a monofocal IOL. Extended depth of focus IOLs are intended to address this need.

ANSI Z80.35 2018 defines EDF IOLs as those IOLs "whose function is the correction of aphakia, with extended range of focus above a defined functional visual acuity threshold to provide useful distance and intermediate vision with monotonically decreasing visual acuity from the best distance focal point." EDF can be achieved by different optical mechanisms including diffractive optics; as is the case for both SYMFONY and AT LARA. While this optical approach has been shown to offer an extended range of vision, patients still experience bothersome visual disturbances at a higher rate than with a monofocal IOL (Symfony SSED 2016).

The VIVITY IOL incorporates a non-diffractive approach to extend the depth of focus and provide improved, intermediate and near vision while maintaining distance vision and a visual disturbance profile similar to that of an aspheric monofocal IOL (CSR for ILI875-C002 2019). The non-diffractive wavefront shaping optic is on the anterior surface of the VIVITY IOL. [redacted]. The combination of the central zone and the outer annular zone transfers enough distance MTF (modulation transfer function) under photopic conditions to provide a continuous range of extended vision. The distance MTF

increases with a larger aperture to improve distance contrast in dim light. VIVITY provides an additional benefit by not using diffractive structures that typically induce visual disturbances.

5.2 Purpose of the Study

This postmarket study is intended to support scientific messaging and to compare the visual disturbance profile of the non-diffractive VIVITY IOL to two marketed diffractive EDF IOLs, SYMFONY and AT LARA.

[redacted]

Results of the study are intended for publication and presentation at ophthalmology conferences globally.

5.3 Risks and Benefits

5.3.1 Known and Potential Risks

Surgical Risk

Complications may occur on the surgery day or throughout the postoperative period. As with any type of intraocular surgery, there is a possibility of complications due to anesthesia, drug reactions, and surgical problems. [redacted]

[redacted]

[redacted]

[redacted]

5.3.2 Potential Benefits

Extended depth of focus (EDF) IOLs offer increased depth of focus across a continuous range of vision to the recipient. Additionally, EDF IOLs have been designed to address key areas of patient dissatisfaction with multifocal IOLs: increased prevalence of photopic phenomena (eg, halos and glare) and lower contrast sensitivity (Rocha 2017, Kondylis 2019).

The VIVITY IOL is a new foldable capsular bag/posterior chamber implanted lens that is indicated to replace the cataractous human lens and correct aphakia with the advantage of providing good distance vision and improved intermediate and near vision without inducing visual disturbances over a monofocal IOL.

6 STUDY OBJECTIVES

6.1 Primary Objective

Table 6–1 Primary Objective

Objective	Endpoint
• To demonstrate superiority of VIVITY over SYMFONY or over AT LARA for the proportion of subjects responding "not bothered at all" by halos on the QUVID questionnaire (Q2.3) at 3 months post-op.	• % of subjects not bothered at all by halos (QUVID)

6.2 Secondary Objectives

Table 6–2 Secondary Objectives

Objectives	Endpoints
• To demonstrate superiority of VIVITY over SYMFONY or over AT LARA for the proportion of subjects responding "not bothered at all" by glare on the QUVID questionnaire (Q3.3) at 3 months post-op.	• % of subjects not bothered at all by glare (QUVID)
• To demonstrate superiority of VIVITY over SYMFONY or over AT LARA for the proportion of subjects responding "not bothered at all" by starbursts on the QUVID questionnaire (Q1.3) at 3 months post-op.	• % of subjects not bothered at all by starbursts (QUVID)

[redacted]

[redacted] [redacted]

[redacted]	[redacted]
[redacted]	[redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted]) [redacted] [redacted]

Objectives	Endpoints
	[redacted]

6.4 Safety Objectives

Table 6–4 Safety Objective

Objective	Endpoints
• To assess safety parameters out to 6 months post-op.	• Adverse events (including SSIs) • Device deficiencies • IOP (clinically significant change) • Slit-lamp exam findings • Dilated fundus exam findings • IOL observations including IOL tilt/decentration • Subjective PCO assessment • Posterior capsulotomy • Intraoperative surgical problems • Other procedures at surgery (combined and/or additional)

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, multi-center, randomized, parallel-group, controlled, assessor- and subject-masked study. Both eyes of a subject must require cataract surgery to qualify for enrollment into this study. To reduce bias, subjects will be randomly assigned in a 1:1:1 ratio

to receive either VIVITY Extended Vision IOL Model DFT015 (test article) or SYMFONY Extended Range of Vision IOL Model ZXR00 (control article), or AT LARA extended depth of focus IOL Model 829MP (control article) in both eyes. *Note: Model number of control devices may be different if a pre-loaded delivery system is used. It should be verified by site staff that the IOL contained within matches the models listed above.*

To further reduce bias, all subjects and site assessors will be masked to subject treatment assignment until the end of the study.

