AcrySof IQ Toric A-code post-market clinical study

CLINICAL STUDY PROTOCOL

Alcon Japan Ltd.

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Protocol No.: ILV814-P001

Version No. 3.0: September 22, 2018

Summary

Protocol No.	ILV814-P001
Objectives	Primary Efficacy To evaluate absolute value of IOL rotation at Visit 4 from Visit 00. • Percentage of eyes with rotation of less than 10 degree* • Percentage of eyes with rotation of less than 20 degree* • Percentage of eyes with rotation of less than 30 degree* * ISO 11979-7:2014(E), 6.2.2 Additional requirements for toric IOLs [redacted]
Study Population	Test Group (A Code): Adult subjects, 20 years of age or older, with no ocular pathology that confound study outcomes, who require cataract extraction by phacoemulsification and eligible Toric IOL implantation for study eye.
Study design	Prospective, single arm, multicenter study
Test Articles	AcrySof IQ Toric, model SN6AT3, SN6AT4, SN6AT5 (A-code)

Variables

Primary Efficacy

Absolute value of IOL rotation at Visit 4 from Visit 00

- Percentage of eyes with rotation of less than 10 degree*
- Percentage of eyes with rotation of less than 20 degree*
- Percentage of eyes with rotation of less than 30 degree*

* ISO 11979-7:2014(E), 6.2.2 Additional requirements for toric IOLs

[redacted]

Table: Definition of Axis Difference

	Intended axis	Visit 00	Visit 00-A	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7
Intended axis		Axis placement error	Misalignment (Axis placement error + Rotation)	Misalignment	Misalignment	Misalignment	Misalignment	Misalignment	Misalignment	Misalignmer
Visit 00			Rotation	Rotation	Rotation	Rotation	Rotation	Rotation	Rotation	Rotation
Visit 00-A				Rotation	Rotation	Rotation	Rotation	Rotation	Rotation	Rotation
Visit 1					Rotation	Rotation	Rotation	Rotation	Rotation	Rotation
Visit 2						Rotation	Rotation	Rotation	Rotation	Rotation
Visit 3							Rotation	Rotation	Rotation	Rotation
Visit 4								Rotation	Rotation	Rotation
Visit 5									Rotation	Rotation
Visit 6										Rotation
Visit 7										

Difference = Column - Row

[redacted]

Safety

[redacted]

- Adverse Events
- Device Deficiencies

Usage	Implant IOL to aphakic eye.
Examinations Schedule	• Visit 0 (Preoperative) • Visit 00 (Surgery day, during surgery) • Visit 00-A（Surgery day, 1 hour +/-30min after surgery） • Visit 1 (Day 1-2) • Visit 2 (Day 7-14) • Visit 3 (Day 30-60) • Visit 4 (Day 120-180) • Visit 5 (Day 330-420) • Visit 6 (Day 630-780) • Visit 7 (Day 990-1140)
Estimated Total Sample Size	Required: 100 subjects (eyes), Planned: 120 subjects (eyes) One eligible eye will be selected as a target eye for efficacy analysis. If both eyes are eligible, the eye in which IOL is implanted first will be selected as a target eye.
Anticipated study period	October 2017 to January 2022 (Enrollment period: October 2017 to September 2018)
Study Sponsor	Alcon Japan Ltd.
Regulations	This study will be conducted in accordance with ICH Harmonized Tripartite Guidelines for Good Clinical Practice or Ministerial Ordinance Regarding Good Clinical Practice Principles for Medical Devices (2005, Ministry of Health, Labour and Welfare Ordinance No.36; hereinafter referred to as “Medical Device GCP”) and Ethical Guidelines for Clinical Studies (2014, Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare Notification No.3), in principle.

CONTENTS

1. Introduction

1.1 History of development

In Japan, in 1985, the intraocular lenses (IOLs) of five companies were approved by the Ministry of Health and Welfare (present MHLW). After IOLs began to be covered by health insurance in 1992, IOL usage has spread rapidly[1]. Subsequently, a range of foldable IOLs were developed[2], and through advances in small incision techniques and their increased use, early recovery of visual acuity, early ambulation, and early rehabilitation became possible. In addition, a series of reconstructive lens surgeries that accompany the insertion of IOLs, have made it an almost complete surgical procedure[3].

In recent years, the cataract surgery is not merely an operation to restore visual acuity, and the needs of refractive cataract surgery, such as not requiring to wear glasses after surgery, is increasing. Miyake et al. reported that 15.4% of patients with cataract surgery had more than 1.5 D of corneal astigmatism[4]. Since this astigmatism cannot be corrected only with the monofocal IOL, a Toric IOL is applied to treat them.

Toric IOLs were first implanted in humans in 1994[5]. Alcon Japan received Regulatory approval of AcrySof Toric IOL in Japan in 2009 and it currently sells the models that can correct corneal astigmatism from 1.03 D to 4.11 D.

One of the important features required for Toric IOL is the rotational stability. Since the astigmatic correction effect of Toric IOL decreases by 3.3% per degree of IOL rotation[5], it is necessary to carry out a surgery to reposition the IOL axis in the case that a large rotation occurs after the surgery.

In Japan, a manufacturing improvement of the AcrySof family of lenses has been implemented in 2017 (A code) [redacted] this study (ILV 814 - P001) will be implemented to clinically confirm the rotational stability of AcrySof IQ toric A code.

This study will be conducted in accordance with ICH Harmonized Tripartite Guidelines for Good Clinical Practice or Ministerial Ordinance Regarding Good Clinical Practice Principles for Medical Devices (2005, Ministry of Health, Labour and Welfare Ordinance No.36; hereinafter referred to as “Medical Device GCP”) and Ethical Guidelines for Clinical Studies (2014, Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare Notification No.3), in principle.

1.2 Information on Safety or Efficacy

Refer to Protocol Supplemental Attachment B ‘Package Insert’

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1 Shinichi Ito. Journal of the Eye 20: 615-620, 2003

2 Ken Hayashi. Japanese Journal of Cataract and refractive Surgery 16: 453-458, 2002

3 Kimiya Shimizu. Journal of the Eye 16(9): 1185-1189, 1999

4 Toshiyuki Miyake. Corneal astigmatism before cataract surgery. Nippon Ganka Gakkai Zasshi 115: 447 453, 2011

5 Shimizu K, et al. Toric intraocular lenses correcting astigmatism while controlling axis shift. J Cataract Refract Surg. 1994, 20, 523 526.

