AcrySof IQ Toric A-code post-market clinical study

Clinical Research Protocol

Alcon Japan Ltd.

Toranomon Minato-ku, Tokyo

[redacted]

Protocol No. ILV814-P001
ClinicalTrials,gov NCT03350503
Ver.4.0：January 29, 2020
Ver.5.0：June 16, 2021

SUMMARY

Protocol No.	ILV814-P001
Objectives	Primary Efficacy To evaluate absolute value of intraocular lens (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 Exploratory Efficacy and Safety To evaluate visual acuity, [redacted] IOL rotation [redacted] Safety endpoints (IOL densitometry, glistenings, Nd: YAG laser treatment for posterior capsular opacification (PCO) and adverse event) until Visit 7.
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	Alcon® AcrySof® IQ Toric Single-Piece IOL (model: SN6AT3, SN6AT4, SN6AT5)

Endpoints

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

Key Exploratory Efficacy

- [redacted] IOL rotation, [redacted]
- [redacted]
- [redacted]

IOL rotation: IOL axis difference between study visits

[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
[redacted]										
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

Other Exploratory Efficacy

- Uncorrected distance visual acuity
- Best corrected distance visual acuity
- [redacted]
- SSNG densitometry

Safety

- Glistening grade
- YAG laser treatment rate for post capsular opacification
- 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 May 2022
Representative Investigator	[redacted]
Study Sponsor	Alcon Japan Ltd.: Creating the trial plan of clinical research and provide funding and services related to conducting research.
Regulations	This study will be conducted in accordance with the principles set forth in the Declaration of Helsinki, the Clinical Trials Act (Act No. 16 of April 14, 2017), the Enforcement Regulations of the Clinical Trials Act (No.17 of February 28, 2018), and other relevant laws, ministerial ordinances, ministerial notifications, etc.
Protocol Effective Date	Approval by the certified review board

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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, Labour and Welfare (MHLW). After IOLs began to be covered by health insurance in 1992, IOL usage has spread rapidly[1]. Subsequently, a range of foldable IOLs was 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 (ILV814-P001) will be implemented to clinically confirm the rotational stability of AcrySof IQ toric A-code.

This study was 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) 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.

With the enforcement of the Clinical Trials Act, this study was to be conducted under the Clinical Trials Act. After completion of the transition to Clinical Trials Act on February 21, 2019, this study will be conducted in accordance with the principles set forth in the Declaration of Helsinki, the Clinical Trials Act (Act No. 16 of April 14, 2017), the Enforcement Regulations of the Clinical Trials Act (No.17 of February 28, 2018), and other relevant laws, ministerial ordinances, ministerial notifications, etc.

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1 Shinichi Ito. Medical insurance and intraocular lenses. Journal of the Eye, 20: 615-620, 2003.
2 Ken Hayashi. New foldable intraocular lenses. Japanese Journal of Cataract and Refractive Surgery, 16: 453-458, 2002.
3 Kimiya Shimizu. Revaluation of cataract surgery. Journal of the Eye, 16(9): 1185-1189, 1999.
4 Toshiyuki Miyake. Corneal astigmatism before cataract surgery. Journal of Japanese Ophthalmological Society, 115: 447-453, 2011.
5 Kimiya Shimizu, et al. Toric intraocular lenses correcting astigmatism while controlling axis shift. J Cataract Refract Surg., 29: 523-526, 1994.

1.2 Information on safety or efficacy

Refer to Protocol Supplemental Attachment B 'Package Insert'.

2. STUDY OBJECTIVES

Primary Efficacy

To evaluate absolute value of IOL rotation at Visit 4 (Day 120-180) from Visit 00 (Surgery day, during surgery).

- 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

Exploratory Efficacy and Safety

To evaluate visual acuity, [redacted] IOL rotation [redacted], Safety endpoints (IOL densitometry, glistenings, Nd: YAG laser treatment for posterior capsular opacification (PCO) and adverse event) until Visit 7(Day 990-1140)

3. TEST ARTICLES

3.1 Test articles

Alcon® AcrySof® IQ Toric Single-Piece IOL (model: SN6AT3, SN6AT4, SN6AT5)

Refer to Protocol Supplemental Attachment B 'Package Insert' for the detail of the test articles.

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 (prior to surgery)]

14), 15), 17): Factors potentially affecting primary and exploratory 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 (during surgery)]

Factors potentially affecting primary and exploratory efficacy endpoint.

5. STUDY DESIGN

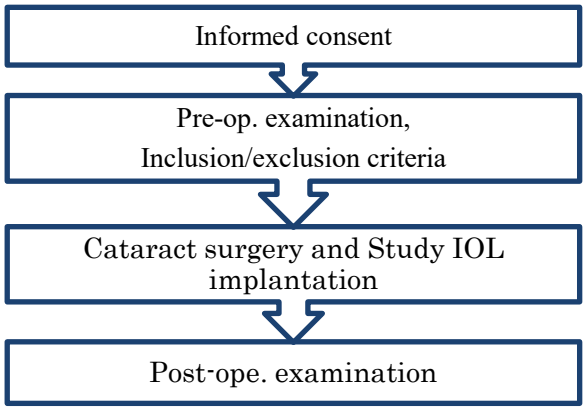
Prospective, single arm, multicenter study

6. STUDY PROCEDURE

6.1 Study 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 Study Outline



6.2 Method of subject selection

Subjects selection and subject identification code assignment are follows.

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 Examination schedule.

Overview of the study procedure is presented in Table 6-1. The examination/observation period is from preoperative to 990-1140 days after surgery. [redacted]

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**
Uncorrected distance visual acuity	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
Best corrected distance visual acuity	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
Corneal keratometory (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**
SSNG densitometry[1]				**X**	**X**	**X**	**X**	**X**	**X**	**X**
Glistening grade				**X**	**X**	**X**	**X**	**X**	**X**	**X**
Slit examination	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
PCO				**X**	**X**	**X**	**X**	**X**	**X**	**X**
YAG laser for PCO				**X**	**X**	**X**	**X**	**X**	**X**	**X**
Adverse Events	**X**	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Device Deficiency		**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**

[1] Evaluate by Pentacam or Pentacam HR

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 (ACD)

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 Case Report Form (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]

[redacted]

[redacted]

・ 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]

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.

・ Visual acuity (Uncorrected distance visual acuity, Best corrected distance visual acuity)

Measure the visual acuity under photopic lighting condition by decimal visual acuity chart.

[redacted]

[redacted]

- Surface light scattering densitometry

  Measure the anterior surface light scattering densitometry by using Pentacam or Pentacam HR. [redacted]

- Slit lamp examination

  Assess the grade of glistening[6] according to Protocol Supplemental Attachment C, evaluate PCO and exam other abnormality. If needed, exam under mydriatic condition. [redacted]

- Nd: YAG laser for posterior capsulotomy

  Record the operation date of Nd: YAG laser for PCO. [redacted].

- Adverse events (whole body) and device deficiencies

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

6.5 Study period (Plan)

October 2017 to May 2022

7. CONCOMITANT THERAPY

No prohibited therapy.

[6] Akira Miyata. Glistening particles on the implanted acrylic intraocular lens. Japanese Journal of Clinical Ophthalmology, 51(4): 729-732, 1997.