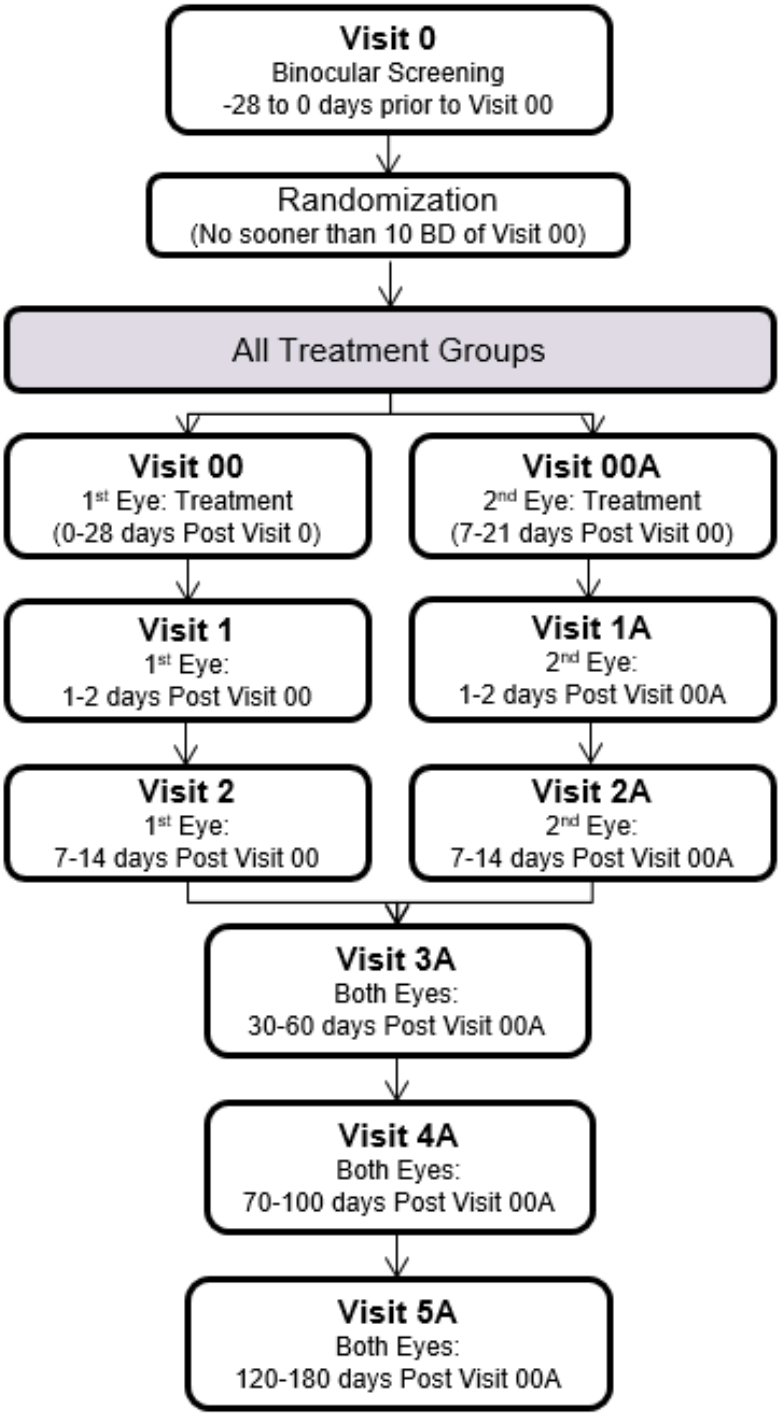
The first operative eye is defined as the eye with the **worse BCDVA**. If the BCDVA is the same in both eyes, the right eye (OD) will be the first operative eye. The second eye implant must occur within 7-21 days of the first eye implant.

A total of 10 scheduled visits are planned and subject participation is expected to last 6-7 months. The visits include a Screening visit (Visit 0), 2 operative visits (Visit 00 and Visit 00A), and 7 postoperative visits at the following intervals: Day 1-2 (Visit 1/1A), Day 7-14 (Visit2/2A), Day 30-60 (Visit 3A), Day 70-100 (Visit 4A), and Day 120-180 (Visit 5A); see Figure 7-1, Study Design.

[redacted]

[redacted]

Figure 7–1 Study Design Diagram



7.2 Rationale for Study Design

To reduce bias this study was designed as a prospective, randomized, subject- and assessor-masked study. The study IOLs are being used under approved indications for the intended population. Test procedures and inclusion/exclusion criteria will be standardized across the multiple sites and common Investigator training will be conducted.

[redacted]

7.3 Rationale for Duration of Treatment/Follow-Up

By 3 months post-op, refractions have typically stabilized; however, subjects will be followed for 6 months total in order to gather comprehensive effectiveness and safety data.

7.4 Rationale for Choice of Control Product

The comparator products, SYMFONY and AT LARA, are marketed EDF lenses in Australia and New Zealand.

7.5 Data Monitoring Committee

Not applicable.

8 STUDY POPULATION

The study population consists of male and female subjects (age 22 years and older) with a diagnosis of cataract requiring extraction. Approximately 218 subjects will be enrolled (consented) at up to 14 sites in Australia and New Zealand, with a target of 9-24 subjects per site. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 6 months.

It is expected that at least 198 subjects will be randomized and at least 180 subjects will complete the study as follows:

- 60 bilaterally implanted with VIVITY
- 60 bilaterally implanted with SYMFONY
- 60 bilaterally implanted with AT LARA

This accounts for a 10% screen failure rate and a 10% rate of subjects who are not bilaterally implanted with the study IOLs or are lost to follow-up.

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:

Note: When criteria are ocular, both eyes must meet criteria.

1.	Adults, at least 22 years of age or older at the time of screening, of either gender, diagnosed with cataract in both eyes.
2.	Planned cataract removal by routine small incision surgery.
3.	Willing and able to complete all required postoperative visits.
4.	Able to comprehend, read and write English and willing to sign an IRB/IEC approved statement of informed consent.
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

8.2 Exclusion Criteria

Subjects fulfilling **any** of the following criteria (holistically or in either eye) are not eligible for participation in this study.

1.	Women of childbearing potential, defined as all women who are physiologically capable of becoming pregnant and who are not postmenopausal for at least 1 year or are less than 6 weeks since sterilization, are excluded from participation if any of the following apply: a. they are currently pregnant, b. have a positive urine pregnancy test result at Screening, c. intend to become pregnant during the study period, d. are breast-feeding. [redacted]
2.	Any disease or pathology, other than cataract, that (in the expert opinion of the Investigator) is expected to reduce the potential postoperative best corrected distance visual acuity [redacted]
[redacted]	[redacted]
[redacted]	[redacted]

	[redacted]
5.	Clinically significant ocular trauma or ocular surface disease that would affect study measurements based on Investigator expert medical opinion.
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
13.	Patients who desire monovision correction.

[redacted]

[redacted]

[redacted]

8.4 Rescreening of Subjects

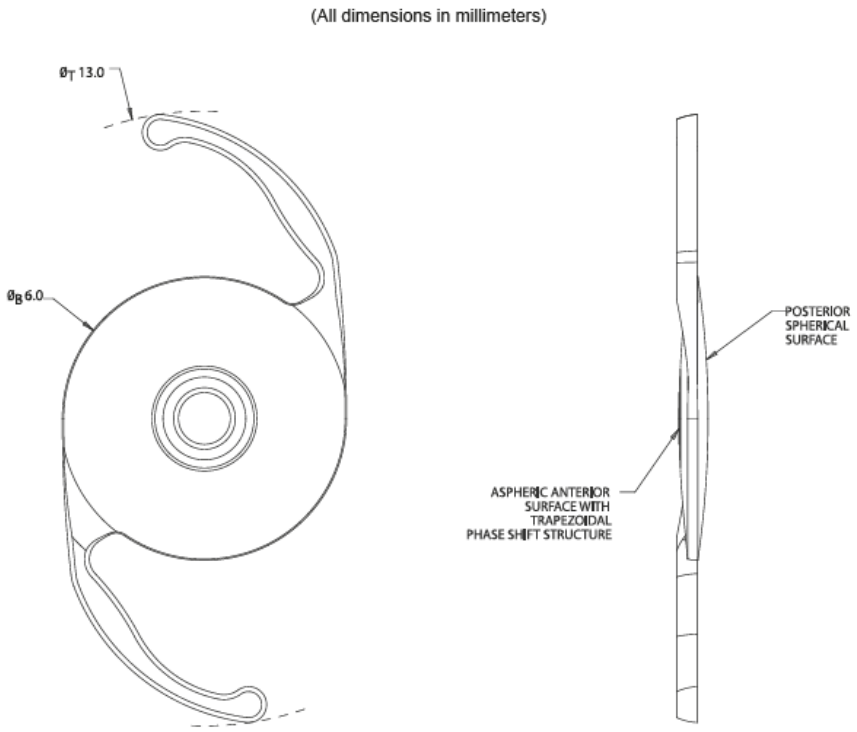
Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s):	ACRYSOF IQ VIVITY Extended Vision IOL Model DFT015
Control Product(s) (If applicable):	TECNIS SYMFONY Extended Range of Vision IOL Model ZXR00
	AT LARA extended depth of focus IOL Model 829MP

