Post-market Clinical Study of AcrySof IQ PanOptix Intraocular Lens In Chinese Population

STUDY ID
ILH297-C004

PROTOCOL

NCT04755231

Medical Device Clinical Trial Protocol

Post-market Clinical Study of AcrySof IQ PanOptix Intraocular Lens

In Chinese Population

Protocol number: ILH297-C004

Name of investigational medical device: AcrySof® IQ PanOptix® Presbyopia Correcting Intraocular Lens

Model and specification: TFNT00

Management category of investigational medical device:

Class III medical device requiring clinical trial examination and approval: Yes □No☑

Similar products within the territory of China Yes☑ No□

Protocol version number and date: V2.0 Nov 5, 2020

Clinical trial institution (leading site): The Second Affiliated Hospital of Zhejiang University

[redacted]

Sponsor: Alcon Research, LLC. ("Alcon")

6201 South Freeway Fort Worth, Texas 76134-2099

Agent: Alcon (China) Ophthalmic Product Co., Ltd.

7/F, No. 20 Building, Jiuxianqiao Road, Chaoyang District, Beijing 100016, China

Filling instructions:

1. For multi-center clinical trials, the clinical trial institutions on the cover only fill in the lead unit, and other institutions are listed in the protocol content.

2. For multi-center clinical trials, the investigator on the cover should fill in the coordinating investigator.

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I. Sponsor's Information

(I) Sponsor's Name

Sponsor: Alcon Research, LLC. ("Alcon")

(II) Sponsor's Address

6201 South Freeway Fort Worth, Texas 76134-2099

[redacted]

(IV) Sponsor's Relevant Qualification Documents

See the business license, medical device business certificate and other qualification documents.

(V) Agent's Name, Address, Contact Information and Relevant Qualification Documents

Agent's name: Alcon (China) Ophthalmic Product Co., Ltd.

Address and contact information: 7/F, No. 20 Building, Jiuxianqiao Road, Chaoyang District, Beijing, China

See the business license, medical device business certificate and other qualification documents.

II. Lists of All Clinical Trial Institutions and Investigators in the Multi-center Clinical Trial

Principal investigator (Coordinating investigator): [redacted] (The Second Affiliated Hospital of Zhejiang University)

The lists of all participating clinical trial institutions and investigators have been attached as separate documents.

III. Clinical Trial Objective and Content

(I) Objective

The objective of this clinical study is to assess the clinical performance of PanOptix® Intraocular Lens (model: TFNT00) in Chinese population, especially the observation of visual acuity and adverse events related to vision (visual disturbance). The data in this clinical study will be submitted to the National Medical Products Administration for renewal registration of PanOptix® Intraocular Lens.

(II) Content

This clinical study is a prospective, single-arm, multi-center, post-marketing clinical study. The study is designed based on the *Guidelines for Clinical Trials of Intraocular Lenses* (hereinafter referred to as the Guidelines), and refers to the content about clinical trials in ISO11979-7.

The product in this clinical study is PanOptix Intraocular Lens (model: TFNT00), which is an ultraviolet and blue light filtering foldable multifocal IOL. It is intended for implantation in the capsular bag in the posterior chamber of the human eye to replace the human eye lens. This position allows the IOL to function as a refractive medium, thereby correcting the aphakic state. The IOL is a biconvex optical surface design, and its front surface includes an aspheric design and a diffractive structure. The diffractive structure divides the incoming light to provide distance, intermediate, and near vision ranges. The IOL provides clinicians with more options by providing a +2.17 D addition power of intermediate visual acuity and a +3.25 D addition power of near visual acuity. This product is suitable for adult patients who require primary implantation of an intraocular lens in the capsular bag in the posterior chamber after cataract extraction with distance, intermediate and near visual acuity requirements so as to improve near, intermediate and distance visual acuity and reduce spectacle dependence.

In this clinical study, subjects will receive binocular implantation of PanOptix Intraocular Lens. In terms of effectiveness, the study will mainly assess the visual performance at Month 6 after surgery; in terms of safety, the study will mainly assess the safety of TFNT00 at Month 6 and Month 12 after surgery. All the effectiveness and safety evaluation indicators will be followed up to Month 12 after surgery, and an interim analysis will be performed on the data when all subjects have completed the 6-month follow-up.