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 notice shall be given as follows.

1) In case that the representative investigator determined discontinuation of the study

The representative investigator shall immediately notify the principal investigator(s) and the sponsor of the discontinuation of the study and its reasons. The representative investigator shall also report these information to the administrator of the investigational site to which the representative investigator belongs, and the certified review board. The principal investigator(s) shall report the discontinuation of the study and its reasons to the administrator of the investigational site to which he/she belongs, and immediately inform the subjects who participant in the study of them and take appropriate actions such as changing to appropriate treatment.

2) In case that the sponsor determined discontinuation of the study

The sponsor shall immediately notify the representative investigator of discontinuation of the study and its reasons and discuss discontinuation of the study with the representative investigator. The representative investigator shall notify the principal investigator(s) of these information. The representative investigator shall also report it to the administrator of the investigational site to which the representative investigator belongs, and the certified review board. The principal investigator(s) shall report the discontinuation of the study and its reasons to the administrator of the investigational site to which he/she belongs, and immediately inform the subjects who participant in the study of them and take appropriate actions such as changing to appropriate treatment.

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.

9.2 Datasets

Datasets used for effectiveness and safety analysis are as follows.

(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).

(2) All-Implanted Analysis Set (AAS)

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

(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. [redacted] 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 Exploratory analysis

Key exploratory variables are as follows.

- [redacted] IOL rotation, [redacted]
- [redacted]
- [redacted]

[redacted]

IOL rotation: IOL axis difference between study visits

[redacted]

Other exploratory variables are as follows.

- Uncorrected distance visual acuity
- Best corrected distance visual acuity
- [redacted]
- SSNG densitometry

9.4.2.1 Statistical hypothesis

No confirmatory hypothesis testing will be conducted.

9.4.2.2 Analysis method (key exploratory analysis)

- [redacted] IOL rotation, [redacted]

Descriptive statistics (mean, SD, N, median, min and max) will be provided for variables below.

- [redacted]
- Absolute value of IOL rotation from Visit 00 axis at each study visit
- [redacted]
- [redacted]
- [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.

- Glistening grade (0,1,2,3)
- YAG laser treatment rate for post capsular opacification
- Adverse events
- Device deficiencies

9.7 Interim analysis

[redacted] 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. [redacted]

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

9.9 Revision of statistical analysis plan

The statistical analysis plan will be prepared before the data base lock. If the statistical analysis plan is necessary to be revised, it will be get approved by the certified review board and the revision will be explained in the CSR of this study.

10. ADVERSE EVENTS, DISEASE OR THE LIKE, AND DEVICE DEFICIENCIES, etc.

10.1 General information

The definitions of the terms are described below.

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 (SAE):

AE 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 AE:

AE that does not meet the criteria for a serious AE.

Adverse Device Effect (ADE):

AE 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:

ADE that has resulted in any of the consequences characteristic of a SAE.

Disease or the Like:

Among AEs, any disease, disability, death or infection which is suspected of being due to the conduct of the study, as well as an abnormal laboratory data and symptoms.

Infection:

A suspicion of concomitant of the pathogens from biological raw materials or biological materials into biological products. In addition, it shall be also reported as an infection when the viral marker such as HBV, HCV, HIV, etc. shows positive.

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 Assessment of AE

Report of AE and Causality Assessment:

All AEs which occurred after the subject consents to participate in the study (related and unrelated to the medical device) will be documented on the AE CRF.

For every AE in the study, the investigator must assess the causality (Related or Not Related to the medical device).

Intensity Assessment of AE:

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:

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.

Outcome:

The outcome shall be assessed as either recovered/resolved, recovering/resolving, not recovered/not resolved, recovered/resolved with sequelae, death or unknown.

10.3 Assessment of disease or the like

Severity Assessment:

Refer to 10.1 the definition of SAE.

Predictability assessment :

For every disease or the like, the investigator must assess the predictability as either ”predictable” or “unpredictable”. If it is not listed in the following documents, etc., and the investigator judge that it cannot be predicted, it shall be "unpredictable”.

1) The clinical research protocol or the explanation document
2) The latest package insert for the test articles
3) The precautions on the container or package of the test articles, or the interview form of the test articles, etc.

10.4 Follow-up of subjects / subjects with AEs

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.

10.5 Actions for disease or the like and device deficiency

10.5.1 Record and report of disease or the like and device deficiency

When the principal investigator or the sub-investigator recognizes an occurrence of a disease or the like or a device deficiency, he/she shall take necessary measures against the subject and prepare the CRF after documenting the occurrences etc. to the patient records. If the sub-investigator recognizes an occurrence of a disease or the like or a device deficiency, he/she shall report its details to the principal investigator.

10.5.2 Report of serious disease or the like and device deficiency that may cause serious disease or the like

1) Principal investigator

When the principal investigator recognizes an occurrence of a serious disease or the like or a device deficiency that may cause serious disease or the like among occurrences of disease or the like which is suspected of being due to the conduct of the study, he/she shall report it to the administrator of the investigational site to which the principal investigator belongs. The principal investigator shall also report it to the representative investigator.

2) Sub-investigator, etc.

When the sub-investigator, etc. recognizes an occurrence of a serious disease or the like or a device deficiency

that may cause serious disease or the like, he/she shall report it to the principal investigator (or the representative investigator if it was occurred at the study site to which the representative investigator belongs.)

3) Representative investigator

When the representative investigator obtains an information of a serious disease or the like or a device deficiency that may cause serious disease or the like, he/she shall report it to the administrator of the investigational site to which he/she belongs, and the certified review board in accordance with the procedure described in 10.7. The representative investigator shall also provide the information to the other principal investigator(s).

10.6 Procedure for reporting to the study sponsor

The investigator will report the SAE, serious disease or the like, or device deficiency which may cause a serious disease or the like to the sponsor within 24 hours after confirming the event or acknowledging the possibility of occurrence of the event.

In addition, after obtaining the detailed information on SAE, serious disease or the like, or device deficiency which may cause a serious disease or the like, the investigator will prepare a report and promptly submit it to the sponsor and the administrator of the investigational site.

If the sponsor receives the report of “death or a life-threatening ADE, disease or the like (device deficiency)” or “serious and unexpected ADE, disease or the like (device deficiency) other than death or a life-threatening event” from the investigator, the sponsor shall give full consideration to promptly notify the information in writing to the representative investigator, the administrators of all investigational sites and all the principal investigators.

10.7 Report of disease or the like to the certified review board and the Minister of Health, Labour and Welfare

10.7.1 Reporting period of disease or the like and device deficiency

When the representative investigator obtain an information of the following disease or the like and device deficiency, he/she shall report it to the administrator of the investigational site and also report it to the certified review board which is written in the clinical research protocol within each reporting period using Clinical Trials Act Form. The order of reporting to the administrator of the investigational site and to the certified review board may be changed. The representative investigator shall provide the information to the manufacturer. The representative investigator shall report the information as the first report within the reporting period as far as he/she obtained, even if the information such as a cause of occurrence of disease or the like is not clear. Afterwards, when the representative investigator obtain more information, he/she shall report the information immediately as the

following report. The report to the Minister of Health, Labour and Welfare shall be made at the periodic report.