2. STUDY OBJECTIVES

Primary Efficacy

- Absolute value of IOL rotation at Visit 4 from Visit 00*
- Percentage of eyes with rotation of less than 10 degrees
- Percentage of eyes with rotation of less than 20 degrees
- Percentage of eyes with rotation of less than 30 degrees

* ISO 11979-7:2014(E), 6.2.2 Additional requirements for toric IOLs

[redacted]

[redacted]

[redacted]

Safety

[redacted]

- Adverse Events
- Device Deficiencies

3. TEST ARTICLES

3.1 TEST ARTICLES

[redacted]

Test Article:

AcrySof IQ Toric (Model: SN6AT3, SN6AT4, SN6AT5)

3.2 Usage

Open the undamaged pouch and transfer the case to a sterile environment. IOL will be implanted to an aphakic eye after phacoemulsification was performed. Adjust the IOL toric mark onto the intended axis which was calculated by the Alcon Toric IOL Calculator.

3.3 Instructions on package and labeling

Not applicable.

3.4 Storage and Management

Do not store intraocular lenses at temperatures over 45°C.

4. SUBJECTS

4.1 Estimated Total Sample Size

One hundred and twenty subjects are planned to be enrolled in this study (Required 100 subjects)

One eligible eye will be selected as a target eye for efficacy analysis. If both eyes are eligible, the eye in which IOL is implanted first will be selected as a target eye.

4.2 Inclusion criteria

1) Adults, 20 years of age or older at the time of informed consent, of either gender or any race, diagnosed with cataracts with planned cataract removal by phacoemulsification.
2) Able to comprehend and willing to sign informed consent and complete all required postoperative follow-up procedures.
3) Calculated lens power within the available range.
4) Eyes for which the implantation of SN6AT3, SN6AT4 or SN6AT5 IOLs is recommended by the Alcon online Toric IOL calculator.
5) Potential postoperative Best Corrected Distance visual acuity (BCDVA) of 0.7 decimal or better in study eye based on Investigator expert medical opinion.
   NOTE: Subjects with any pathology that could reduce visual potential should not be enrolled in this study.
6) Clear intraocular media other than cataract in study eye
7) Eyes whose predicted postoperative refraction is emmetropia.

< Rationale for inclusion criteria >

1), 3), 4): To confirm eligible for Toric IOL

2): Required for Medical Device GCP

5), 6): Conditions to minimize the potential non-IOL confounding factors which may affect the primary efficacy endpoint.

7): To avoid effect of post operative uncorrected visual acuity.

4.3 Exclusion criteria

Exclusion Criteria (Prior to surgery)

1) Clinically significant corneal abnormalities per the Investigator's expert medical opinion.
2) Previous corneal transplant.
3) Previous refractive surgery or planned refractive surgery procedures throughout the entire duration of the subject participation in the clinical study (including, but not limited to LASIK, astigmatic keratotomy and limbal relaxing incisions)
4) History of or current retinal conditions or predisposition to retinal conditions, including previous history of or a predisposition to retinal detachment or presence of diabetic retinopathy that the Investigator determines that

could confound outcomes (NOTE: Including but not limited to background diabetic retinopathy, diabetic macular edema or proliferative diabetic retinopathy, macular degeneration)

5) Amblyopia
6) Rubella, congenital, traumatic, atopic or complicated cataracts
7) Any recurrent severe anterior or posterior segment inflammation of any etiology, and /or history of any disease producing an intraocular inflammatory reaction
8) Iris neovascularization
9) Glaucoma (uncontrolled with medication) or ocular hypertension
10) Optic nerve atrophy
11) Subjects with diagnosed degenerative eye disorders
12) Pregnancy current or planned during the course of the study
13) Any subject currently participating in another investigational drug or device study that may confound the results of this investigation
14) Subjects who may reasonably be expected to require an ocular surgical treatment at any time during the study (other than Nd:YAG capsulotomy)
15) Situations where the need for a large capsulotomy can be anticipated by the Investigator's expert medical opinion (e.g., diabetics, retinal detachment in the fellow eye, peripheral retinal pathology, etc.)
16) Subjects who are expected to require retinal laser treatment
17) Patient with the poor mydriasis and who is expected that it cannot confirm Toric mark even if they were dilated
18) Patient with corneal irregular astigmatism
19) Disqualified by the investigator or the sub investigator because of systemic or ophthalmic diseases.

< Rationale for exclusion criteria >

14), 15), 17): Factors potentially affecting primary efficacy endpoint.

Others: General safety considerations.

Exclusion Criteria (During surgery)

1) Eyes with any other additional procedures during the cataract surgery and IOL implant due to intraoperative complications that required further intervention (including but not limited to posterior capture rupture, vitreous loss, zonular dehiscence that may make the IOL implant less stable, etc.)
2) Significant anterior chamber bleeding
3) Uncontrolled intraocular pressure
4) Unrecognized (pre-existing but discovered during surgery) ocular conditions or complications in which the IOL stability could be compromised, including zonular weakness.
5) Bag-sulcus, sulcus-sulcus or unknown placement of the haptics.
6) Any capsulorhexis other than continuous curvilinear capsulorhexis (e.g., no anterior radial inconsistencies in the capsulorhexis such as anterior capsular tears or any areas of 'can-opener' capsulotomy).

< Rationale for exclusion criteria >

Factors potentially affecting primary efficacy endpoint.