The clinical study will be carried out at approximately 8 clinical trial institutions with relevant qualifications, and approximately 142 implanted subjects (284 eyes) will be included.

See Table 3-1 for a summary of the study protocol. The acronyms and abbreviations used in this protocol are shown in Table 3-2.

Table 3-1 Protocol summary

Study Title	Post-market Clinical Study of AcrySof IQ PanOptix Intraocular Lens in Chinese Population
Study Objective	To assess the clinical performance of PanOptix® Intraocular Lens in Chinese population, especially the observation of visual acuity and adverse events related to vision (visual disturbance).
Study Product	Intraocular Lens AcrySof IQ PanOptix Presbyopia Correcting Intraocular Lens (Model: TFNT00)
Study Design	A prospective, single-arm, multi-center, post-marketing clinical study
Sample size	Enrolled: 158 subjects Implanted: 142 subjects (284 eyes) Completed: At least 127 subjects (254 eyes) available for evaluation at 12 months
Sites	It is expected that 8 sites will participate in the clinical study in China

Study Population	Adult Chinese subjects, 18 years of age or older, who require primary implantation of an intraocular lens in the capsular bag in the posterior chamber after cataract extraction with distance, intermediate and near visual acuity requirements so as to improve near, intermediate and distance visual acuity and reduce spectacle dependence.
Inclusion Criteria	Eligible subjects must meet all of the following inclusion criteria: 1) Able to comprehend and sign an informed consent form. 2) Adult Chinese subjects, 18 years of age or older, diagnosed with **bilateral** cataracts. 3) Pre-operative regular corneal astigmatism of less than 1.0 D. 4) Planned bilateral cataract removal by routine phacoemulsification. 5) Calculated IOL power between +6.0 D and +34.0 D. (when targeted for emmetropia 0.0 D) 6) Able to complete all study visits required in the protocol. 7) Pre-operative best corrected distance visual acuity (BCDVA) worse than or equal to 0.3 LogMAR in each eye. 8) Potential postoperative best corrected distance visual acuity (BCDVA) of 0.3 logMAR or better in both eyes based on the investigator expert medical opinion.
Exclusion Criteria	Subjects who do not meet the inclusion criteria or meet any of the following exclusion criteria will be excluded: 1) History of anterior segment (corneal, anterior chamber, sulcus) or posterior segment (uveal, vitreo-retinal) pathologic change including retinal vascular occlusive disease, retinal detachment or peripheral retinal laser photocoagulation, ARMD, glaucoma, diabetic retinopathy, retinitis pigmentosa and any pathologic changes associated with the optic nerve. 2) Corneal Endothelial Cell Count less than 2000 cells/mm^2. 3) History of recurrent anterior segment/posterior segment inflammation. 4) Clinically significant corneal diseases (epithelium, stromal, and/or endothelium) may, according to the investigator's medical opinion, adversely affect visual outcomes. These ocular pathologies include but are not limited to old significant corneal scars (including Salzman’s nodular degeneration), active or inactive keratitis with compromise of the refractive capability of the cornea, keratoconjunctivitis sicca with compromise of visual function, active keratouveitis, endothelial dystrophy (Fuch’s and non-guttate),keratoconus, etc. (Note: Patients with any pathological manifestations that may potentially affect postoperative visual acuity should not be included in this study) 5) Clinically significant/severe dry eye that would affect study measurements based on the investigator’s expert medical opinion. 6) History of previous intraocular or corneal (refraction or trauma related) surgery. 7) Currently or planning to be pregnant/lactating or has another condition with associated fluctuation of hormones that could lead to refractive changes. 8) Current or past history of amblyopia or monofixation syndrome with poor