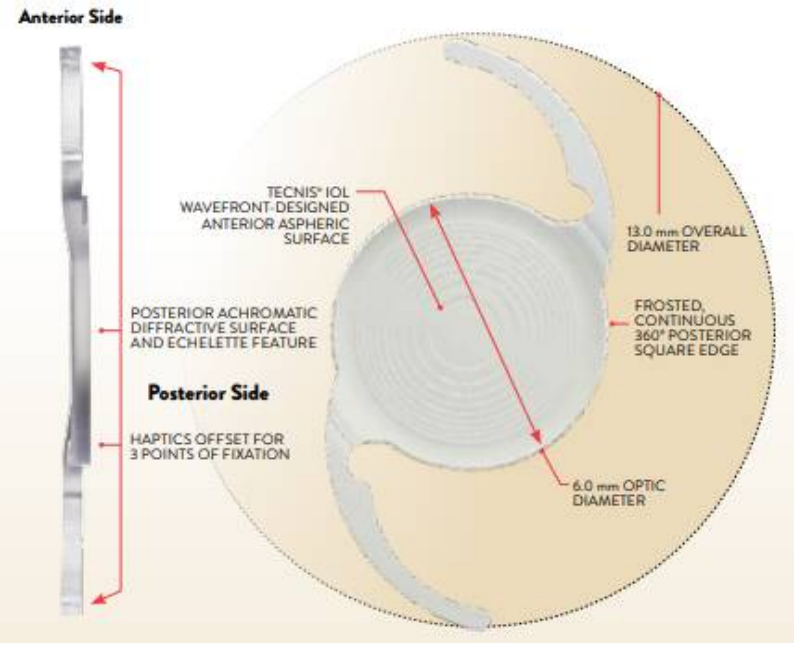
Table 9–1 Test Product

Test Product	ACRYSOF IQ VIVITY Extended Vision IOL Model DFT015 
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	The VIVITY IOL is intended for primary implantation for the visual correction of aphakia in adult patients with < 1.00 D of preoperative corneal astigmatism, in whom a cataractous lens has been removed by extracapsular cataract extraction. The VIVITY IOL is intended for capsular bag placement only. It is also indicated for refractive lens exchange.

Product description and parameters available for this study	• Optic Type: Biconvex wavefront focusing optic • Optics Material: Ultraviolet and blue light filtering Hydrophobic Acrylate/ Methacrylate Copolymer • Optic Powers: 15.0 to 25.0 D in 0.5 D steps • Index of Refraction: 1.55 • Haptic Configuration: STABLEFORCE™ Modified L-Haptics • Haptic Material: Ultraviolet and blue light filtering Hydrophobic Acrylate/ Methacrylate Copolymer (Boettner 1962) • Optic Diameter (mm): 6.0 • Overall Length (mm): 13.0 • Haptic Angle: 0°
Formulation	N/A
Usage	IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject.
Packaging description	Each IOL will be individually packaged and will have a unique serial number. The IOL package will contain the following items: • The IOL • A subject registration card (Lens Implant Card) • A subject identification card • Adhesive labels containing the IOL information and unique serial number • Directions on where to find the electronic package insert containing directions for product use
Labeling description	The test article will be supplied in a standard Alcon IOL carton. The carton is labeled with the following information: name of the lens, model number, overall diameter, optic diameter, diopter power, serial number, name of the manufacturer, storage conditions, expiration date, sterile, and single use. Each package is also labeled with the clinical protocol number.

Storage conditions	Refer to product Directions For Use. The VIVITY consignment provided for the study must be stored in a safe, secure location with limited access separated from general stock. Transportation of product from one address to another must be documented and a Transportation Log (or similar documentation) utilized for appropriate accountability.
Additional information	N/A
Supply	The Sponsor will provide a consignment of test articles to each investigative site. The Investigator is responsible for maintaining the consignment, ensuring that an adequate number of IOLs are available in each dioptric power. To obtain additional IOLs, the Investigator must contact the Sponsor.

Table 9–2 Control Product Model ZXR00

Control Product(s)	TECNIS SYMFONY Extended Range of Vision IOL Model ZXR00 

Manufacturer	Johnson & Johnson Vision 1700 East St. Andrew Place Santa Ana, California 92705 USA
Indication for Use	The SYMFONY IOL is indicated for primary implantation for the visual correction of aphakia, in adult patients with less than 1.0 D of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near VA, while maintaining comparable distance VA.
Product description and parameters available for this study	• Optic Type: Biconvex aspheric optic • Optics Material: Optically clear, soft foldable, UV-blocking hydrophobic acrylic • Optic Powers: For study purposes, limited to 15.0 to 25.0 D in 0.5 D steps • Index of Refraction: 1.47 • Haptic Configuration: TRI-FIX design, haptics offset from optic, one-piece lens • Haptic Material: Soft foldable, UV-blocking hydrophobic acrylic • Haptic Color: Clear • Optic Diameter (mm): 6.0 • Overall Length (mm): 13.0 • Haptic Angle: No angulation but offset from optic body
Formulation	N/A
Usage	IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject.

Packaging description	Each IOL will be individually packaged in manufacturer's packaging and will have a unique serial number. The IOL package will contain the following items: • The IOL • A subject registration card (Lens Implant Card) • A subject identification card • Adhesive labels containing the IOL information and unique serial number • A package insert containing directions for use
Labeling description	This control article will be supplied in a standard Johnson & Johnson Vision IOL carton. The carton is labeled with the following information: name of the lens, model number, overall diameter, optic diameter, diopter power, serial number, name of the manufacture, storage condition, expiration date, sterile, and single use.
Storage conditions	Refer to product Directions For Use. Once an IOL is designated for study use, it is considered IP and must be stored in a safe, secure location with limited access separated from general stock. Transportation of product from one address to another must be documented and a Transportation Log (or similar documentation) utilized for appropriate accountability.
Additional identifying information	N/A
Supply	The Investigator will procure this control product. [redacted].