5. STUDY DESIGN

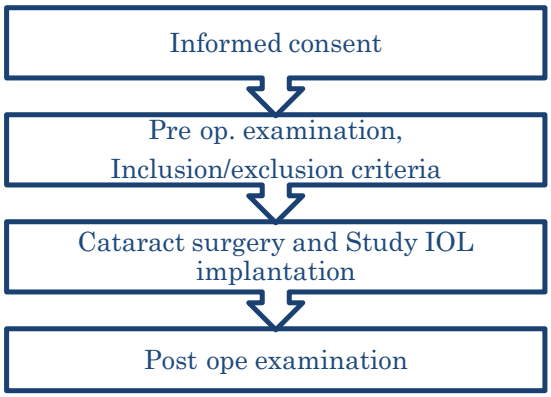
Prospective, single arm, multicenter study

6. STUDY PROCEDURE

6.1 Outline

The outline of this study is shown in Figure 6-1. The subject who has corneal astigmatism and was judged by Alcon Toric IOL Calculator to be eligible implantation of SN6AT3, SN6AT4, SN6AT5 and will be implanted recommended IOL model will be enrolled. The subjects are examined from pre-operative visit to 3 years post-operatively. One hundred and twenty subject will be enrolled.

Figure 6-1 Outline of This Study



6.2 Method of Subject Selection

Subjects will be selected by following method.

1) After an explanation of the study details is given to a prospective subject, his/her consent to participate in the study will be obtained.
2) The subject identification code will be assigned to a subject whose consent is obtained.
3) The investigator will assess the eligibility of the subject through examinations and observations needed to assess the eligibility based on the inclusion and exclusion criteria.
4) One eligible eye will be selected as a target eye for efficacy analysis. If both eyes are eligible, the eye in which eye will be implanted IOL first will be selected as a target eye.

6.3 Examinations Schedule

Overview of the study procedure is presented in Table 6-1.

Table. 6-1 OVERVIEW OF STUDY PROCEDURES

		Nominal Time ± Visit Window Limits								
	Visit 0	**Visit 00**	**Visit 00-A**	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**
Procedure/ Assessment	Pre-operative	Surgery day, during surgery	Surgery day, 1 +/-0.5 hour after surgery	Day 1-2	Day 7-14	Day 30-60	Day 120-180	Day 330-420	Day 630-780	Day 990-1140
Informed Consent	**X**									
Demographics	**X**									
Medical History	**X**									
Inclusion/Exclusion	**X**	**X**								
Manifest refraction	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
[redacted]	■			■	■	■	■	■	■	■
[redacted]	■			■	■	■	■	■	■	■
Corneal keratometery (K1, K2, Ax)	**X**									
Corneal topography	**X**									
Toric calculator	**X**									
Axial length	**X**									
Anterior chamber depth	**X**									
[redacted]				■						
[redacted]		■					■			
[redacted]		■	■	■	■	■	■	■	■	■
Surgical records		**X**								
Toric mark axis		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
[redacted]				■	■	■	■	■	■	■
[redacted]				■	■	■	■	■	■	■
Slit examination	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
[redacted]				■	■	■	■	■	■	■
[redacted]				■	■	■	■	■	■	■
Adverse Events	**X**	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Device Deficiency		**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**

[redacted]

6.4 Examinations Procedure

1) Visit 0 (Pre-operative)

After an explanation of the study details is given to a prospective subject, his/her consent to participate in the study will be obtained. The subject identification code will be assigned to a subject whose consent is obtained. The investigator will assess the eligibility of the subject and select the target eye. The registration form for the subject will be sent to the sponsor.

After the subject consents to participate in the study, the following examinations are performed. When a routine clinical assessment is performed before obtaining informed consent, data from these assessments may be used as study data.

- Subject Demographics:

  Gender, age (at the day of consented), medical history of eye, ophthalmic surgical history and eye complications
- Manifest refraction

  Record the spherical and cylindrical refraction and axis at the time of BCVA measurement with the visual acuity test chart.
- Visual acuity (Uncorrected distance visual acuity, Best corrected distance visual acuity):

  Measure the visual acuity under photopic lighting condition by decimal visual acuity chart.
- Keratometry (K1, K2, Axis)

  Measure the corneal curvature by auto keraometer. Measurement is less than 0.25 D step.
- Corneal topography

  Measure the corneal irregular astigmatism by corneal topography or any other measurement instrument. Confirm the subject doesn't have corneal irregular astigmatism.
- Target refraction

  Record the target refraction which was expected by IOL power calculation.
- Toric Calculator

  Record the IOL model, Toric IOL target axis, calculate formula, corneal refraction power, axial length, anterior chamber depth(ACD), anticipated residual astigmatism (D, degree) by Alcon online toric IOL calculator.
- Axial length

  Measure the axial length by optical measurement method.
- Anterior chamber depth

  Measure the anterior chamber depth (distance between corneal endothelial and anterior surface of crystalline lens capsular) using by optical measurement method.
- Slit lamp examination

  Confirm the presence or absence of adverse events. If any adverse event is present, record data on the event in the Adverse Event CRF according to Section 10 "Adverse Events and Device Deficiencies, etc." of the protocol.
- Adverse events

Collect the information of the adverse events (whole body) occurred after the subject consents.

2) Visit 00 (Surgery day, during surgery)

・ Exclusion criteria

Confirm the exclusion criteria of during surgery.

・ Information of IOL model

Record the implanted IOL model and IOL power (D).

[redacted]

・ Angle of IOL axis

After IOL implantation, confirm the IOL alignment to intended axis using by surgical guidance system.

Photographic documentation of the implanted IOL, end of surgery, with visible IOL axis marks and – on the same picture – visible structures of the eye which are stable in time and allow a determination of the rotational angle of the IOL around the optical axis relative to the said structures of the eye.

IOL axis is evaluated [redacted] using with the anterior segment photograph. Each investigator will capture and send the anterior segment photograph [redacted] for analysis. The measurement of the toric mark angle chooses any reference marks such as conjunctiva or the iris and measures the angle to make with the toric mark of IOL and records it. Measurement methodology will be described in measurement instructions. Measurement method is according to the manual specified separately.

・ Adverse events (whole body) and Device deficiencies

Collect the information of the adverse events (whole body) and device deficiencies.

3) Visit 00-A (post-operative 1 +/- 0.5 hours)

[redacted]

・ Angle of IOL axis

Photographic documentation of the implanted IOL, on the day of surgery, with visible IOL axis marks and – on the same picture – visible structures of the eye which are stable in time and allow a determination of the rotational angle of the IOL around the optical axis relative to the said structures of the eye. Preferred structures are limbal vessels. The pupil might be dilated.