	stereoscopic vision. 9) Systemic medications that, in the opinion of the investigator, may confound the outcome or increase the risk to the subject (e.g. Tamsulosin Hydrochloride – Flomax) or other medications including anticholinergics, alpha adrenergic blocking agents with similar side effects (e.g. small pupil/floppy iris syndrome) 10) Any subject currently participating in another investigational drug or device study that may confound the results of this investigation. 11) Any other ocular or systemic co-morbidity that, in the investigator's medical opinion, may confound the results of this study or prohibit the completion of the study assessments or increase the risk for the subject. 12) Subjects with conditions that increase the risk of zonular rupture during cataract extraction procedure that may affect the postoperative centration or tilt of the IOL (e.g., patients of exfoliation Syndrome, Marfan syndrome). 13) Any other planned ocular surgical procedures including but not limited to limbal relaxing incision (LRI)/Astigmatic Keratotomy and laser-assisted in situ keratomileusis (LASIK). 14) Subjects who desire monovision correction.
Reasons for non-implantation* (During Surgery)	1) Surgical complications including but not limited to loss of zonular integrity/zonular weakness, zonular rupture, anterior or posterior capsule rupture interfering with the stability of the IOL, any evidence of fluid misdirection during the cataract procedure with progressive shallowing of the anterior chamber, uncontrollable IOP. Mechanical manipulation of the pupil during surgery. 2) Mechanical or Surgical Manipulation of the pupil. 3) Excessive iris mobility. 4) Inability to place the IOL in the capsular bag due to surgical complications. *If the first eye implantation was aborted and the **IOL did not touch the eye**, then the subject is required to discontinue from the study and standard of care for IOL is followed. If the implantation was aborted and **the IOL did touch the eye,** then the subject is encouraged to attend all follow-up study visits for safety evaluation on this eye only. Please refer to Table 7-6 for detail information.
Primary Effectiveness Endpoints	All effectiveness endpoints will be described for each visit, with postoperative Month 6 visit results being the key endpoint. • The percentage of eyes with Best Corrected Distance Visual Acuity (BCDVA) of 0.3 LogMAR or better • Mean monocular and binocular BCDVA • Mean monocular and binocular Distance Corrected Intermediate Visual Acuity (DCIVA) (60 cm) • Mean monocular and binocular Distance Corrected Near Visual Acuity (DCNVA) (40 cm)
[redacted]	[redacted]

<table>
<tr><td></td><td></td></tr>
<tr><td>Primary Safety Endpoints</td><td>All safety endpointswill be discribed at each visit, with postoperative Month 6 and Month 12 results being the key endpoints.
Estimate the rates of ocular adverse events
Estimate the rates of secondary surgical interventions (SSIs)
Estimate rates of severe and most bothersome visual disturbances as reported by the subjects using a questionnaire (QUVID)</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Follow-up</td><td>
<table>
<tr><td>The surgery day is Day 0</td><td>First eye</td><td>Second eye</td></tr>
<tr><td>Day -28 to Day 0</td><td colspan="2">Visit 0 (screening of both eyes)</td></tr>
<tr><td>Surgery day (Day 0)</td><td>Visit 00 (Day 0)</td><td>Visit 00A*(Day 0)</td></tr>
<tr><td>Post-op Days 1-2</td><td>Visit 1 (Day 1)</td><td>Visit 1A (Day 1)</td></tr>
<tr><td>Post-op Days 7-14</td><td>Visit 2 (Week 1)</td><td>Visit 2A (Week 1)</td></tr>
<tr><td>Second eye: Post-op Days 30-60</td><td colspan="2">Visit 3A (Month 1)</td></tr>
<tr><td>Second eye: Post-op Days 90-120</td><td colspan="2">Visit 4A (Month 3)</td></tr>
<tr><td>Second eye: Post-op Days 180-210</td><td colspan="2">Visit 5A (Month 6)</td></tr>
<tr><td>Second eye: Post-op Days 360-390</td><td colspan="2">Visit 6A (Month 12)</td></tr>
</table>
* The second eye implantation occurs at 7-28 days after the first eye implantation.
</td></tr>
<tr><td>Statistical</td><td>Sample size calculation:</td></tr>
</table>