Table 9–3 Control Product Model 829MP

Control Product(s)	AT LARA extended depth of focus IOL Model 829MP 
Manufacturer	Carl Zeiss Meditec AG Göschwitzer Straße 51-52 07745 Jena Germany
Indication for Use	The AT LARA IOL is indicated for implantation for the visual correction of aphakia in patients with and without presbyopia in whom a cataractous lens has been removed by extracapsular cataract extraction, and aphakia following refractive lensectomy in presbyopic patients.

Product description and parameters available for this study	• Optic Type: Diffractive aspheric • Optics Material: Hydrophilic acrylic (25%) water content with hydrophobic surface properties • Optic Powers: For study purposes, limited to 15.0 to 25.0 D in 0.5 D steps • Index of Refraction: 1.49 • Haptic Configuration: 4-haptic • Haptic Material: Hydrophilic acrylic (25%) water content with hydrophobic surface properties • Haptic Color: Clear • Optic Diameter (mm): 6.0 • Overall Length (mm): 11.0 • Haptic Angle: 0^{o} plate haptic
Formulation	N/A
Usage	IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject.
Packaging description	Each IOL will be individually packaged in manufacturer's packaging and will have a unique serial number. The IOL package will contain the following items: • The IOL • A subject registration card (Lens Implant Card) • A subject identification card • Adhesive labels containing the IOL information and unique serial number • A package insert containing directions for use
Labeling description	This control article will be supplied in a standard Zeiss IOL carton. The carton is labeled with the following information: name of the lens, model number, overall diameter, optic diameter, diopter power, serial number, name of the manufacture, storage condition, expiration date, sterile, and single use.

Storage conditions	Refer to product Directions For Use. Once an IOL is designated for study use, it is considered IP and must be stored in a safe, secure location with limited access separated from general stock. Transportation of product from one address to another must be documented and a Transportation Log (or similar documentation) utilized for appropriate accountability.
Additional identifying information	N/A
Supply	The Investigator will procure this control product. [redacted]

[redacted]

[redacted]

9.3 Treatment Administration

Subjects will be randomized to treatment group prior to surgery, no sooner than 10 business days prior to Visit 00. The lens to which the subject is randomized, must be implanted in both eyes. [redacted]

Each study surgeon will follow his/her **routine** cataract procedure for all study surgeries. It is permitted to have 1 study-trained surgeon at each site perform IOL implantations. For surgeons with experience prior to the start of the trial, femtosecond laser-assisted cataract surgery (FLACS) is permitted, however it is **NOT** required. The laser may **ONLY** be used for the following:

- Primary and sideport incisions
- Capsulorhexis
- Lens fragmentation

Use of any intraoperative power assessment is not permitted during surgery.

9.4 Treatment Assignment / Randomization

Subjects will be randomized in a 1:1:1 ratio to receive treatment with the VIVITY or the SYMFONY or the AT LARA IOLs.

Only after signing the ICF, will a subject be assigned a subject number by the electronic data capture system.

A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the IRT system. The randomization list will be generated and maintained by the Study Sponsor.

No sooner than 10 business days of Visit 00, each eligible subject will be randomized via the IRT system to one of the treatment arms. The Investigator or unmasked delegate will access the respective system after confirming that the subject meets all the eligibility criteria. A randomization number will be automatically assigned to the subject according to the subject randomization list but will not be communicated to the site user. The IRT system will inform the site user of the treatment assignment.

9.5 Treatment Masking

This study is double-masked (effectiveness assessor and subject) with subjects randomized for bilateral implantation with one of the three studied IOLs.

The effectiveness assessor and subject masking will be maintained throughout the conduct of the study until all study data is validated and final database lock occurs. [redacted]

[redacted]

[redacted]

9.6 Accountability Procedures

Upon receipt of test article from the Sponsor, the Investigator or delegate must conduct an inventory of all lenses by serial number, complete study-specific confirmation of receipt procedures [redacted] and retain any required documentation in the Investigator's clinical study records.

For all IP (test and control articles) the Investigator or delegate must maintain records of use and implantation for each subject throughout the study. [redacted]

Return to the Study Sponsor recoverable test articles associated with a device deficiency. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies [redacted]

At the conclusion of the study, the Investigator will be responsible for returning all used and unused study supplies (including test and control articles) as instructed by the Sponsor. [redacted]

9.7 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 (include herbal therapies, vitamins, and all over-the-counter as well as prescription medications).

  Note: Throughout the subject's participation, obtain information on any changes in medical health and/or the use of concomitant 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

The following section outlines the assessments performed in this clinical study. The Investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified site personnel.

Assessments [redacted] are outlined in Table 3–1, Schedule of Study Procedures and Assessments.

During the course of the study, it is possible that the window of visits may overlap; in such cases the subject may complete both visits on the same day at the discretion of the Investigator (and the data would be entered for each respective visit in EDC).

10.1 Informed Consent and Screening

The Investigator or delegate must explain the purpose and nature of the study, and have the subject or legally authorized representative 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. (Note that data from exams and assessments specified in Section 10.2.1 that were completed within 30 days of screening can be used as per discretion of Investigator.)

Additionally, the individual obtaining consent from the subject and a witness, if applicable, must sign and date the informed consent document. The subject should be provided with

enough time for his/her decision on participation in the study, and should have options to discuss with his/her family members or relatives about the participation in the investigation.

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. Note that the applicable privacy regulation requirements must be met.

10.2 Visits and Examinations

Data from the Investigator's previous routine clinical evaluation (ie, slit-lamp examination, dilated fundus examination, IOP, biometry and keratometry) may fulfill Visit 0 requirements, if the data comply with the following:

1. meet the conditions of this protocol [redacted]
2. apply for all 3 IOLs being tested; and
3. were collected within 30 days of screening.

10.2.1 Visit 0: Preoperative Screening Visit (-28 - 0 Days Prior to Visit 00)

1. After the subject signs the consent, assess **inclusion/exclusion criteria**. The subject must meet all inclusion criteria and must not meet any exclusion criteria prior to surgery.
2. Obtain the subject's **demographic** information (including age, race and sex), **medical/ocular history** within 30 days prior to signing the ICF, and **concomitant medications** for ocular and non-ocular conditions used by the subject at the time of the visit.
3. Perform a **urine pregnancy** test, IF the subject is a woman of childbearing potential (defined as all women who are physiologically capable of becoming pregnant and who are not postmenopausal for at least 1 year or are less than 6 weeks since sterilization).
4. Adjust room to **photopic lighting** for distance (4 m).
5. Perform **manifest refraction** (OD, OS).
6. Measure and record monocular **BCDVA** at 4 m (OD, OS).
7. Measure optical **keratometry** and optical **biometry** according to the Investigator's standard of care noting all available measurements including corneal thickness, crystalline lens thickness, white-to-white, anterior chamber depth (ACD) and axial length (AL).