The reporting period for Specified Clinical Trials using a medical device that has been already approved or a medical device within indication

Disease or the like	Expecting infection		Infection	
	Unpredictable	Predictable	Unpredictable	Predictable
(1) Death	15 days	15 days	15 days	15 days
(2) In-patient hospitalization or prolonged hospitalization	15 days	30 days	15 days	15 days
(3) A life-threatening illness or injury	15 days	30 days	15 days	15 days
(4) Any potentially sight-threatening event or permanent impairment to a body structure or a body function	15 days	30 days	15 days	15 days
(5) A congenital anomaly/birth defect	15 days	30 days	15 days	15 days
(6) A medically important event or reaction	15 days	30 days	15 days	15 days
(7) Other disease or the like: every year (within 2 months of the end of the period)	Periodic report	Periodic report	15 days	Periodic report

Report period of device deficiency

Device deficiencies that may cause disease or the like (1)-(6): within 30 days

Other device deficiencies: unnecessary to report

10.7.2 Periodic report

1) Report to the certified review board

Regarding disease or the like which is suspected of being due to the conduct of the study and applies to the periodic report, the representative investigator shall report the information to the administrator of the investigational site and report to the certified review board using the format of Clinical Trials Act at the periodic report. Periodic report shall be made every year from the date of publication of the trial plan in the Registry of Clinical Trials (jRCT), the database maintained by the MHLW.

2) Report to the Minister of Health, Labour and Welfare

The representative investigator shall make the periodic report to the Minister of Health, Labour and Welfare using the format of Clinical Trials Act.

10.7.3 Action to opinions of the certified review board

When the certified review board states opinions to the representative investigator, the representative investigator shall respect such opinions and take necessary measures. The representative investigator shall report the opinions

of the certified review board to the administrator of the investigational site to which he/she belongs. If a specific action is required based on the opinions of the certified review board, the requirement shall be also reported. The representative investigator shall provide the information with other principal investigator(s). When the principal investigator obtain the information from the representative investigator, he/she shall report it to the administrator of the investigational site to which he/she belongs to, and also share the information with the sub-investigator(s).

10.8 Other measures to be taken

When AE, disease or the like, or device deficiency etc. was occurred, the principal investigator shall determine the following and take an action in accordance with the clinical research protocol. If the principal investigator makes the following 2) or 3) decisions, he/she shall inform the representative investigator of it. The representative investigator shall take necessary measures if he/she obtained information from other principal investigator or if the representative investigator made the following 2) or 3) decisions.

1) Discontinuation of the study in each subjects
2) Discontinuation or completion of the study
3) Revision of the explanation document or consent document

10.9 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.

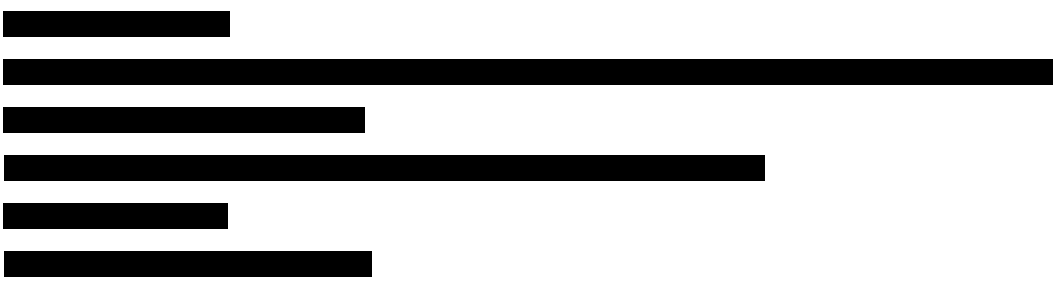
10.10 Information provision of safety information

When the safety information is identified, the investigator will provide the necessary information to the sponsor.

11. ETHICS

11.1 Certified review board

Prior to the study initiation, the representative investigator asks the certified review board to inspect and evaluate the planned study from the ethical, scientific and medical points of view with an ultimate goal of protecting the human rights and welfare of the subjects, 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.



11.2 Ethical consideration

The study is implemented after a contract on implementation of the study is concluded between the sponsor and each study site following inspection and authorization of the study by the certified review board.

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 will be conducted in accordance with the principles set forth in the Declaration of Helsinki, the Clinical Trials Act (Act No. 16 of April 14, 2017), the Enforcement Regulations of the Clinical Trials Act (No.17 of February 28, 2018), and other relevant laws, ministerial ordinances, ministerial notifications, etc.

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 AEs

In the event of acknowledging any AEs, the investigator or the subinvestigator should promptly 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 study, the sponsor should supply the information in writing to all the principal investigators and the heads of all study sites and take necessary actions.

3) Avoiding emergent risks

In the event of deviating from the clinical research 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 reason of the protocol deviation to the administrator of the investigational site, the representative investigator, and the study sponsor.

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. Explains the cost to reduce such burden as transportation expenses

12. PROTOCOL etc. AMENDMENTS

When the protocol, etc. are revised, the sponsor and the investigator will exchange an agreement in writing. The representative investigator will hear the opinion and obtain approval of the protocol amendments from the certified review board which is described in the clinical clinical research protocol. And then, the principal investigator will obtain approval of the protocol amendments from the administrator of the investigational site based on the results of the review.

13. CONSIDERATIONS FOR DOCUMENTATION AND COMPLETION OF CASE REPORT FORM

The investigator will complete the CRF by himself or herself based on source data in accordance with the protocol and the preparation procedure of the CRF. After preparation of the CRF, the investigator will sign or name and seal and date it, and submit it to the sponsor through the monitor.

14. MONITORING

The monitoring will be entrusted to the sponsor under the responsibility of the principal investigator and conducted under the supervision of the principal investigator. The Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals. The clinical investigation will be monitored to ensure the following items. The monitor will report the monitoring results to the Monitoring manager and the principal investigator. The principal investigator who received the report will notify the representative investigator of the contents of the report, if necessary. The representative investigator who received the notification will share the information of the notification to the other principal investigators.

1) The rights and well-being of the subjects are protected.
2) The reported data are accurate, complete, and verifiable from the source documents.
3) The study is conducted in compliance with the current approved protocol (and amendment[s], if applicable), with the Clinical Trials Act (Act No. 16 of April 14, 2017), the Enforcement Regulations of the Clinical Trials Act (No.17 of February 28, 2018), and other relevant laws, ministerial ordinances, ministerial notifications, etc.

15. RETENTION OF THE RECORDS

The principal investigators shall preserve the protocol, source documents, informed consent forms agreed, informed consent form and other records that must be preserved in accordance with the Clinical Trials Act (Act No. 16 of April 14, 2017), the Enforcement Regulations of the Clinical Trials Act (No.17 of February 28, 2018), and other relevant laws, ministerial ordinances, ministerial notifications, etc. Above documents excluding medical records should be retained five years after the date of completion of the study. The storage period of clinical record depend on Medical Practitioners Act and other related regulations.

At the end of the retention period, documents should be anonymized and disposed of in an appropriate manner.