Considerations	• Enrolled: 158 subjects • Implanted: 142 subjects (284 eyes) • Completed: 127 evaluable subjects (254 eyes) [redacted] **Analysis plan:** • There are no statistical hypotheses for the safety and effectiveness objectives in this study. • Planned analyses include a descriptive summary of all effectiveness and safety endpoints. Monocular effectiveness and safety endpoints will be presented separately by the first and second implanted eyes and all eyes. • Descriptive statistics generated for all endpoints will be based upon the data type (i.e., whether the data are categorical or continuous) being analyzed. For categorical endpoints, sample size, number in the category, and percent in the category will be presented. For continuous endpoints, sample size, mean, median, standard deviation, minimum, maximum, and two-sided 90% confidence intervals will be presented. • Visual acuity will be summarized as a continuous variable. Additionally proportion of subjects who achieve BCDVA of 0.3 logMAR or better will be presented. [redacted] • An interim analysis of all data is planned at approximately 6 months after the second eye had been implanted for all subjects.

Table 3-2 shows the acronyms and abbreviations used in this protocol

Acronym	English name	Chinese name
ACD	Anterior chamber depth	前房深度
ADE	Adverse device effect	医疗器械不良反应

AE	Adverse event	不良事件
AL	Axial length	眼轴长度
ARMD	Age-related macular degeneration	年龄相关性黄斑变性
BCDVA	Best corrected distance visual acuity	最佳矫正远视力
cm	Centimeter	厘米
CRF	Case report form	病例报告表
D	Diopter	屈光度
DCIVA	Distance corrected intermediate visual acuity	远距离矫正下中距离视力
DCNVA	Distance corrected near visual acuity	远距离矫正下近视力
DD	Device deficiency	器械缺陷
DEP	Deviations and evaluability plan	方案偏离和可评估性计划
DFU	Directions for use	使用说明书
EDC	Electronic data capture	电子数据采集
FLACS	Femtosecond laser-assisted cataract surgery	飞秒激光辅助下白内障手术
FAS	Full analysis set	全分析集
GCP	Good Clinical Practice	临床试验质量管理规范
GPCMS	Global Product Complaint System	全球产品投诉管理系统
ICF	Informed consent form	知情同意书
IEC	Independent ethics committee	伦理委员会
IOL	Intraocular lens	人工晶状体
[redacted]	[redacted]	[redacted]
IOP	Intraocular pressure	眼内压
IP	Investigational product	研究产品
ISO	International Organization for Standardization	国际标准化组织
m	Meter	米
μm	Micrometer	微米
mm	Millimeter	毫米
mmHg	Millimeters of mercury	毫米汞柱
MIOL	Multifocal intraocular lens	多焦点人工晶状体
N/A	Not applicable	不适用
Nd:YAG	Neodymium-doped yttrium aluminium garnet	掺效乙铝石榴石激光
OD	Right eye	右眼

OS	Left eye	左眼
OVD	Ophthalmic viscosurgical devices	粘弹剂
PC	Posterior capsulotomy	后囊切开术
PCO	Posterior capsular opacification	后囊膜混浊
PI	Principal Investigator	主要研究者
PP	Per protocol	符合方案集
QUVID	Questionnaire for Visual Disturbances	视觉干扰症状调查问卷
RD	Retinal detachment	视网膜脱离
SADE	Serious adverse device effect	器械严重不良反应
SAE	Serious adverse event	严重不良事件
SAS	Safety analysis set	安全性分析集
SD	Standard deviation	标准差
SOP	Standard operating procedures	标准操作流程
SSI	Secondary surgical intervention	二次手术介入
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
UNSV	Unscheduled visit	计划外访视
US	United States	美国
USADE	Unanticipated serious adverse device effect	非预期的严重不良反应
VA	Visual acuity	视力

IV. Background Information of the Clinical Trial

Cataract is the leading blinding eye disease worldwide, and surgery is currently the only effective treatment. In recent years, with the increasing improvement of cataract extraction techniques and the application of a variety of new functional IOLs in clinical practice, patients also have higher requirements for visual quality after cataract extraction, including postoperative distance, intermediate and near vision, spectacle independence rate, etc. Therefore, cataract extraction has entered the era of refractive surgery from the era of blindness prevention surgery.