[redacted]

8. **Select and document** the subject's required lens power for each of the 3 IOLs (VIVITY, SYMFONY and AT LARA). [redacted].

[redacted]

9. Perform **slit-lamp examination** of the anterior segment of both eyes. [redacted]

10. Subject **questionnaires** completed: QUVID [redacted]

[redacted]

13. Perform a **dilated fundus** examination of both eyes. *Note: if this exam was completed on this subject ≤ 30 days prior to the date of screening that data may be used (per the Investigator's discretion) and this test is not required to be repeated.*

14. Record any **adverse events**.

15. Ensure that all inclusion/exclusion criteria have been met and that all preoperative screening assessments have been performed. Upon meeting eligibility criteria, subjects will be scheduled for surgery.

NOTE: The eye with the worse BCDVA will be the first eye implanted. If the distance BCDVA in both eyes is the same, the right eye (OD) will be implanted first.

10.2.2 Visit 00: Surgery Visit 1st Eye (0-28 days after Visit 0)

1. In preparation for the operative visit, randomize the subject. It is recommended that subjects are contacted prior to randomization to 1) confirm willingness to continue trial participation, and 2) confirm scheduled surgical date and time.

[redacted].

2. Record **operative eye.**
3. Record changes in **medical/ocular history** and **concomitant medications for** ocular and non-ocular **conditions**.
4. Verify **inclusion/exclusion criteria**. Subjects must meet all requirements to proceed to surgery.
5. Prepare subject for surgery in accordance to site specific operating procedures and ensure that all IOL power calculations have been completed.
6. Perform **surgery** and **implantation** with the IOL to which the subject was randomized.
7. Record any surgical problems, complications, or other procedures (including SSIs) that occurred during surgery. Other procedures include those performed outside of routine cataract surgery. **Other planned procedures at the time of surgery are exclusionary**.
8. Record **final incision size**.
9. Record **lens information** that is located on the IOL sticker. Both successful and aborted (if applicable) test and control article information should be recorded.
10. Assess if any **IOL damage** has occurred. If an IOL is damaged/defective and not implanted, it must be returned to the respective manufacturer as a **device deficiency**.
11. Record any **surgical problems**, **complications** or **secondary surgical interventions** for the operative eye, if applicable.
12. Record any **adverse events**.
13. Record any **device deficiencies**.

10.2.3 Visit 1: Postoperative for 1st Eye (1-2 days after Visit 00)

1. Record changes in **medical/ocular history** and **concomitant medications** for ocular and non-ocular conditions.
2. Perform **slit-lamp examination** of the anterior segment. *Note that only unmasked site staff can perform slit-lamp exam.*
3. Record **IOL observations**, if any.
4. Record **lens decentration and/or tilt**, if applicable.

5. Record **subjective posterior capsule opacification** and information for any **posterior capsulotomy** that has occurred since surgery, if applicable for operative eye.
6. Perform **tonometry** to measure the intraocular pressure.
7. Record **secondary surgical interventions** that have occurred since surgery, if applicable.
8. Record any **adverse events**.
9. Record any **device deficiencies**, if applicable.

10.2.4 Visit 2: Postoperative for 1st Eye (7-14 days after Visit 00)

1. Record changes in **medical/ocular history** and **concomitant medications** for ocular and non-ocular conditions.
2. Adjust room to **photopic lighting for distance** at 4 m.
3. Perform **manifest refraction** at 4 m.

[redacted]

5. Perform **slit-lamp examination** of the anterior segment. [redacted]
6. Record **IOL observations**, if any.
7. Record **lens decentration and /or tilt**, if applicable.
8. Record **subjective posterior capsule opacification** and information for any **posterior capsulotomy** that has occurred since surgery, if applicable for operative eye.
9. Perform **tonometry** to measure the intraocular pressure.
10. Record **secondary surgical interventions** that have occurred since surgery, if applicable.
11. Record any **adverse events** (both volunteered and elicited).
12. Record any **device deficiencies**, if applicable.

10.2.5 Visit 00A: Surgery Visit 2nd Eye (7-21 days after Visit 00)

Follow all procedures listed in Section 10.2.2, starting with Step 2, for the 2nd operative eye.

10.2.6 Visit 1A: Postoperative for 2nd Eye (1-2 days after Visit 00A)

Follow all procedures listed in Section 10.2.3 for the 2nd operative eye.

10.2.7 Visit 2A: Postoperative for 2nd Eye (7-14 days after Visit 00A)

Follow all procedures listed in Section 10.2.4 for the 2nd operative eye.

10.2.8 Visit 3A: Postoperative for Both Eyes (30-60 days after Visit 00A)

1. Subject **questionnaires** completed: QUVID, [redacted].
2. Record changes in **medical/ocular history** and **concomitant medications** for ocular and non-ocular conditions.
3. Adjust room to **photopic lighting for distance** at 4 m.
4. Perform **manifest refraction** at 4 m for each eye.

[redacted]

[redacted]

7. Perform **slit-lamp examination** of the anterior segment. *Note that only unmasked site staff can perform slit-lamp exam.*
8. Record **IOL observations**, if any.
9. Record **lens decentration and /or tilt**, if applicable.
10. Record **subjective posterior capsule opacification** and information for any **posterior capsulotomy** that has occurred since surgery, if applicable.
11. Perform **tonometry** to measure the intraocular pressure.
12. Record **secondary surgical interventions** that have occurred since surgery, if applicable.
13. Record any **adverse events** (both volunteered and elicited).
14. Record any **device deficiencies**, if applicable.

10.2.9 Visit 4A: Postoperative for Both Eyes (70-100 days after Visit 00A)

Note: Due to the large number of assessments and exams indicated for this visit the subject may be allowed to complete Visit 4A in two sessions (both occurring between 70-100 days after Visit 00A).