16. CONFIDENTIALITY AND PUBLICATION OF STUDY

All information related to this clinical study including the protocol and the clinical study results are the property of the sponsor, and the investigator and all 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. The representative investigator will register the summary of the study to jRCT before conducting the study, and will properly update it based on the revision of the trial plan or the study progression.

When publishing the results of this clinical study in the congresses or medical journals etc., the investigators and all other medical staff engaged in the clinical study must obtain prior approval from the sponsor. The sponsor can confirm the contents of presentation before publication. After completion of the study, the sponsor and the investigators will report the results 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 CRF are indicated accurately.

With reference to [Assessment of AE] and [Comment of the investigator, etc.], there are no source data and they are information directly indicated on the CRF.

The source data is all materials or documents that will become the basis of the data which is recorded in the CRF as results of the study. The source data in this study shall be patient records (including worksheets), informed consent forms agreed, informed consent form and other records, the photographic imaging data and the results of the central evaluation. The CRF shall be a source data if the description such as investigator’s opinion is written directly in the CRF.

18. QUALITY CONTROL AND QUALITY ASSURANCE OF THE STUDY

The quality control will be entrusted to the sponsor under the responsibility of the principal investigator. The sponsor will carry out the quality control in compliance with the sponsor’s standard operational procedures (SOP) for a clinical research under the supervision of the principal investigator.

The quality assurance will be entrusted to the sponsor under the responsibility of the principal investigator. The sponsor will carry out the quality assurance in compliance with the sponsor’s SOP for the audit and the audit procedure of this study under the supervision of the principal investigator.

The auditor will evaluate that the study is properly conducted according to the protocol, SOP of the department in charge of clinical research design/planning/implementation (Medical Affairs, Clinical Development, Clinical Biometrics), the Clinical Trials Act (Act No. 16 of April 14, 2017), the Enforcement Regulations of the Clinical Trials Act (No.17 of February 28, 2018), and other relevant laws, ministerial ordinances, ministerial notifications, etc. The auditor will report the audit results in accordance with the audit procedure of this study.

19. OBLIGATIONS OF INVESTIGATORS

19.1 Obligations of principal investigators

Agreement on and compliance with clinical research protocol(s)

Prior to reaching an agreement with the sponsor on the clinical research protocol(s) and CRFs, the principal investigator(s) shall confer with the sponsor on the basis of the clinical research 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 study. The same shall apply if the clinical research protocol(s) or CRF are revised.

The principal investigator shall reach agreement with sponsor on the content of the clinical research protocol(s) and CRFs, and as evidence of agreement to comply with the clinical research protocol(s), the principal 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 clinical research protocol(s) or CRFs are revised, or if, due to a directive of the administrator of the investigational site based on the opinion the certified review board, the clinical research protocol(s) or CRF is corrected.

Selection of study subjects

In the selection of trial subjects, the principal investigator 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 clinical research protocol(s), carefully consider whether to request participation in the study, taking into consideration such factors as the subject's general state of health, symptoms, age, sex, capacity to consent, dependency on investigator, etc., and participation in other trials.

Obtaining consent of subjects

The principal investigator 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 Clinical Trials Act.

Medical treatment of subjects

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

The administrator of the investigational site and the principal investigator shall ensure that the subject is provided with adequate medical treatment for all study-related AEs that constitute clinical problems during and after the subject's participation in the study. Further, when the principal investigator or sub-investigator becomes aware of the need for medical treatment of an AE, he/she shall so inform the subject.

The principal investigator or the sub-investigators shall confirm whether the subject has an another primary care physician or not, and with the subject's consent, inform the primary care physician of the subject's participation in the study.

If a subject desires to withdraw or withdraws participation during the study, the subject is not obliged to clarify the reason for withdrawal, but the principal investigator or sub-investigators 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.

Submission of documents to the certified review board

Before and during the study period, the principal investigator shall keep current those documents that are subject to review by the certified review board and are to be submitted by the principal investigator. If these documents are augmented, updates or revised, all must be submitted promptly to the representative investigator.

Permission from the administrator of the investigational site

The principal investigator should start the clinical research after the certified review board has approved the conduct of the study or approved the conduct study, subject to any modification, and after obtaining the permission of the administrator of the investigational site based on the approval from the certified review board and confirming publication of such medical institution site in the jRCT.

Use, etc., of the investigational product(s)

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

Compliance with clinical research protocol(s)

The principal investigator or sub-investigators shall not undertake any deviation from or modification of study trial protocol(s) without prior written agreement between the principal investigator and the sponsor and written approval based on prior inspection by the certified review board. 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).

Management of the deviations

Deviation is defined as a condition in which the study is non-compliance from the ministerial ordinance or clinical research protocol pertaining to the conduct of the Specified Clinical Trials. Deviations, regardless of the reason, shall be managed as follows. The principal investigator or sub-investigator must record all deviations from the clinical research protocol, regardless of the reason.

1) When the principal investigator finds a deviation, he/she shall promptly report it to the administrator of the investigational site and notify the representative investigator.
2) If a significant deviation is identified that may affect the human rights, safety of subjects, the progress of the clinical research and the reliability of the results (e.g., non-compliance with inclusion/exclusion criteria, termination criteria, etc.), the principal investigator shall promptly request the representative investigator to hear the opinion of the certified review board listed in the protocol.
   Significant deviations do not include failure to comply with the protocol for unavoidable medical reasons, such as to avoid immediate danger to the subjects.
3) When the sub-investigator becomes aware of a deviation, he/she shall promptly report it to the principal investigator.

Recording and reporting the CRF

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

The principal 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 principal investigator shall also inspect modifications or revisions to CRFs undertaken by sub-investigators, and confirm that there is no problem.

The principal 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 principal investigator shall prepare a record explaining the reason therefore, submit it to the sponsor, and retain a copy.

In modifying or correcting CRFs, the principal 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 principal investigator should submit records of modification and correction of the CRFs to the sponsor and retain a photocopy of each record.

19.2 Obligations of representative investigator

Reporting of the significant deviations

When the representative investigator recognize the significant deviation that may affect the human rights and safety of subjects, the progress of the research, and the reliability of the results (e.g., non-compliance with inclusion/exclusion criteria, termination criteria, etc.), he/she shall promptly hear the opinion of the certified review board listed in the protocol.

Significant deviations do not include failure to comply with the protocol for unavoidable medical reasons, such as to avoid immediate danger to the subjects.

The periodical reports to the certified review board

The representative investigator shall report the status of the progress of the Specified Clinical Trials to the administrator of the investigational site every year from the date of submission of the Trial Plan to the Minister of Health, Labour and Welfare, and within two months after the expiration of the period. In addition, the representative investigator should make periodic reports to the certified review board listed in the research protocol. The following items shall be reported on the status of progress/implementation;

- Number of subjects

- Occurrence of disease or the like and its progress
- Occurrence of deviations and subsequent actions
- Evaluation of safety and scientific validity
- Matters concerning the involvement of manufacturers described in the conflict of interest management standards

The periodical reports to the Minister of Health, Labour and Welfare

The representative investigator shall report the status of the progress of the Specified Clinical Trials with the following matters to the Minister of Health, Labour and Welfare within one month from the date on which the certified review board listed in the trial plan stated opinion;

- Name of the certified review board described in the Trial Plan
- Adequacy of continuation of this research judged by the certified review board
- Number of subjects
- Occurrence of the disease or the like and its progress
- Occurrence of deviations and subsequent actions
- Evaluation of safety and scientific validity
- Matters concerning the involvement of manufacturers described in COI management standards

Discontinuation of clinical research / Reporting of the study completion

When discontinuing the entire clinical research, the representative investigator should state the reason for the termination in the discontinuation notice (Clinical Trials Act format) and submit it to the certified review board within 10 days from the discontinuation date. At the same time, a notification form for discontinuation of the Specified Clinical Trials (Ministerial Ordinance Form) must be entered and notified to the Minister of Health, Labor and Welfare.