In recent years, the design and materials of multifocal intraocular lenses (MIOL) have been continuously improved, and MIOL is thus more and more clinically used, thereby greatly improving the accuracy of distance, intermediate and near vision after surgical treatment of cataract patients [1].

The investigational product PanOptix IOL used in this study is a multifocal intraocular lens. It was approved by the National Medical Products Administration on December 26, 2019. At the same time, after registration, the production enterprises still need to complete the following tasks: clinical follow-up should be carried out after the product is marketed, focusing on the visual acuity and adverse events related to vision (visual disturbance) of Chinese patients after implantation. Statistical analysis of the follow-up data should also be conducted to form a clinical follow-up report, which should be submitted when renewing the registration.

At present, PanOptix IOL has been approved for marketing in the United States, Australia, Japan, Europe and other countries and its safety and effectiveness have been widely recognized internationally. PanOptix IOL provides patients with good visual acuity at far distance, intermediate distance of 60 cm and near distance of 40 cm by creating an addition power of +2.17 D **IOL plane** intermediate vision (equivalent to +1.64 D **spectacle plane**) and an addition power of +3.25 D **IOL plane** near vision (equivalent to +2.48 D **spectacle plane**).

PanOptix IOL has the same material and overall dimensions as AcrySof IQ ReSTOR +3.0 D IOL which has been approved globally, but there are differences in the diffraction optical design of the optical zone. PanOptix IOL is a non-sequential diffraction design to provide distance and near vision equivalent to ReSTOR +3.0 D, as well as better intermediate vision. From the current global clinical data, PanOptix IOL can effectively provide continuous vision from near to distance, and no unanticipated risks related to IOL optical design have been found.

This study aims to assess the clinical performance of PanOptix IOL in Chinese population, especially the observation of visual acuity and adverse visual reactions, so as to prove that it has good distance, intermediate and near vision in Chinese population, can reduce the spectacle dependence, and have tolerable and acceptable adverse reactions related to vision.

V. Product Characteristics, Structural Composition, Working Principle, Mechanism of Action and Test Scope

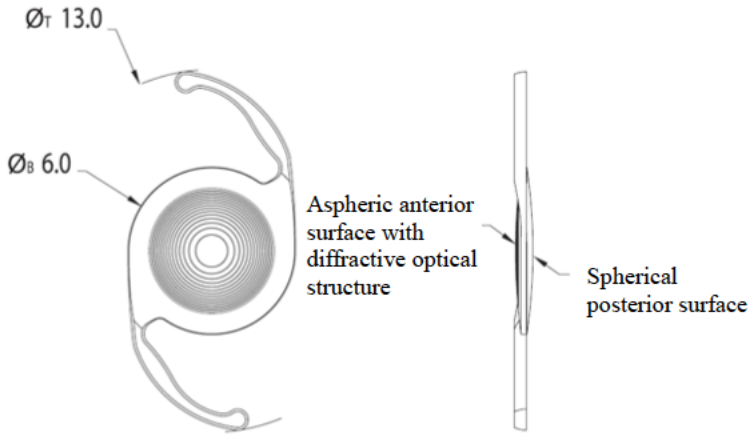
(I) Product Characteristics

PanOptix IOL (model and specification: TFNT00) is an ultraviolet and blue light filtering foldable multifocal IOL. The intraocular lens adopts a single-piece design, including a central optical zone and two open-loop intraocular lens loops (Figure 5-1). The optical part is composed of a proprietary hydrophobic acrylate material with a blue light filtering chromophore, which can filter light in the blue wavelength range of 400-475 nanometers in a manner close to the human lens (Boettner and Wolter, 1962). The biconvex optical zone is made of a soft acrylic material, which can be folded before implantation, so it can be implanted into the eye through an incision smaller than the optical diameter of the lens. The optical zone diameter of the intraocular lens is 6.0mm. The total diameter is 13.0mm. Its power range is 6.0-30.0D (in increments of 0.5 D) and 31.0 D-34.0 D (in increments of 1.0 D). After being surgically implanted into the eye, the intraocular lens is gradually fully deployed. The optical diffraction

structure is located in the 4.5mm portion in the center of the optical zone, and divides the incoming light to create a +2.17 D intermediate and a +3.25 D near addition power. The anterior surface is designed with negative spherical aberration to compensate for the positive spherical aberration of the human cornea. The effect of this aspheric design feature has not been evaluated clinically.