1. Subject **questionnaires** completed: QUVID, [redacted].
2. Record changes in **medical/ocular history** and **concomitant medications** for ocular and non-ocular conditions

[redacted]

[redacted]

6. Perform **manifest refraction** at 4 m. [redacted].

[redacted]

17. Measure optical **keratometry** and optical **biometry** according to the Investigator's standard of care noting all available measurements including anterior chamber depth (ACD) and axial length (AL), corneal thickness, crystalline lens thickness and white-to-white.
18. Perform **slit-lamp examination** of the anterior segment. *Note that only unmasked site staff can perform slit-lamp exam.*
19. Record **IOL observations**, if any.
20. Record **lens decentration and /or tilt**, if applicable.
21. Record **subjective posterior capsule opacification** and information for any **posterior capsulotomy** that has occurred since surgery, if applicable.
22. Perform **tonometry** to measure the intraocular pressure.
23. Record **secondary surgical interventions** that have occurred since surgery, if applicable.
24. Record any **adverse events** (both volunteered and elicited).
25. Record any **device deficiencies**, if applicable.

10.2.10 Visit 5A: Postoperative for Both Eyes (120-180 days after Visit 00A)

1. Subject **questionnaire** completed: QUVID.
2. Record changes in **medical/ocular history** and **concomitant medications** for ocular and non-ocular conditions.
3. Adjust room to **photopic lighting for distance** at 4 m.
4. Perform **manifest refraction** at 4 m.

[redacted]

7. Perform **slit-lamp examination** of the anterior segment. [redacted]
8. Record **IOL observations**, if any.
9. Record **lens decentration and /or tilt**, if applicable.
10. Record **subjective posterior capsule opacification** and information for any **posterior capsulotomy** that has occurred since surgery, if applicable.
11. Perform **tonometry** to measure the intraocular pressure.
12. Record **secondary surgical interventions** that have occurred since surgery, if applicable.
13. Record any **adverse events** (both volunteered and elicited).
14. Record any **device deficiencies**, if applicable.

10.2.11 Unscheduled Visits

If a subject is examined more than once during any of the scheduled follow-up periods, or between scheduled follow-up periods due to a potential issue, an unscheduled visit form should be completed, reporting any study parameters or any relevant data collected at this visit. If, during the visits specific for the second eye, a clinical observation is made on the first eye implanted, an unscheduled visit form should be completed to record the first eye data. The following exams and assessments are recommended and should be completed as per the Investigator's expert opinion; in the event this is not possible, the data that is available should be reported.

1. Record changes in **medical/ocular history** and **concomitant medications** for ocular and non-ocular conditions.
2. Perform **manifest refraction** at 4 m.

[redacted]

4. Perform **slit-lamp examination** of the anterior segment of both eyes. *Note that only unmasked site staff can perform slit-lamp exam except in cases of medical emergency.*
5. Record **IOL observations**, if any for the operative eye(s).
6. Record **lens decentration and/or tilt**, if applicable.
7. Record **subjective posterior capsule opacification** and information for any **posterior capsulotomy** that has occurred since surgery, if applicable for operative eye(s).
8. Perform **tonometry** to measure the intraocular pressure of both eyes.
9. Perform a **dilated fundus** examination of both eyes.
10. Record **secondary surgical interventions** for the operative eye(s) that have occurred since surgery, if applicable.
11. Record any **adverse events** (both volunteered and elicited).
12. Record any **device deficiencies**, if applicable.

[redacted]

10.3 Discontinued Subjects

10.3.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent and prior to randomization are considered screen failures. The Investigator must document the reason for screen failure in the subject's case history source documents.

Subject numbers must not be re-used.

10.3.2 Discontinuations

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

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.

If a subject discontinues from study treatment, every effort must be made to keep the subject in the study and to continue with the study assessments as specified in the schedule of study procedures and assessments until the final visit.

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

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

10.3.3 Schedule of Procedures and Assessments for Subjects Discontinued from Investigational Product

Subjects who discontinue IP (ie, have study lens explanted), will continue in the study through Visit 5A and be followed for safety. At minimum, safety examinations must include the assessments associated with appropriate medical care. Standard post-surgical assessments are bulleted below:

- UCDVA and/or BCDVA
- Slit-lamp Examination
- Dilated Fundus Examination

10.3.4 Subject Lost to Follow Up

If a subject unavoidably misses a scheduled exam, he/she should be rescheduled within the same exam period. The investigational site should show diligence in trying to schedule the subject for all exams. The site must document all attempts to contact the subject in the subject's chart, including dates, times, method of contact, etc. If a subject is unable to return for the Final Study Visit, the Exit Case Report Form should be completed with the

appropriate reason for discontinuation indicated. If attempts to contact the subject are unsuccessful, then the Exit Case Report Form for that subject is completed after the last window closes and documented as Lost to Follow-up. The date at which the subject was considered lost to follow-up should also be recorded.

[redacted]

10.5 Clinical Study Termination

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

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

- The Study Sponsor must:
    - Immediately notify the Investigator(s) and subsequently provide instructions for study termination.
    - Inform the Investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension.
- The Investigator must:
    - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
    - Provide subjects with recommendations for post-study treatment options as needed.

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

10.5.1 Follow-up of subjects after study participation has ended

Following this study, the subject will return to their eye care professional for their routine eye care.

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 General Information

Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent, regardless of subject enrollment status (screen failure or randomized.

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 test article. Refer to the Glossary of Terms for categories of AEs and SAEs.

Figure 11–1 Categorization of All Adverse Events

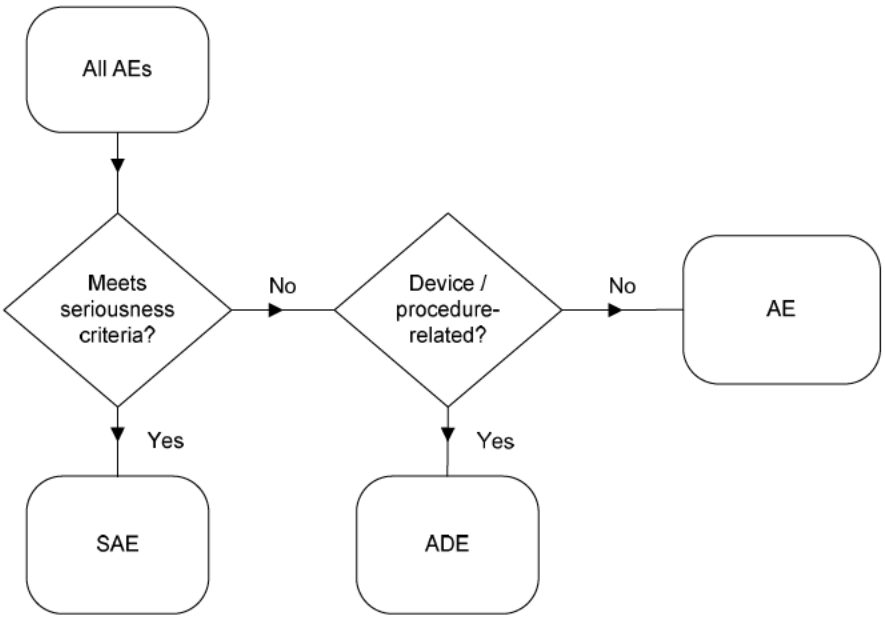
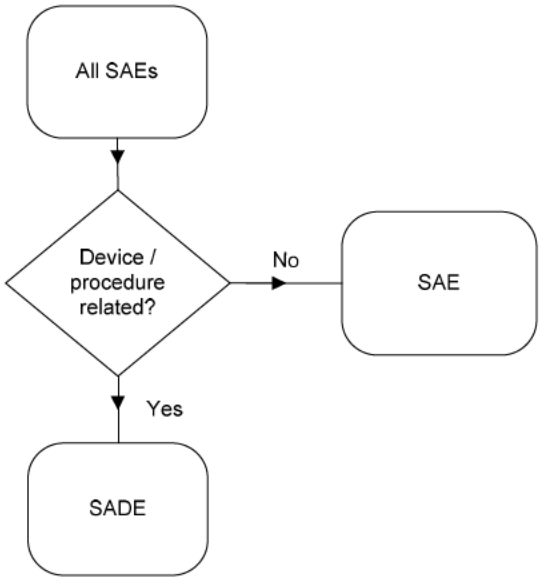