The representative investigator shall provide information with the principal investigator and, if necessary, hear the opinion of the certified review board regarding the timing and the method of completion of the study due to the subject's measures. Even if representative investigator submit a discontinuation notice, he/she shall continue to report disease or the like and periodic reports, etc. until the research is completed. If the trial plan needs to be changed, the change shall be notified.

In the case where the representative investigator submits a notification of discontinuation and completes the measures of the subject, he/she shall prepare a CSR within 1 year from the date of study discontinuation or the end of the period for collecting data related to all evaluation items, whichever is later. The representative investigator shall submit the CSR to the certified review board. In addition, the representative investigator shall also submit the CSR to both the administrator of the investigational site and the Minister of Health, Labor and Welfare.

Publication of research results and completion report

The representative investigator shall prepare the primary outcome report within a year from the date of the end of the collection period of the primary endpoint data, and hear the opinion of the certified review board using the

review request form for change (Clinical Trials Act format).After approval, the report should be registered in the jRCT and reported to the administrator of the investigational site. And the representative investigator shall submit the notification for changes in trial plan (Ministerial Ordinance Form) to the Minister of Health, Labor and Welfare.

The representative investigator shall prepare a CSR and a summary of CSR (Clinical Trials Act Exhibit Form) within a year of the completion from the date of the end of all data collection periods, and shall hear the opinion of the certified review board after preparation of a termination notice (Clinical Trials Act form). The representative investigator shall register the summary of CSR in the jRCT within one month of approval from the certified review board, and shall report it to the administrator of the investigational site and submit the summary of CSR along with the clinical research protocol and statistical analysis plan to the Minister of Health, Labor and Welfare.

The representative investigator shall provide information about the above to each principal investigators, and the principal investigators shall report it to the administrators of the investigational sites.

Retention of the records

The principal investigator shall refer to "15. RETENTION OF THE RECORDS" and storage the relevant materials appropriately.

Others

The representative investigator should report to the certified review board and the Minister of Health, Labour and Welfare as necessary and appropriate, including applications for changes and reports as stipulated in “Report of disease or the like to the certified review board and the Minister of Health, Labour and Welfare”.

20. INFORMED CONSENT

Time to obtain consent

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

Methods for explaining to trial subjects

The principal investigator (or sub-investigator) will give explanations to study 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 study subjects can understand.

Methods for obtaining consent

(1) The principal 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 study

subjects.)

(3) Supply the study subject with the consent document and explanation document describing aforementioned necessary information and take sufficient time for the study subject to decide whether or not he/she should participate in the clinical study.

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

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

(6) After obtaining the consent document signed and dated by the study subject, the principal 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 study subject with the copy (duplicate for the study subject) of the consent document and the explanation document before the study subject participates in the clinical study.

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

Items mentioned for the written informed consent form and explanatory documents

The items mentioned for the written informed consent form and explanatory documents are in accordance with "Clinical Study Protocol (version 3.0)" because the informed consent has been already obtained from all of the study subjects in this study.

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

(2) The purpose of the study.

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

(4) The study method (including the aspects of the trial that are experimental, subject's inclusion/exclusion criteria, and when the study 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 study 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 study.

(8) That participation in the study is voluntary; that the study subject can refuse to participate in the study or can withdraw from the study 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 study monitor, auditor, Institutional Review Board (IRB), and regulatory authorities are allowed to examine the source data, that the confidentiality of the study 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 study or their rights, or if they develop a health problem associated with the study.
(13) The compensation and medical treatment the study subjects can receive should they develop a health problem associated with the study.
(14) The number of subjects expected to be enrolled in the study (including discrete variable).
(15) That if information is received that may affect the will of the subjects regarding the subjects' ongoing participation in the study, that information will be passed on promptly to the subjects.
(16) The circumstances under which or the reasons subjects will be withdrawn from the study.
(17) The specifics about any expense the study subjects will have to pay.
(18) The specifics about any cash or the like that will be paid to the study subjects (including the arrangement for calculating the sum to be paid).
(19) Responsibilities of the study subjects.
(20) Information about IRB.
(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 principal 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 study subject's intention to continuously participate in the clinical study or in other cases, the principal investigator shall immediately report it to the representative investigator. The representative investigator inform the other principal investigator of it immediately. The principal investigator shall revise the explanatory document as needed (refer to "12. PROTOCOL AMENDMENTS"). The representative investigator will hear the opinion and obtain approval of the revision of explanatory document from the certified review board which is described in the clinical clinical research protocol. And then, the principal investigator will obtain approval of the revision of explanatory document from the administrator of the investigational site based on the results of the review.

21. PROVIDE SERVICES RELATED To CONDUCTING RESEARCH

In this clinical research, Alcon Japan provides the following services. The following services will be entrusted to Alcon Japan under the responsibility of the principal investigator and conducted supervised by the representative investigator.

Details of the services to be provided: Creating a protocol, data management, monitoring, statistics, analysis, audit, creating reports, registration and updating of jRCT etc.

22. CONFLICT OF INTEREST

Alcon Japan Ltd. is the sponsor of this clinical study. Alcon Japan Ltd. and the administrator of the investigational site 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.

Regarding cost of the central evaluation, Alcon Japan Ltd. [redacted] will sign a contract for collaborative research about the central evaluation. Financial cost of the central evaluation will be sponsored by Alcon Japan Ltd. in accordance with the contract. [redacted]