Angle of IOL axis is evaluated [redacted] using with the anterior segment photograph. Measurement method is according to the manual specified separately.

4) Visit 1, 2, 3, 4, 5, 6, 7 (Post-operative)

・ Manifest refraction

Record the spherical and cylindrical refraction and axis at the time of BCVA measurement with the visual acuity test chart.

[redacted]

・ Angle of IOL axis

Photographic documentation of the implanted IOL, on the every visit after surgery, with visible IOL axis marks and – on the same picture – visible structures of the eye which are stable in time and allow a determination of the rotational angle of the IOL around the optical axis relative to the said structures of the eye. Preferred structures are limbal vessels. The pupil might be dilated.

Angle of IOL axis is evaluated [redacted] using with the anterior segment photograph. Measurement method is according to the manual specified separately.

[redacted]

・ Slit lamp examination

[redacted]

・ Adverse events (whole body) and Device deficiencies

[6] Akira Miyata. Glistening particles on the implanted acrylic intraocular lens. Jpn J Clin Ophthalmol 51(4): 729-732, 1997

Collect the information of the adverse events (whole body) and device deficiencies.

6.5 Study period

October 2017 to January 2022

7. CONCOMITANT THERAPY

No prohibited therapy

8. DISCONTINUED SUBJECTS

8.1 Discontinued Subjects

Subjects are discontinued the study in the following cases:

1) Upon onset of adverse events which make study continuation difficult.
2) Upon cancellation of consent to the study by the subject.
3) Upon request of the subject to discontinue the study.
4) Hospital referral or move of the subject during the study, making it difficult to continue the study.
5) If the investigators judge it necessary to discontinue the study.

Upon discontinuation of the study, if the investigators decided the examination or observation is necessary, the examination or observation should be carried out as far as possible under the subject's consent, and reason of discontinuation is entered in the case report form. In case which continuation of the study is difficult because of discontinued visit of the subject to the clinic, the subject is followed as possible over telephone, by mail or other appropriate means and the reason for discontinued visit, survival/death of the subject, presence/absence of adverse events, etc., are entered in the case report form.

8.2 Discontinuation of the entire study

If discontinuation of the entire study has become inevitable for reasons of reports on serious safety information, problems pertaining to the quality of the test articles, and so on, the Sponsor is required to immediately inform the investigator and the head of each study site of discontinuation of the study and its reason in writing.

9. Statistical Analysis

9.1 Evaluability

Subject evaluability based on pre specified deviations and their impact on analysis sets will be determined prior to locking the database. Protocol deviations and their impact on analysis sets, eg, individual visits and data points to be excluded will be pre specified in the Deviation and Evaluability Plan (DEP).

9.2 Datasets

Datasets used for effectiveness and safety analysis are as follows.

9.2.1 Safety Analysis Set

The pre treatment safety analysis set will include all subjects who consented to participate in the study. The pre treatment safety analysis set will be the set that will be used to summarize occurrence of adverse experiences prior to exposure to the test article. The treatment emergent safety analysis set will include all eyes with attempted implantation with the test article (successful or aborted after contact with the eye).

9.2.2 All Implanted Analysis Set (AAS)

All-Implanted Analysis Set (AAS) will include all eyes with successful test article implantation.

9.2.3 Best Case Analysis Set (BAS)

Best-Case Analysis Set (BAS) will include all eyes with successful test article implantation that had

- at least 1 postoperative visit,
- no major protocol violation.

The pre treatment safety analysis set will be used to summarize occurrence of adverse experiences prior to exposure to the test article. The treatment emergent safety analysis set will be used for safety analysis after implantation of test article. Non target eyes will be included in safety analysis if the eye is implanted with test article. The AAS and BAS will be used for primary effectiveness analysis in the study, with priority given to AAS results. The AAS will be used for exploratory analysis in the study.

9.3 Demographic factors and baseline characteristics

For all datasets (Safety Analysis Set, AAS, BAS), demographic factors (sex, age, axis length, planned IOL angle, pre operative astigmatism, IOL model, pre operative astigmatism volume), descriptive statistics will be provided. For sex, age (<60, 60 69, 70 79, ≥ 80), axial length (<22, 22 26.9, 27≤ mm), planned IOL angle (0 45° or 135 180°, 46 136°), pre operative astigmatism (with the rule, against the rule, oblique), IOL model (SN6AT3, SN6AT4, SN6AT5), the N and percentage will be provided. For age, axis length and pre operative astigmatism volume, arithmetic mean, standard deviation, N, median, min and max) will be provided.

9.4 Effectiveness Analysis

The objective of this study is to describe safety and effectiveness for patients who are implanted with AcrySof IQ Toric (A-code). The one eye will be selected as the target eye for effectiveness analysis. The first implanted eye will be the target eye in case both eyes have no deviation from inclusion/exclusion criteria.

9.4.1 Primary Analysis

Primary effectiveness variable is the absolute value of IOL rotation at Visit 4 from Visit 00.

Primary analysis is to provide N and percentage of eyes which satisfy the following criteria*.

- Absolute value of IOL rotation of less than 10 degrees
- Absolute value of IOL rotation of less than 20 degrees
- Absolute value of IOL rotation of less than 30 degrees

* ISO 11979-7:2014(E), 6 2 2 Additional requirements for toric IOLs

9.4.1.1 Statistical Hypothesis

No confirmatory hypothesis testing will be conducted for primary analysis.

9.4.1.2 Analysis Method

The number and percentage of eyes will be provided for each category of absolute value of IOL rotation at Visit 4 from Visit 00.

- < 10 degrees / ≥10 degrees
- < 20 degrees / ≥20 degrees
- < 30 degrees / ≥30 degrees

9.4.2.1 Statistical Hypothesis

[redacted]

[redacted]

[redacted]

[redacted].

9.5 Missing Data Imputation

No missing data imputation will be conducted.

9.6 Safety Analysis

A patient listing of adverse experiences prior to exposure to the test article will be provided. Safety variables after exposure to the test article are as follows. Each safety variable will be

summarized descriptively. Descriptive statistics (mean, standard deviation, N, median, min and max) will be provided for actual value and change from appropriate baseline at each visit for continuous variables. For categorical variables, N and percent will be provided for each category.