Figure 5-1

Physical characteristics



(II) Structural Composition, Working Principle, Mechanism of Action of the Product

The structural composition of PanOptix IOL is shown in Table 5-1 below.

Table 5-1

Physical characteristics and structural composition

Physical characteristics	Description
Optical type	Single-piece IOL with diffractive aspheric optic
UV Cutoff at10%T	401nm for 21 D
Refractive index	1.55
Optic Powers	+6.0D~+30.0D (in increments of 0.5 D) +31.0~+34.0D (in increments of 1.0 D), +2.17 D intermediate and a +3.25 D near add power
Haptic Configuration	STABLEFORCE* modified-L Haptics
Lens Material	Ultraviolet and blue light filtering Acrylate/Methacrylate Copolymer
Optical Diameter（mm）	6.0
Overall Length (mm)	13.0
Haptic Angle	0°

Mode of action

The AcrySof IQ PanOptix IOL Model TFNT00 is intended to be positioned in the lens capsule in the posterior chamber of the eye, replacing the Natural crystalline lens. This position allows the lens to function as a refractive medium in the correction of aphakia. This IOL has a biconvex optic containing an aspheric design and a diffractive structure on the anterior surface. The diffractive structure divides incoming light to provide a range of vision from distance to intermediate to near. This IOL provides an option for clinicians to provide patients an intermediate add power of +2.17 D and a near add power of +3.25 D.

(III) Trial Scope

The study population of this trial includes adult Chinese subjects, 18 years of age or older, who require primary implantation of an intraocular lens in the capsular bag in the posterior chamber after cataract extraction with distance, intermediate and near visual acuity requirements so as to improve near, intermediate and distance visual acuity and reduce spectacle dependence. The preoperative regular corneal astigmatism in each eye of the subject is less than 1.0 D. The calculated IOL power needs to be between +6.0 D and +34.0 D (when targeted for emmetropia 0.0 D). The preoperative best-corrected distance visual acuity in each eye is worse than or equal to 0.3 LogMAR. The potential postoperative best corrected distance visual acuity is better than 0.3 logMAR in both eyes. Planned cataract removal by routine phacoemulsification. Able to complete all study visits required in the protocol. Able to comprehend and sign an informed consent form.

VI. Indications and Contraindications, Precautions of the Product

Scope of application

This product is suitable for adult patients who require primary implantation of an intraocular lens in the capsular bag in the posterior chamber after cataract extraction with distance, intermediate and near visual acuity requirements so as to improve near, intermediate and distance visual acuity and reduce spectacle dependence.

Contraindications

There are no known contraindications when using PanOptix intraocular lenses as recommended.

Precautions

For details, see the product instructions: warnings, reminders and instructions for use.

VII.Overall Design

(I) Trial Design

1. Trial Objective

The primary objective of this clinical study is to assess the clinical performance of PanOptix Intraocular Lens (model: TFNT00) in Chinese population, especially the observation

of visual acuity and adverse events related to vision (visual disturbance).

2. Test Method Selection and Justification

This clinical study is a prospective, single-arm, multi-center, post-marketing clinical study. The study is designed based on the *Guidelines for Clinical Trials of Intraocular Lenses* [2] (hereinafter referred to as the Guidelines), and refers to the content about clinical trials in ISO11979-7: 2018 [3].

3. Measures to Reduce and Avoid Bias

(1) Qualified clinical study institutions will be invited to carry out the multi-center clinical trial to control the central effect in sample size allocation. Before the start of the experiment, the study staff will be trained in the protocol and the standard operating procedures.

(2) The surgeon at each site is the investigator himself/herself, who has rich and mature cataract surgery experience, and can ensure that patients undergo high-standard cataract surgery.

(3) A unified distance, intermediate and near visual acuity chart will be used to detect visual acuity [redacted].

(4) Unified questionnaire [redacted] QUVID) will be used for subjective survey assessment.