23. REFERENCES

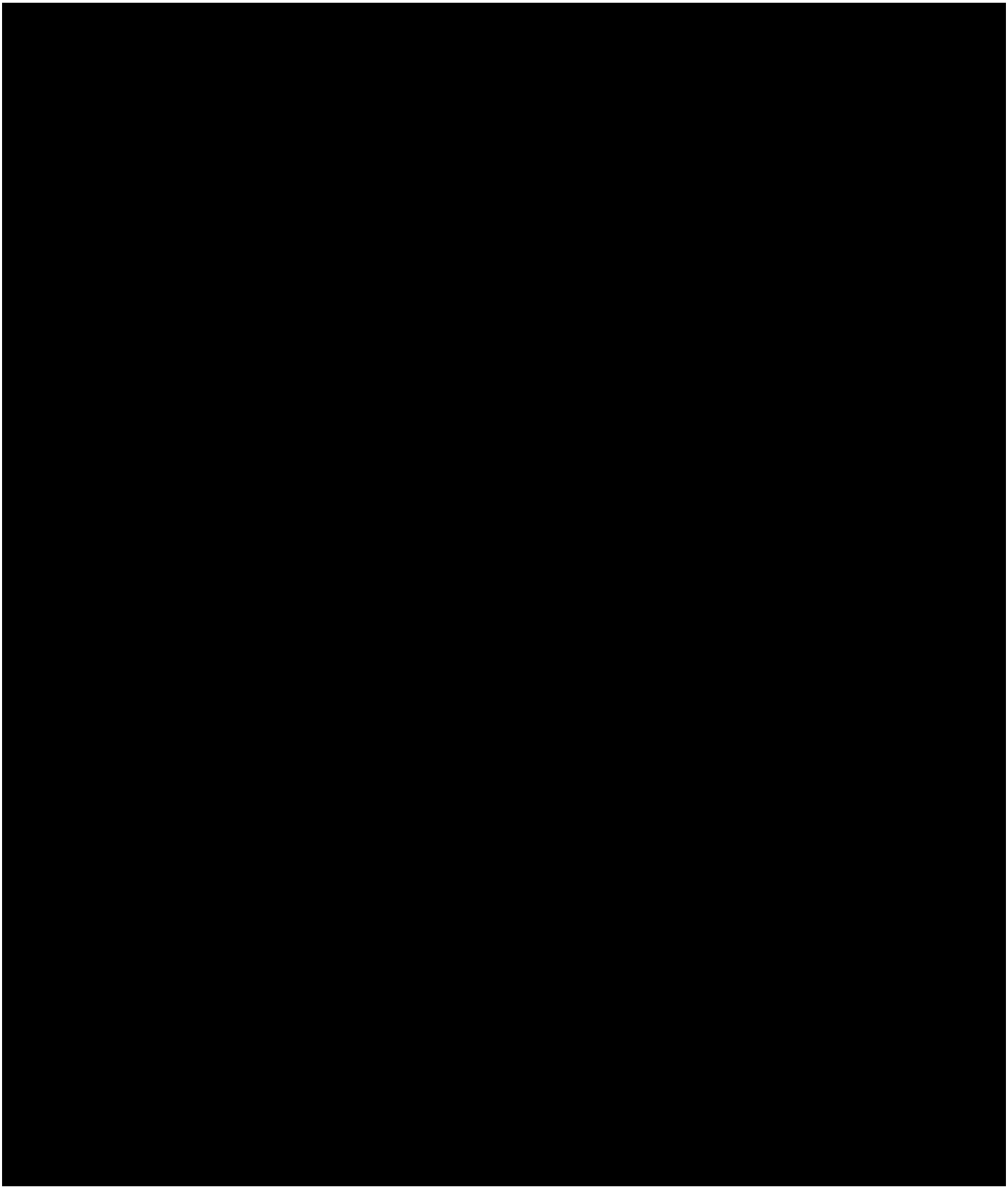
1） Shinichi Ito. Medical insurance and intraocular lenses. Journal of the Eye, 20: 615-620, 2003.

2） Ken Hayashi. New foldable intraocular lenses. Japanese Journal of Cataract and Refractive Surgery, 16: 453-458, 2002.

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

4） Toshiyuki Miyake. Corneal astigmatism before cataract surgery. Journal of Japanese Ophthalmological Society, 115: 447-453, 2011.

5） Kimiya Shimizu, et al. Toric intraocular lenses correcting astigmatism while controlling axis shift. J Cataract Refract Surg., 29: 523-526, 1994.



AcrySof IQ Toric A-code Post Market Clinical Study

Clinical Research Protocol
Supplemental Attachment

A Clinical Trial System, Participating Facilities and Principal Investigators
B Package Insert: Alcon® AcrySof® IQ Toric Single-Piece IOL
C Grading Scales for Glistening
[redacted]
[redacted]
F Creation and Storage of Records Relating to the Provision of Samples and Information

Alcon Japan Ltd.

Toranomon Minato-ku, Tokyo

[redacted]

Protocol No.：ILV814-P001
Ver.4.0: January 5, 2021
Ver.5.0: March 22, 2021

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

1. CLINICAL TRIAL SYSTEM

1.1 Sponsor

Alcon Japan Ltd. Representative: Richard Kozloski, CEO

1-23-1 Toranomon, Minato-ku, Tokyo, 105-6333, Japan

TEL: 03-6899-5061/FAX: 03-6257-3650

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Supplemental Attachment B: Package Insert

40-500-123-005
15-22 アルコン® アクリソフ® IQ トーリック シングルピース
**2017年4月改訂（第7版）
*2011年8月改訂（第6版）

医療機器承認番号：22000BZX01199000

機械器具72 視力補正用レンズ
高度管理医療機器 後房レンズ JMDNコード：35658100

アルコン® アクリソフ® IQトーリック シングルピース

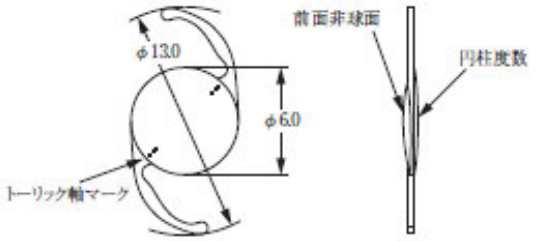
（モデル：SN6AT3、SN6AT4、SN6AT5、SN6AT6、SN6AT7、SN6AT8、SN6AT9）

再使用禁止

【禁忌・禁止】
＜使用方法＞
1. 再使用禁止。
2. 再滅菌禁止。

【形状・構造及び原理等】
[材質]
光学部：紫外線・青色光吸収剤含有アクリル樹脂
支持部：紫外線・青色光吸収剤含有アクリル樹脂
紫外線・青色光吸収剤：エチルメタクリルアミド系

[形状]
光学部形状：非対称両凸



（単位：mm）

[仕様]
モデルの仕様の詳細は、別表あるいは外箱若しくはレンズケース（容器）に記載してある表示値を参照のこと。

[滅菌方法]
エチレンオキサイドガス滅菌

【使用目的又は効果】
角膜乱視を有する無水晶体眼の視力補正

【使用方法等】
無菌的に取り出し、術後の無水晶体眼に挿入する。

[レンズパワーの計算][1)2)3)4)]
A-定数は参考値である。
眼内レンズ度数を算定する場合には、術者の経験、手術手技及び眼内レンズの予測固定位置等に基づき、決定すること。

モデル	A-定数
SN6AT3, SN6AT4, SN6AT5, SN6AT6, SN6AT7, SN6AT8, SN6AT9	119.0

＜使用方法等に関連する使用上の注意＞
1. 本眼内レンズは、嚢内に挿入すること。[前房への挿入及び毛様溝への固定の安全性及び有効性は確認されていない]
**2. 開封前に、眼内レンズの種類、度数及び使用期限について表示を確認すること。[種類や度数が異なった眼内レンズを使用した場合、摘出交換手術が必要になるおそれがある]
3. 開封後、眼内レンズは無菌的に取り扱うこと。
4. 挿入前に、眼内レンズに損傷、その他の異常がないことを確認すること。[破損している眼内レンズを挿入した場合、組織を侵襲したり、眼内レンズの固定状態に影響するおそれがある]
**5. 挿入前に、眼内レンズ表面に異物や塵埃等付着物の無いことを確認すること。[異物等が付着したまま眼内に挿入されると、術後炎症を引き起こすおそれがある]
6. 挿入前に、眼灌流液（ビーエスエスプラス®500眼灌流液0.0184%等）で眼内レンズをよく濯ぐこと。眼灌流液以外の液体では決して眼内レンズを洗浄しないこと。
7. 眼内レンズを折り畳んで挿入するときは、適切な挿入器具を選び、予めその使用方法に十分習熟してから行うこと。鑷子は、眼内レンズに損傷をきたさないよう、縁の丸く研磨され、表面に鋸状の刻みのないものを使用すること。