- [redacted]
- [redacted]
- Adverse Events
- Device Deficiencies

9.7 Interim Analysis

Interim analysis will be conducted twice after all subjects complete Visit 4 (Day 120 180) and Visit 6 (Day 630 780) visits to evaluate safety and effectiveness of the test lens. The primary analysis will be conducted after all subjects complete Visit 4. The final analysis will be conducted after all subjects complete Visit 7 (Day 990 1140). Interim analyses are not intended to stop the study early. Also, the interim analysis will be performed in the same way of the final analysis at Visit 7.

9.8 Sample Size Justification

According to ISO standards*, at least 100 subjects should be enrolled to investigate IOL rotation. The 120 subjects will be enrolled assuming that dropout rate is around 16%.

* ISO 11979-7:2014(E), 6.2.2 Additional requirements for toric IOLs

10. ADVERSE EVENTS and DEVICE DEFICIENCIES, etc.

10.1 General Information

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

Adverse Event (AE):

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects after signed informed consent, users or other persons, whether or not related to the investigational medical device (test article). *For subjects, this definition includes events related to the test article or the procedures involved. For users or other persons, this definition is restricted to events related to the test article.*

Serious Adverse Event:

Adverse event that led to any of the following, or that needed treatment not to lead to the following results:

- 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 congenital anomaly/birth defect,

e) a medically important event or reaction.

Non-serious Adverse Event

Adverse event that does not meet the criteria for a serious adverse event.

Adverse Device Effect (ADE)

Adverse event related to the use of an investigational medical device (test article).

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 article.

Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Device Deficiency

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance.

Safety Information:

Information about quality, efficacy and safety for medical device and information which is needed for appropriate use, including:

- Use error
- Abnormal Use
- Product tampering
- Product counterfeiting
- Product theft

10.2 Procedure for Reporting of Serious Adverse Events (SAE)

The investigator will report the serious adverse event or the risk of causing serious adverse event to Alcon within 24 hours after confirming the event.

After obtainment of detailed information on the serious adverse event, the investigator will prepare a report and immediately submit it to Alcon and the head of the medical institutions.

Contact for emergent communication

[redacted]

When the SAE is correspond to “Death or a life-threatening ADE” or “Serious and unexpected ADE other than Death or a life-threatening event”, the sponsor will immediately notify them to heads of all medical institutions and all investigators by document.

10.3 Report of Adverse Events and Evaluation of the Causal Relationship

All adverse events (related and unrelated to the medical device) will be documented on the Adverse Event Case Report Form (CRF).

10.4 Intensity Assessment of Adverse Events

For every AE, the investigator must assess the intensity (severity). Events should be classified as mild, moderate, or severe. These classifications should be based on the following definitions:

Intensity:	
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.

10.5 Follow-up of Subjects / Subjects with Adverse Events

In the event of acknowledging any adverse events, the investigators should immediately take appropriate actions irrespective of the presence or absence of causal relationship with the test article. And the investigators will make a follow-up of the adverse event if it is possible. When the subject needs medical treatment, the investigators should inform the subject of the matter.

For subjects who are experiencing ongoing unresolved adverse events at the time of their study completion or early discontinuation from the study, it is recommended that the investigator schedule an appropriate follow-up visit in order to determine the outcome of the event.

10.6 Pregnancy of subjects

Women who is planning to become pregnant during this study period or women who are pregnant at the time of study entry are excluded from participation.

10.7 Provision of safety information

Investigators provide safety information which is needed to make a detailed report on demand from the sponsor.

11. ETHICS

11.1 Independent ethics committee / Institutional review board

Prior to the start of the study, the Independent ethics committee (IEC)/the institutional review board (IRB) of each participating institution is required to inspect and evaluate the planned study as to the acceptability of implementing the study, appropriateness of the contents of the protocol, case report form, questionnaire and informed consent document, and other matters related to the study from the ethical, scientific and medical points of view, with an ultimate goal of protecting the human rights and welfare of the subjects.

The inspection and examination by the IEC/IRB may be performed again also during a certain period of time after the start of the study or when the head of the participating institution sees the necessity of additional inspection/examination so that the study may be monitored continuously.

11.2 Ethical consideration

The study is implemented after a contract on implementation of the study is concluded between the Sponsor and each participating institution following inspection and authorization of the study by the IEC/IRB of each participating institution.

If deemed necessary to ensure safe implementation of the study, the protocol of this study may be revised in accordance with the provisions set forth in “Section 12. PROTOCOL AMENDMENTS”.

This study is carried out in accordance with the principles set forth in the Declaration of Helsinki and the protocol. This study will be conducted in accordance with ICH Harmonized Tripartite Guidelines for Good Clinical Practice or the Ministerial Ordinance Regarding Good Clinical Practice Principles for Medical Devices (2005, Ministry of Health, Labour and Welfare Ordinance No.36; hereinafter referred to as “GCP”) and Ethical Guidelines for Clinical Studies (2014, Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare Notification No.3), in principle.

11.3 Protection of subjects’ privacy

To protect the privacy of individual subjects, only identification codes is used to represent the subjects whose data are used in case reports, etc., so that leakage of the identifiable individual information about the subjects can be prevented.

11.4 Specifications to secure safety of study subjects

1) Actions to take for adverse events

In the event of acknowledging any adverse events, the investigator or the subinvestigator should immediately

take appropriate actions irrespective of the presence or absence of causal relationship with the test article.

2) Supply of new information

In the case of obtaining safety-related new and significant information related to the clinical trial, the sponsor should supply the information in writing to the investigator and the subinvestigator and the head of the study site and take necessary actions.

3) Avoiding emergent risks

In the event of deviating from the study protocol to avoid the emergent risk and secure safety of the study subject or because of other unavoidable clinical reasons, the investigator will retain the record and submit the documentation and justification of the protocol deviation to the sponsor and the head of the study site.

11.5 Compensation for health hazards

If any subject has sustained health hazards arising from this study, best healthcare is provided to that subject. The Sponsor needs to be covered by insurance for liability arising from clinical trial.