(5) Subjects will be selected in strict accordance with the inclusion and exclusion criteria.

(6) A verifiable and traceable data collection management system will be established to ensure that the data is true and reliable. Qualified monitors will be employed to check the original data to ensure that the data is true and complete, and that the research process is standardized and recorded.

4. Investigational Medical Device

The investigational medical device used in this study is: AcrySof IQ PanOptix Intraocular Lens. There is no control medical device.

Table 7-1 Investigational medical device

Item name	Intraocular Lens AcrySof IQ PanOptix Presbyopia Correcting Intraocular Lens (model: TFNT00)
Manufacturer	6065 Kyle Lane Huntington WV, 25702 USA
Indication	This product is suitable for adult patients who require primary implantation of an intraocular lens in the capsular bag in the posterior chamber after cataract extraction with distance, intermediate and near visual acuity requirements so as to improve near, intermediate and distance visual acuity and reduce spectacle dependence.

Product description and parameters	• Optical type: Single-piece IOL with diffractive aspheric optic • Intraocular lens material (optic + loop structure): Ultraviolet and blue light filtering Acrylate/Methacrylate Copolymer • Optic power: +6.0D~+30.0D (in increments of 0.5 D), +31.0~+34.0D (in increments of 1.0 D), +2.17 D intermediate and a +3.25 D near add power • Refractive index: 1.55 • Haptic Configuration: STABLEFORCE* Modified-L Haptics • Optic diameter (mm): 6.0 • Overall length (mm): 13.0 • Haptic Angle: 0°
Usage	IOLs are implantable medical devices and intended for long-term use over the lifetime of the pseudophakic subject.
Number/Amount of product to be provided to the subject	Each subject is planned to be bilaterally implanted with the test articles.
Packaging description	Alcon standard commercial packaging contains the following items: • IOL • Subject registration card (lens implantation response card) • Subject identification card (implant card) provided to the patient • Self-adhesive label with IOL information and unique serial number • eIFU reference card, which provides IFU access information. See ifu.alcon.com
Label description	Packed in standard Alcon IOL cartons. The carton is marked with the following information: lens name, model, total diameter, optical zone diameter, degree, serial number, manufacturer's name, storage conditions, expiration date, sterility and single use.
Additional information	In order to successfully implant the IOL in the eyes of study subjects, the surgeons participating in the study must be licensed ophthalmologists, have experience in cataract surgery, and have received protocol training.

5. Subject Selection

(1) Inclusion criteria

1	Able to comprehend and sign an informed consent form.
2	Adults aged at and above 18 years, diagnosed with bilateral cataracts.
3	Pre-operative regular corneal astigmatism of less than 1.0 D.
4	Planned cataract removal by routine phacoemulsification.
5	Calculated IOL power between +6.0 D and +34.0 D (when targeted for emmetropia 0.0 D)
6	Able to complete all study visits required in the protocol.
7	Pre-operative best corrected distance visual acuity worse than or equal to 0.3 LogMAR in each eye.
8	Potential postoperative best corrected distance visual acuity of 0.3 logMAR or better in both eyes based on the investigator expert medical opinion.

(2) Exclusion criteria

1	History of anterior segment (corneal, anterior chamber, sulcus) or posterior segment (uveal, vitreo-retinal) pathologic change including retinal vascular occlusive disease, retinal detachment or peripheral retinal laser photocoagulation, ARMD, glaucoma, diabetic retinopathy, retinitis pigmentosa and any pathologic changes associated with the optic nerve.
2	Corneal Endothelial Cell Count less than 2000 cells/mm^2.
3	History of recurrent anterior segment/posterior segment inflammation.
4	Clinically significant corneal diseases (epithelium, stromal, and/or endothelium) may, according to the investigator's medical opinion, adversely affect visual outcomes. These ocular pathologies include but are not limited to old significant corneal scars (including Salzman's nodular degeneration), active or inactive keratitis with compromise of the refractive capability of the cornea, keratoconjunctivitis sicca with compromise of visual function, active keratouveitis, endothelial dystrophy (Fuch's and non-guttate), keratoconus, etc. (Note: Patients with any pathological manifestations that may potentially affect postoperative visual acuity should not be included in this study)
5	Clinically significant severe dry eye that would affect study measurements based on the investigator's expert medical opinion.
6	History of previous intraocular or corneal (refraction or trauma related) surgery.
7	Currently or planning to be pregnant/lactating or has another condition with associated fluctuation of hormones that could lead to refractive changes.
8	Current or past history of amblyopia or monofixation syndrome with poor stereoscopic vision.
9	Systemic medications that, in the opinion of the investigator, may confound the outcome or increase the risk to the subject (e.g. Tamsulosin Hydrochloride – Flomax) or other medications including anticholinergics, alpha adrenergic blocking agents with similar side effects (e.g. small pupil/floppy iris syndrome)
10	Any subject currently participating in another investigational drug or device study that may confound the results of this investigation.