Figure 11–2 Categorization of All Serious Adverse Events



[redacted]

Device Deficiencies

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 for the identified or suspect device deficiency and report any subject harm separately.

11.2 Monitoring for Adverse Events

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

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

Changes in any protocol-specific parameters and/or questionnaires evaluated during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in a protocol-specific parameter or questionnaire response that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

11.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (ie, before informed consent is signed) are not considered AEs in the study and should be recorded in the Medical History section of the eCRF.

[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 articles on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the Study Sponsor immediately as follows:

- All SAEs must be reported immediately (within 24 hours) of the Investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reported within 10 calendar days of the Investigator's or site's awareness.
- A printed copy of the completed ***Serious Adverse Event and Adverse Device Effect*** and/or ***Device Deficiency*** eCRF must be included with product returns.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document 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 Adverse Device Effect (for related AEs) and Serious Adverse Event eCRF.

[redacted]

Any AEs and device deficiencies for non-study marketed devices/products will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives may be contacted for any protocol related question [redacted]

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 on 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 AE that is upgraded from non-serious to serious or from unrelated to related.

11.4 Return Product Analysis

Study Sponsor representatives and their contact information are provided i[redacted]

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

11.5 Unmasking of the Study Treatment

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

11.6 Follow-Up of Subjects with Adverse Events

The Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

The Investigator should provide the Study Sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ongoing at time of subject exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (ie, database lock).

All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

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

11.7 Pregnancy in the Clinical Study

Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case-by-case basis. An Alcon form will be utilized to capture all pregnancy-related information until birth of the child.

12 ANALYSIS PLAN

[redacted]

12.2 Analysis Sets

The primary analysis set for effectiveness analyses will be the All-Implanted Analysis Set (AAS). AAS includes all eyes with successful study IOL implantation. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Safety Analysis Set includes all eyes that had contact with a study IOL (successful or aborted implant).

12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by IOL group and overall using descriptive statistics based on the type of variable. For categorical variables summary statistics will include sample size, number in category, and % in each category. For continuous variables, number of subjects/eyes, mean, median, standard deviation, minimum, and maximum will be reported.

12.4 Effectiveness Analyses

Each effectiveness hypothesis will be tested independently for each of the following IOL groups 1) VIVITY vs. SYMFONY, and 2) VIVITY vs. AT LARA. There will be no comparison between the two non-Alcon comparators. [redacted]

[redacted]

[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoints

The primary endpoint is the percent (%) of subjects not bothered at all by halos as reported by the subject using the QUVID questionnaire at 3 months.

12.4.1.1 Statistical Hypotheses

The primary effectiveness objective is to demonstrate the superiority of Vivity to Symfony or AT LARA in % of subjects not bothered at all by halos at 3 months post-bilateral implantation.

The null and alternative hypotheses in support of the primary effectiveness objective are:

H_0: $p_{Vivity} \leq p_{Comparator}$
H_A: $p_{Vivity} > p_{Comparator}$

Where p_{vivity} and $p_{comparator}$ refer to the percent of subjects not bothered at all by haloes in the VIVITY group and the comparator groups respectively. The two comparator groups are SYMFONY and AT LARA.

12.4.1.2 Analysis Methods

The superiority hypothesis for each comparator will be evaluated using a two-sample test of proportions. The null hypothesis is rejected if the 1-sided p-value is less than 0.0125. Primary analysis will be based on AAS. [redacted]

12.4.2 Analysis of Secondary Effectiveness Endpoints

The secondary effectiveness endpoints are:

- % of subjects not bothered at all by glare (QUVID)
- % of subjects not bothered at all by starbursts (QUVID)

12.4.2.1 Statistical Hypotheses

If the primary null hypothesis is rejected, the following null and alternative hypothesis for the secondary endpoints will be tested independently for each comparator in the order of glare, then starburst, if glare is successful:

H_0: $p_{Vivity} \leq p_{Comparator}$
H_A: $p_{Vivity} > p_{Comparator}$

Where p_{vivity} and $p_{comparator}$ refer to the percent of subjects not bothered at all by haloes in the VIVITY group and the comparator groups respectively. The two comparator groups are SYMFONY and AT LARA.

12.4.2.2 Analysis Methods

The superiority hypothesis for each comparator will be evaluated using a two-sample test of proportions. The null hypothesis is rejected if the 1-sided p-value is less than 0.0125. Primary analysis will be based on AAS. [redacted]

[redacted]

[redacted]

12.5 Handling of Missing Data

There will be no imputation for missing data.

12.6 Safety Analyses

The safety endpoints are:

- Adverse events (including SSIs)
- Device deficiencies
- IOP (clinically significant change)
- Slit-lamp exam findings
- Dilated fundus exam findings
- IOL observations including IOL tilt/decentration
- Subjective PCO assessment
- Posterior capsulotomy
- Intraoperative Surgical problems
- Other procedures at surgery (combined and/or additional)

There are no safety hypotheses for this study. For all safety measures, descriptive statistics generated will be based upon the type of variable. For categorical variables summary statistics will include sample size, number in category, and % in each category. For continuous variables, number of subjects/eyes, mean, median, standard deviation, minimum, and maximum will be reported.