11.6 Payment to subjects

[redacted] the Sponsor pays an amount of money, predetermined through negotiation with each participating medical institution, to each subject. This payment is not intended to force any subject to remain in the study.

12. PROTOCOL AMENDMENTS

When the protocol, etc. are revised, the sponsor and the investigator will exchange an agreement in writing. subjects are enrolled, depending on the necessity.

13. CONSIDERATIONS FOR DOCUMENTATION AND COMPLETION OF CASE REPORT FORM

The investigator, etc. will complete the case report form by himself or herself based on source data in accordance with the protocol and the preparation procedure of the case report form. After preparation of the case report form, he or she will sign and date it, and submit it to the sponsor through the person in charge of monitoring.

14. MONITORING

The Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals. 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.
- The study is conducted in compliance with the current approved protocol (and amendment[s], if applicable), with current Good Clinical Practices (GCPs), Ethical Guidelines for Clinical Studies and

with applicable regulatory requirements, in principle.

The monitor will report the monitoring results to study manager.

15. RETENTION OF THE RECORDS

The records for this clinical study shall be stored properly: At expiration of the retention period of the records, the sponsor will notify the medical institutions thereof.

Medical institutions and investigators shall preserve the protocol, source documents, informed consent forms agreed, informed consent form and other written information, records on GCP and Ethical Guidelines for Clinical Studies (2014, Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare Notification No.3). Above documents excluding medical records should be retained either five years after the date of completion of the study, or three years after the date of publication/presentation the final study result whichever date is later. The storage period of clinical record depend on Medical Practitioners Act and other related regulations.

16. CONFIDENTIALITY AND PUBLICATION OF STUDY

All information related to this clinical study including the protocol and therapeutic results are the property of the sponsor, and the investigator and other medical staff engaged in the clinical study must keep such information confidential.

The sponsor can submit the results of this clinical study to the health authority and use the results as “Information on Proper Use” of the product. Sponsor will register the summary of the study to open database (The Database Center of the National University Hospitals, JAPIC Clinical Trials Information, or JMACCT Clinical Trials Registry, etc.) before conducting the study, and will properly update it based on the revision of the protocol or study progression.

When publishing the results of this clinical study in the congresses or medical journals, the investigators and other medical staff must obtain prior approval from the sponsor. The sponsor can confirm the contents of presentation beforehand.

After completion of the study, sponsor and the investigators will report the result of the study after taking necessary steps for protecting the right and benefits of the subjects, related persons, sponsor, investigators, and so on.

17. DIRECT ACCESS TO SOURCE DATA AND DOCUMENTS

The investigator and the study site must make source data available to the sponsor or the regulatory authority at their request. Such direct access to source data will be performed so that the sponsor or the regulatory authority may confirm whether the clinical study is conducted in accordance with the protocol and whether data of the case report form are indicated accurately.

With reference to [Evaluation] and [Comment of the investigator, etc.], there are no source data and they are information directly indicated on the case report form.

18. QUALITY CONTROL AND QUALITY ASSURANCE OF THE STUDY

Quality control and Quality assurance shall be carried out in accordance with GCP standard operational procedures (SOP) and Quality assurance SOP of the Sponsor.

Quality Assurance will evaluate that the study is properly conducted according to the protocol, Standard Operation Procedures of Phase-IV / Clinical Infometrics, ICH Harmonized Tripartite Guidelines for Good Clinical Practice or Medical device GCP (2005, Ministry of Health, Labour and Welfare Ordinance No.36) and its amendments, and Ethical Guidelines for Clinical Studies (2003, Ministry of Health, Labour and Welfare Notification No.255) and its amendments.

19. OBLIGATIONS OF INVESTIGATORS

Selection of Trial Subjects

In the selection of trial subjects, investigator(s) and sub-investigators shall, from the standpoint of human rights and on the basis of the standards for selection and exclusion set forth in the trial protocol(s), carefully consider whether to request participation in the trial, taking into consideration such factors as the subject's general state of health, symptoms, age, sex, capacity to consent, dependency on investigator(s), etc., and participation in other trials.

Obtaining Consent of Subjects

Investigator(s) and sub-investigators shall obtain consent for the subject to participate in the trial from the subject or legally acceptable representative thereof, in accordance with GCP.

Medical Treatment of Subjects

The investigator shall have the responsibility for all decisions on medical treatment relating to the trial.

The director of the institution and the investigator shall ensure that the subject is provided with adequate medical treatment for all trial-related adverse events that constitute clinical problems during and after the subject's participation in the trial. Further, when an investigator or sub-investigator becomes aware of the need for medical treatment of an adverse event, he or she shall so inform the subject.

If a subject desires to withdraw or withdraws participation during the trial, the subject is not obliged to clarify the reason for withdrawal, but the investigator or sub-investigator shall make appropriate efforts, based on full respect for the rights of the subject, to determine the reason.

After this study, the investigator shall provide the best treatment for the subjects using the result of this study.

Agreement on and Compliance with Trial Protocol(s)

Prior to reaching an agreement with the sponsor on the trial protocol(s) and case report forms (CRF), the investigator shall confer with the sponsor on the basis of the trial protocol(s), CRF, and other required materials and information submitted by the sponsor, and shall give full consideration to the ethical and scientific suitability of conducting the trial. The same shall apply if the trial protocol(s) or CRF are revised.

The investigator shall reach agreement with sponsor on the content of the trial protocol(s) and CRFs, and as evidence of agreement to comply with the trial protocol(s), the investigator and sponsor shall date and affix their

signatures or personal seals to a trial contract or alternative document. The same shall apply if the trial protocol(s) or CRFs are revised, or if, due to a directive of the director of the institution based on the opinion the IRB, the trial protocol(s) or CRF is corrected.

Submission of Documents to the IEC/IRB

Before and during the trial period, the investigator(s) shall keep current those documents that are subject to review by the IEC/IRB and are to be submitted by the investigator(s). If these documents are augmented, updates or revised, all must be submitted promptly to the director of the institution.

Directive and Decisions of the Director of the Study site

When the IEC/IRB gives its approval to conduct the trial on condition of certain revisions, and the investigator has been informed in writing of the directives and decisions of the director of the institution based thereon, the investigator shall commence the trial in accordance with these directives and decisions.