【使用上の注意】
＜使用注意＞（次の患者には慎重に適用すること）
**1. 小児（「重要な基本的注意」の項参照）
2. 角膜内皮障害
3. 緑内障
4. ぶどう膜炎
5. 糖尿病網膜症
6. 網膜剥離
7. 先天性眼異常
8. 脈絡膜出血
9. 重篤な眼疾患の合併
10. 浅前房
11. 小眼球
12. 角膜ジストロフィ
13. 視神経萎縮
14. 高眼圧
15. 散瞳不良
16. 弱視
17. 角膜移植の既往のあるもの
18. 虹彩炎
19. 角膜異常
20. 黄斑変性症
21. 網膜変性症
22. 臨床的に顕著な黄斑、網膜色素上皮の変化
23. 角膜不正乱視
24. 色覚異常
25. 次の状態にある患者
－capsulorrhexis（CCC 法）以外の前嚢切開を施術されている患者
－手術中に放射状の嚢亀裂が生じた、又はその疑いのある患者
－capsulorrhexis（CCC 法）が完全に行われていることを直接視認できない状態の患者
－水晶体乳化吸引術以外での水晶体摘出患者
－大きな前嚢切開径が必要と思われる患者（糖尿病患者、対側眼の網膜剥離、周辺部の網膜病変等）
26. アトピー性疾患
27. 偽落屑症候群及びチン小体脆弱例
28. チン小帯断裂及び水晶体脱臼（亜脱臼を含む）
29. 虹彩血管新生
30. 重篤な術中の有害事象発生症例
31. その他、全身的、眼科的理由により医師が慎重適応と判断した場合

[2～31 原疾患の悪化やその他有害事象が発現しやすくなる可能性があるため]

色覚が正常な患者において、本眼内レンズによる色の識別に対する悪影響は認められていない。遺伝性の色覚異常や眼疾患（緑内障、糖尿病網膜症、慢性のぶどう膜炎、その他網膜や視神経疾患等）による続発性色覚異常を有する患者における、本眼内レンズの視覚への影響についての臨床試験は実施していない。

*＜重要な基本的注意＞
1. 手術に先立ち、本眼内レンズ挿入の対象となる患者に、本眼内レンズの使用にともなって予期される効果と有害事象等の危険性について十分に説明すること。
2. 使用注意にあたる患者については、合併症の発生率が高くなる可能性や、十分な視力が得られない可能性があるため、十分な設備と使用経験を持つ眼科専門医のもとで、術後のフォローアップを含め適切に適用すること。
3. 小児については、小児の特性等について十分な知識と経験を有する眼科専門医のもとで眼内レンズ挿入術を行うこと。特に2歳未満の小児においては、眼球のサイズから器具の挿入や操作が難しくなること、成長に伴う眼軸長の変化によって再手術の可能性が高くなることが報告されていることからも、その旨を含めた十分なインフォームドコンセントを保護者に対して行うこと。
4. 活動期にあるぶどう膜炎や小児のぶどう膜炎患者については、外科的侵襲を加えることで、ぶどう膜炎の悪化や新たな合併症を引き起こすおそれがあるため、あらかじめ薬物治療を行い、炎症を鎮静化させた上で、眼内レンズ挿入術を行うこと。
5. 眼内レンズに損傷をきたさないよう、十分注意して操作を行うこと。
6. 「モナーク®ハンドピース」「IOLデリバリーシステム（カートリッジ）」等弊社が推奨する挿入器具の取扱い方法及び使用上の注意については、各製品の添付文書を参照のこと。
7. このレンズは後房が破裂していたり、チン小帯が損傷していたり、大きな後嚢切開を予定している場合には挿入しないこと。
8. 本眼内レンズは、予定している円柱軸の回転により、その乱視矯正効果が弱くなる。30°以上の円柱軸のずれは術後屈折乱視を悪化させる可能性がある。必要がある場合は、レンズが水晶体嚢へ癒着する前の、なるべく早い時期にレンズ再配置を実施すべきである。いくつかの臨床例において、挿入の4週間以内にこの癒着が起こることが報告されている。
9. レンズの前面及び後面にある全ての粘弾性物質を注意深く除去すること。残った粘弾性物質は、本眼内レンズの予定している円柱軸をずらすようにレンズを回転させる可能性がある。
10. 臨床試験では、切開位置を耳側切開に統一したため、耳側以外の切開での有効性は確立されていない。
11. 強度乱視の患者では、光学理論上、歪んだ見え方を生じる可能性がある。本眼内レンズが関係する因子としては、残存した乱視度数誤差または眼内レンズの軸ずれがある。
12. 本眼内レンズは、経年的に発症してくる乱視に対しては矯正できない。

＜相互作用＞（他の医薬品、医療機器等との併用に関すること）
〈併用注意〉（併用に注意すること）
本製品とIOLデリバリーシステム（カートリッジ）と組合せて使用する場合は、下表に示す組み合わせを厳守すること。異なる組合せのカートリッジを使用すると、眼内レンズを損傷するおそれがある。
眼内レンズモデルとカートリッジタイプの組合せ

眼内レンズモデル	カートリッジタイプ
SN6AT3, SN6AT4, SN6AT5	B
	C†
	D††
SN6AT6, SN6AT7, SN6AT8, SN6AT9	B
	C†††
	D††††

†30.0Dまでの使用に限る。
††25.0Dまでの使用に限る。
†††27.0Dまでの使用に限る。
††††23.0Dまでの使用に限る。

＜不具合・有害事象＞
眼内レンズ挿入術に伴い、以下のような不具合・有害事象が発生することがある。その際、レンズ挿入中止や摘出・再挿入が必要になる他、場合によっては、失明または不可逆的な視力障害等の重大な健康被害をきたすおそれがある。

〈その他の不具合〉
1. レンズ光学部損傷（破損、キズ等）
2. レンズ支持部損傷（破損、脱落、変形等）
3. レンズ表面への異物付着
4. レンズ表面反射
5. レンズ光学部の変色・偽着色・グリスニング
6. レンズ混濁
7. レンズ脱臼
8. レンズ偏位
9. レンズ落下