[redacted]

12.8 Sample Size Justification

Approximately 218 subjects will be enrolled to achieve 180 subjects who complete the study.

[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]. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

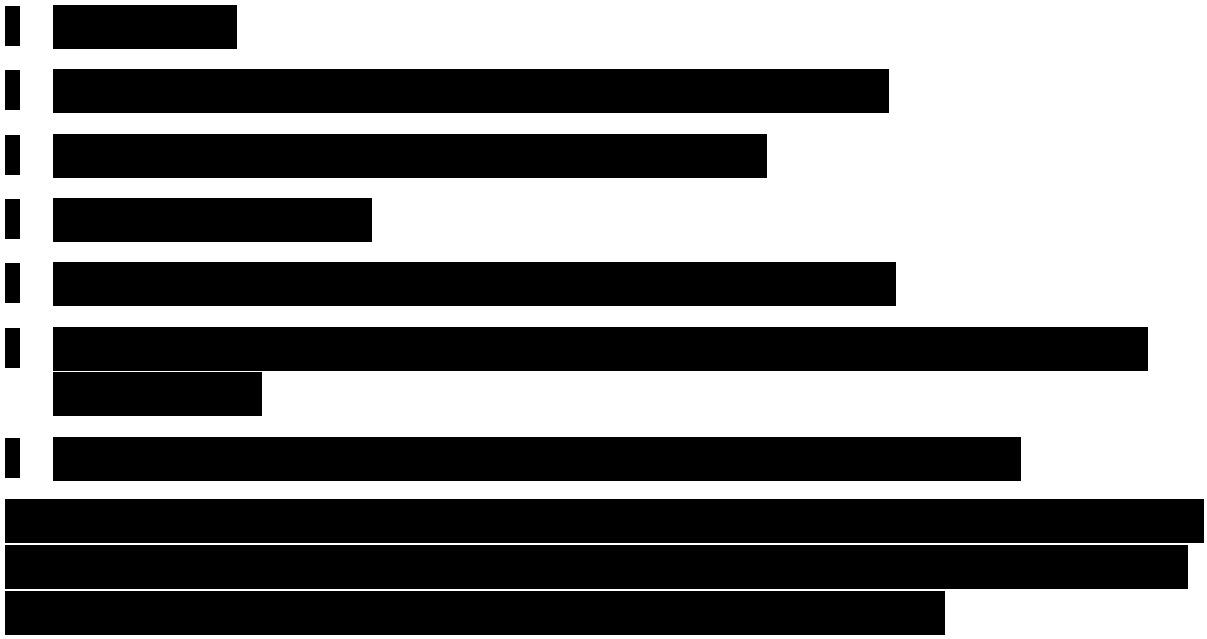
[redacted]

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.

If electronic records are maintained, the method of verification must be determined in advance of starting the study.

[redacted]



Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The Principal Investigator is responsible for reviewing and certifying that the CRFs are accurate and complete. The only subject identifiers recorded on the CRFs will be subject number, and subject demographic information.

13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, additional data clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's CRF.

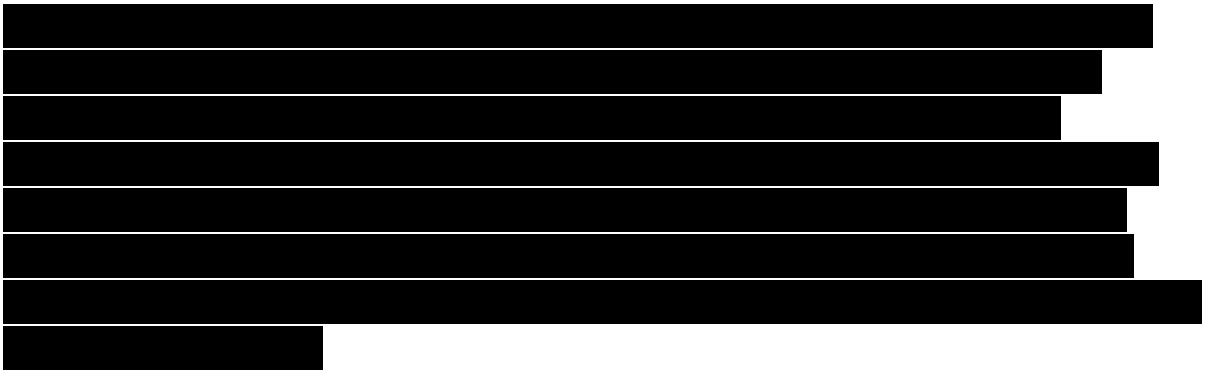
13.4 Sponsor and Monitoring Responsibilities

The Study Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals according to the study monitoring plan. The clinical investigation will be monitored to ensure that the rights and well-being of the subjects are protected, the reported data are accurate, complete, and verifiable from the source documents, and the study is conducted in compliance with the current approved protocol (and amendments[s], if applicable), with current GCP, and with applicable regulatory requirements.

The site may not screen subjects or perform the informed consent process on any subject until it receives a notification from an appropriate Study Sponsor representative that the site may

commence conducting study activities. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone, written and fax correspondence. Close-out visits will take place after the last visit of the last subject at the site.

A Coordinating Investigator may be identified by the Study Sponsor to review and endorse the final study report. In cases where a Coordinating Investigator is engaged, the Study Sponsor will select the Coordinating Investigator based upon their experience, qualifications, active study participation, and their willingness and availability to take on this role.



13.5 Regulatory Documentation and Records Retention

The Investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the Study Sponsor and the Investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is to be kept separately.

13.6 Quality Assurance and Quality Control

The Study Sponsor will secure agreement from all involved parties to ensure direct access to all study related sites, source data and documents, and reports for the purpose of monitoring and auditing by the Study Sponsor, and inspection by domestic and foreign regulatory authorities. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Agreements made by the Study Sponsor

with the Investigator/Institution and any other parties involved in the clinical study will be provided in writing as part of the protocol or as a separate agreement.

14 ETHICS

This clinical study must be conducted in accordance with the ethical principles contained within:

- The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.
- Notification of Intent to Supply Unapproved Therapeutic Goods under Clinical Trial Notification (CTN) Scheme (May 2011).
- SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.
- Notifications and timelines for reporting protocol deviations should be based upon applicable IRB/IEC requirements.

The Investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The Investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. Deviations from this protocol, regulatory requirements and/or GCP must be recorded and reported to the Sponsor prior to database lock. If needed, corrective and preventive action should be identified, implemented, and documented within the study records. Use of waivers to deviate from the clinical protocol is prohibited.

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

Voluntary informed consent must be obtained in writing from every subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or their delegate, must explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

[redacted]

[redacted]

[redacted]

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