When the IEC/IRB gives its approval to continue a trial in progress or to continue a trial on condition of certain revisions, and the investigator has been informed in writing of the directives and decisions of the director of the institution based thereon, the investigator shall continue the trial in accordance with these directives and decisions.

When the IEC/IRB cancels its approval to an item related to a trial in progress (including its termination or suspension) and the investigator has been informed in writing of the directives and decisions if the director of the institution based thereon, the investigator shall comply with these directives and decisions.

Use, etc., of the Investigational Product(s)

The investigator shall ensure that the investigational product(s) are used only in accordance with methods that comply with the approved trial protocol(s).

Deviations etc. from Trial Protocol(s)

The investigator or sub-investigators shall not undertake any deviation from or modification of the trial protocol(s) without prior written agreement between the investigator and the sponsor and written approval based on prior inspection by the IEC/IRB. This is not, however, applicable in the case of changes related solely to cases that are medically unavoidable in order to avoid imminent danger to the subject, or in the case of management matters (e.g., a change in telephone number).

The investigator or sub-investigators shall keep a record of all actions deviating from the trial protocol(s). The investigator or sub-investigators shall prepare a record describing the reason(s) etc. therefore, submit the record regarding to deviation in order to avoid imminent danger to the subject to the sponsor, and retain a copy. The investigator or sub-investigators may undertake deviations from or modification of the trial protocol(s) within prior written agreement between the investigator and the sponsor and written approval based on prior inspection by the IEC/IRB in medically unavoidable situation, in order to avoid imminent danger to the subject, In such an event, the investigator notify as soon as possible the sponsor, as well as the director of the institution and, via the director of the institution, to the IEC/IRB, of the nature of and reasons for the deviation or modification, together

with a proposal for revision of the trial protocol(s), if appropriate, and obtain their approval, and at the same time shall obtain in writing the approval of the director of the institution and, via the director of institution, the agreement of the sponsor.

Recording and Reporting the CRF

The Investigator or sub-investigators shall prepare CRFs in accordance with the trial protocol(s), affix thereto his or her signature or personal seal, and submit them to the sponsor. The investigator shall retain copies of the CRFs submitted.

The investigator shall inspect CRFs prepared by sub-investigators prior to their submission to the sponsor, and upon confirming that there is no problem, affix thereto his or her signature or personal seal. The investigator shall also inspect modifications or revisions to CRFs undertaken by sub-investigators, and confirm that there is no problem.

The investigator shall ensure that the data in the CRFs and all other documents submitted to the sponsor are accurate, complete, legible, and submitted in a timely manner, and that a subject identification code is used for identifying subjects.

Data in the CRFs that are based on original materials shall not conflict with the original materials. When there is any discrepancy with the original, the investigator shall prepare a record explaining the reason therefore, submit it to the sponsor, and retain a copy.

In modifying or correcting CRFs, the investigator or sub-investigators shall follow the manual provided by the sponsor. If there is any modification or correction whatever in a CRF, it must be dated and the signature or personal seal affixed. An explanation of the change must be provided if the change is critical. Further the modification or correcting shall not be such as to render the initial writing unclear (i.e., an audit trail shall be maintained).

The investigator should submit records of modification and correction of the case report form to the Sponsor and retain a photocopy of each record.

Reports, etc. in the Course of the Trial

In order to be available for ongoing review by the IEC/IRB, the investigator shall submit a written overview of the status of the trial to the director of the institution annually, or more frequently when requested by the IEC/IRB.

With respect to any trial modification that could have a significant effect on the conduct of the trial or could increase the risk to subjects, the investigator shall promptly submit a written report to the sponsor, the director of the institution and, via the director of the institution, to the IEC/IRB.

Except in cases in which the trial protocol(s), etc. provide that urgent notification is not required, the investigator shall notify the sponsor promptly of all serious adverse events. After the urgent notification, a detailed written report shall be made in due course.

With respect to adverse events that are specified in the trial protocol(s) as serious for evaluation the safety of the investigational product(s), the investigator shall report to the sponsor, observing the reporting requirements and deadlines set forth in the trial protocol(s).

The investigator shall report all serious adverse events to the director of the institution promptly and in writing.

In this case, the investigator shall identify those of the reported serious adverse events involving serious and unpredictable adverse device effects.

With respect to serious adverse events or serious adverse device effects, including cases of death, shall submit to the sponsor, director of the institution or IEC/IRB any additional information (autopsy reports, final treatment records or other requisite information that they may request).

Termination or Suspension of the Trial

When for any reason the trial is terminated or suspended, the investigator shall notify the subjects promptly to that effect, and shall ensure that subjects receive appropriate medical treatment and post-treatment. When the investigator terminates or suspends the trial, the investigator shall notify the director of the institution promptly and in writing to that effect, and shall provide a detailed written explanation for the termination or suspension.

Completion of the Trial

When the trial is completed, the investigator shall notify the director of the institution in writing to that effect, and report in writing an overview of the trial results.

Storage of records

The investigator shall retain essential documentation relating to the conduct of the trial in accordance with the directives of the director of the institution.

20. INFORMED CONSENT

Time to obtain consent

The investigator or sub-investigator will obtain written consent by the trial subject prior to the commencement of the study.

Methods for explaining to trial subjects

The investigator (or sub-investigator) will give explanations to trial subjects. Study collaborators can give supplemental explanations.

The explanations should be given based on the explanation/consent document using terms which are the most easy to understand (non-technical terms). Questions made by trial subjects should be answered appropriately in the way the trial subjects can understand.

Methods for obtaining consent

(1) The investigator (or sub-investigator) who has given explanations will sign and date the consent document.
(2) If any study collaborator has given supplemental explanations, the study collaborator will also sign and date the consent document. (Study collaborators are not allowed to solely give all necessary explanations to trial subjects.)
(3) Supply the trial subject with the consent document and explanation document describing aforementioned necessary information and take sufficient time for the trial subject to decide whether or not he/she should

participate in the clinical study.

(4) Before obtaining consent, take sufficient time for the trial subject to sufficiently review the consent items and ask any questions. Answer the questions in a convincing manner.