〈その他の有害事象〉
1. 角膜浮腫
2. 角膜炎（角膜びらんを含む）
3. 角膜内皮障害
4. 急性角膜代償不全
5. デスメ膜剥離
6. 結膜炎・結膜下出血
7. 前房出血
8. 前房蓄膿
9. 虹彩損傷
10. 虹彩炎（虹彩毛様体炎）
11. 虹彩癒着
12. 虹彩脱出
13. 瞳孔異常（ブロック、捕獲、変形、散大等）
14. ぶどう膜炎
15. チン小帯断裂
16. 毛様体炎膜
17. 後嚢破損
18. 後発白内障
19. 硝子体炎
20. 硝子体出血・混濁
21. 硝子体脱出
22. 網膜組織（黄斑等）の剥離・円孔・裂孔等
23. 網膜剥離
24. 脈絡膜剥離
**25. 脈絡膜出血
26. 黄斑浮腫・変性
**27. 駆逐性出血
28. 眼内炎
29. フィブリン析出
30. 続発緑内障
31. 眼圧上昇（一過性眼圧上昇、高眼圧を含む）
32. 眼圧低下
33. 色視症
34. 視機能低下（視力・コントラスト感度）
35. 予想屈折値誤差
36. 創口閉鎖不全

＜その他の注意＞
1. 折り曲げによる鑷子痕が光学部に残るのを防ぐため、使用するすべての器具類は、よく洗浄してから使用すること。
2. 挿入器具については、各製品の添付文書に従って注意深く操作すること。
3. 室温より低い温度の場所で保管している場合は、使用前に眼内レンズを室温に保つこと。ただし、人為的に加温するなど急激な温度変化を与えないこと。
4. 眼内レンズを取り出す際、光学部を鑷子で把持しないこと。また、眼内レンズの折り曲げ操作をするまでは支持部を持つこと。
5. 支持部を変形させるような操作は行わないこと。

6. 光学部表面及び支持部に損傷を与えないよう、注意深く操作すること。眼内レンズを操作中には、光学部をきつく把持したり、光学部に繰り返し強い力をかけないこと。
7. capsulorrhexis（CCC法）によるPMMA、シリコーンおよびアクリルの後房レンズの挿入に際して、浅前房と誘発近視を伴う術後の水晶体嚢の拡張（capsular bag distension）が合併することがある、との報告がある。[5]
8. 眼内レンズを固定する際、支持部と光学部が密着している場合は、フックあるいは鑷子等を用いて支持部と光学部を離し、手術終了前に眼内レンズの位置を矯正しておくこと。眼内レンズの支持部と光学部を密着したまま放置すると、眼内レンズの中心固定に支障をきたすことがある。
9. 本製品に同封されている眼内レンズ患者用カードに必要事項を記入し、患者に提供すること。他の医療機関を受診する際は、眼内レンズ患者用カードを提示するよう患者を指導すること。

【臨床試験】

11医療機関にて球面モデル（SA60T3、SA60T4及びSA60T5）について術前の直乱視または斜乱視度数が0.75D以上、あるいは倒乱視度数が1.00D以上の角膜乱視を有する老人性白内障患者を対象に、既承認のアルコン® アクリソフ® シングルピース[1]を比較対照とした臨床試験を米国にて実施した。眼内レンズの挿入例数および眼数は、本レンズ256例301眼、対照レンズ261例285眼であり、裸眼視力および残存円柱屈折力を比較し、本レンズのIOL回転量を測定した。

その結果、第1術眼の術後330－420日における分数視力20/40以上の達成率は、本レンズ92.2%（224/243眼）、対照レンズ81.4%（193/237眼）であった。また、残存円柱屈折力1.00D以下の割合は、本レンズ88.0%（213/242眼）、対照レンズ48.1%（114/237眼）であり、本レンズの残余乱視は軽度であった。

IOL回転量（角膜強主経線軸とIOL弱主経線軸のずれ）は、レンズ挿入時0.3° ±1.4°であり、正確に眼内に挿入された。術後330－420日までにIOL回転量が5°以内であった割合は、78.0%以上であり、IOL回転量は少なく、眼内で安定していた。なお、本レンズの不具合は、挿入後にレンズが眼内で回転したことに対処した「位置修正処置」および「IOL交換」の1眼（0.3%）2件が認められた。

[1]医療機器承認番号：21100BZY00116000

6医療機関で、予測術後角膜乱視が第1術眼で4.11～4.62D、第2術眼で3.60～4.62Dの老人性白内障患者15例を対象に、臨床試験を実施した。眼内レンズの挿入眼数は、第1術眼にSN60T9を15眼、第2術眼にSN60T9を3眼、SN60T8を12眼であり、歪んだ見え方に関するアンケートを実施し、術後の乱視の軽減及び眼内レンズの軸ずれを測定した。

その結果、術後120－180日での第1術眼の乱視軽減率は、85.67±15.58%であり、目標乱視度数との誤差が、0.50D以内は33.3%（5/15例）、1.00D以内は93.3%（14/15例）であった。また、手術時、眼内レンズ軸の目標位置と実際に挿入した位置の差は、0.3° ±0.7°であった。被験者アンケートで術後、歪んで見えると答えたのは2/15例であったが、眼内レンズ軸ずれとは関係がなかった。重篤な有害事象は、残存屈折異常調整のためレンズ軸を修正する二次手術を施行した1例1眼のみであり、レンズとの関連性は否定されている。歪んだ見え方の処置として二次手術が行われた症例はなかった。他に安全性で問題となる所見は認められなかった。

【保管方法及び有効期間等】

＜保管方法＞

高温多湿や直射日光を避けること。
45℃以上の高温では保存しないこと。

＜有効期間＞

使用期限は外箱に記載。

【主要文献及び文献請求先】

＜主要文献＞

1) Hoffer, K.J. The Hoffer Q formula: A comparison of theoretic and regression formulas. *J. Cataract Refract. Surg.* 19: 700-712, 1993.
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[文献請求先・製品情報お問い合わせ先]

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（別表）各モデルの代表度数の仕様

	項 目	単 位	SN6AT3	SN6AT4	SN6AT5	SN6AT6	SN6AT7	SN6AT8	SN6AT9
仕様	光学部径	mm	6.0	6.0	6.0	6.0	6.0	6.0	6.0
	全長	mm	13.0	13.0	13.0	13.0	13.0	13.0	13.0
	有効光学部径	mm	6.0	6.0	6.0	6.0	6.0	6.0	6.0
	円柱屈折力	D	1.50	2.25	3.00	3.75	4.50	5.25	6.00

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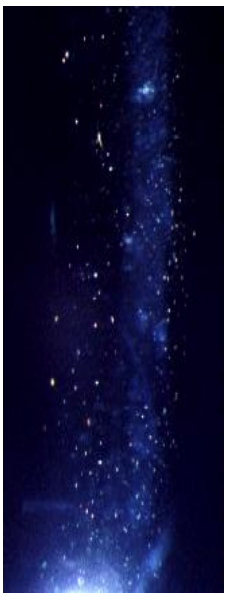
Supplemental Attachment C: Grading Scales for Glistening

Frequency of the glistening in optic segment of IOL shall be observed by slit-lamp and assessed using following scales.

Grade 0	Grade 1	Grade 2	Grade 3
No glistening	Mild ($50/mm^3$)	Moderate ($100/mm^3$)	Severe ($200/mm^3$)
			

Reference: Akira Miyata. Glistening particles on the implanted acrylic intraocular lens. Japanese Journal of Clinical Ophthalmology, 51(4): 729-732, 1997.