(5) Obtain the trial subject's spontaneous written consent to participate in the clinical study.

(6) After obtaining the consent document signed and dated by the trial subject, the investigator (or sub-investigator) will enter the date of consent in the CRF and in the medical record. All consent documents must be retained.

(7) Supply the trial subject with the copy (duplicate for the trial subject) of the consent document and the explanation document before the trial subject participates in the clinical study.

(8) If the explanation document or consent document is subject to revision during the participation of the trial subject, follow the above procedures and re-obtain consent.

Items Mentioned for the Written Informed Consent Form and Explanatory Documents

(1) The fact that the clinical study involves research.

(2) The purpose of the trial.

(3) The name and title of the investigator or sub-investigator, and how he or she can be contacted.

(4) The trial method (including the aspects of the trial that are experimental, subject's inclusion/exclusion criteria, and when the trial is randomized, the probability of randomization for each treatment).

(5) The expected clinical benefits, and the foreseeable risks or inconveniences to the subjects. (If any benefits for the subject will not be expected, it must be informed to the subject.)

(6) When the persons to be enrolled as trial subjects are patients, the availability of other medical treatments for their condition, and the potential major benefits and risks of such treatments as are available.

(7) The expected duration of the subjects' participation in the trial.

(8) That participation in the trial is voluntary; that the trial subject can refuse to participate in the trial or can withdraw from the trial at any time and that the subjects will not be disadvantaged or lose any benefit to which they are entitled if they refuse to enroll in the trial or if they withdraw from the trial after enrolling.

(9) Handling of investigational products in case of withdrawing from the clinical study.

(10) That the trial monitor, auditor, IRB, and regulatory authorities are allowed to examine the source data; that the confidentiality of the trial subjects will be protected when those data are examined by those persons; and that the subjects authorize the perusal of those data by those persons by sealing and/or signing the written consent form.

(11) That the subjects' confidentiality will be protected even when the results of the clinical study are published.

(12) The person in the study site whom the subjects should contact for further information about the trial or their rights, or if they develop a health problem associated with the trial.

(13) The compensation and medical treatment the trial subjects can receive should they develop a health problem associated with the trial.

(14) The number of subjects expected to be enrolled in the trial (including discrete variable).

(15) That if information is received that may affect the will of the subjects regarding the subjects' ongoing participation in the trial, that information will be passed on promptly to the subjects.

(16) The circumstances under which or the reasons subjects will be withdrawn from the trial.
(17) The specifics about any expense the trial subjects will have to pay.
(18) The specifics about any cash or the like that will be paid to the trial subjects (including the arrangement for calculating the sum to be paid).
(19) Responsibilities of the trial subjects.
(20) Information about Institutional review board.
(21) The name of the study and the fact that the head of medical institute approved the conduct of the study
(22) The procedure of disclosure of information
(23) The fact that the documents related to protocol and procedure of the study are available, as far as there is no interruption regarding protection of personal information and originality of the study, depending on the request from subject etc.. Also procedure of its access.
(24) Handling of personal information (including the procedure of anonymity, if applicable)
(25) The procedure of storing and disposal of the information
(26) Conflict of Interest of the investigator, medical institution etc. regarding the study, including funding source, personal income and so on.
(27) If there is a possibility that the sample or information of subjects might be used in future study or provided to other research institution, the fact and assumed contents when informed consent is obtained.

Revision of Informed Consent Form and Explanatory Documents

If the investigator acknowledges the necessity of revising the explanatory document used for obtaining consent, in the case of the obtainment of the information which may affect the trial subject's intention to continuously participate in the clinical study or in other cases, immediately revise the explanatory document and have the revision approved by the IEC/IRB.

21. CONFLICT OF INTEREST

Alcon Japan Ltd. is sponsor of this clinical study. Alcon Japan Ltd. and head of the medical institution will sign a contract for the clinical study. Financial cost of the study will be sponsored by Alcon Japan Ltd in accordance with the contract.

[redacted]

[redacted]

Financial information to medical institutions paid by Alcon Japan Ltd. is disclosed at Homepage of Alcon Japan Ltd.

22. REFERENCES

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3） Kimiya Shimizu. Journal of the Eye 16(9): 1185-1189, 1999

4） Toshiyuki Miyake. Corneal astigmatism before cataract surgery. Nippon Ganka Gakkai Zasshi 115: 447 453, 2011

5） Kimiya Shimizu, et al. Toric intraocular lenses correcting astigmatism while controlling axis shift. J Cataract Refract Surg. 1994, 20, 523-526.

6） Akira Miyata. Glistening particles on the implanted acrylic intraocular lens. Jpn J Clin Ophthalmol 51(4): 729-732, 1997

AcrySof IQ Toric A-code Post Market Clinical Study

CLINICAL PROTOCOL Supplemental Attachment

A Clinical trial system, participating facilities and principal investigators

B Package Insert AcrySof® IQ Toric Single piece

[redacted]

D Measurement of IOL rotation

[redacted]

[redacted]

[redacted]

Alcon Japan Ltd.

1-23-1 Toranomon, Minato-ku, Tokyo

Protocol No.: ILV814-P001

Version No.2.0: September 22, 2018

Supplemental Attachment A:
Clinical Trial System, Participating Facilities and Principal Investigators

1. Clinical Trial System

(1) Sponsor

Alcon Japan Ltd. [redacted]
1-23-1 Toranomon, Minato-ku, Tokyo, 107-0052
[redacted]
[redacted]

(2) Study Supervisor

[redacted]

(3) Clinical Development Director

[redacted]

(4) Study Manger

[redacted]

(5) Persons in Charge of Monitoring (delegate)

[redacted]

(6) Statistical Analysis Manager

[redacted]

(7) Data Manager

[redacted]

(8) Input of Study Data and Data Analysis

[redacted]
[redacted]
[redacted]

(9) Reliability Assurance Manager

[redacted]

(10) Central Evaluation (Measurement of IOL axis and CCC area)

[redacted]

(11) Sponsor Medical Expert

[redacted]

2. Medical Institutions and Investigators

No.	Medical Institutions	Job title	Principal investigator	Location
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]