11	Any other ocular or systemic co- morbidity that, in the investigator's medical opinion, may confound the results of this study or prohibit the completion of the study assessments or increase the risk for the subject.
12	Subjects with conditions that increase the risk of zonular rupture during cataract extraction procedure that may affect the postoperative centration or tilt of the IOL (e.g., patients of exfoliation Syndrome, Marfan syndrome).
13	Any other planned ocular surgical procedures including but not limited to limbal relaxing incision (LRI)/Astigmatic Keratotomy and laser-assisted in situ keratomileusis (LASIK).
14	Subjects who desire monovision correction.

(3) Criteria and procedure for stopping the trial/trial treatment

1) Termination of clinical trial

The trial may be terminated in the following cases: a) If there is new safety information indicating that continuing the trial or operation may endanger the safety of the subjects; b) the sponsor's administrative decision.

The ethics committee should follow up and supervise the clinical trial of the clinical trial institution, and may require the suspension or termination of the clinical trial in writing at any time if it finds that the rights and interests of subjects cannot be guaranteed or other situations alike.

The sponsor should ensure that all investigators who conduct the clinical trial strictly abide by the clinical trial protocol. If the sponsor finds that the clinical trial institution and investigator do not comply with relevant laws and regulations, the GCP and the clinical trial protocol, the case should be pointed out and corrected; if the case is serious or persists without correction, the sponsor should terminate the trial at that site.

Suspended clinical trials shall not be resumed without the consent of the ethics committee. If deciding to suspend or terminate the clinical trial, the sponsor should inform the medical device clinical trial management department of all clinical trial institutions within 5 days, and explain the reason in writing. The medical device clinical trial management department of clinical trial institutions should timely notify the corresponding investigators and ethics committees. After the completion of the clinical trial, the sponsor should inform the food and drug regulatory authority of the province, autonomous region, or municipality directly under Central Government where the sponsor is located.

2) Subjects' withdrawal from the clinical trial

Subjects can stop the study or study treatment at any time for any reason. For the best interests of the subjects, the investigator can terminate the subjects' participation in the trial at any time during the trial.

Subjects can be discontinued from the study or study treatment due to special circumstances during the operation.

a. Surgical complications including but not limited to loss of zonular integrity/zonular weakness, zonular rupture, anterior or posterior capsule rupture interfering with the stability of the IOL, any evidence of fluid misdirection during the cataract procedure with progressive shallowing of the anterior chamber, uncontrollable IOP.

b. Mechanical or Surgical manipulation of the pupil.

c. Excessive iris mobility.

d. Inability to place the IOL in the capsular bag due to surgical complications.

If 1st eye implantation was aborted and **the IOL did not touch the eye**, then the subject is required to discontinue from the study and standard of care for IOL implantation is followed. If the implantation was aborted and **the IOL did touch the eye**, then the subject is encouraged to attend all follow-up study visits for safety evaluation on this eye only**..**

See the text below: Table 7-6 Subject Status after Reasons for Non-implantation.

3) Procedures to stop the trial

Subjects who discontinue the study refer to individuals who voluntarily withdraw from the study after signing the informed consent form or are required to withdraw from the study by the investigator.

Except for screening failure, if the subject withdraws from the study, the investigator should complete the early withdrawal procedure in accordance with the "Research Procedures and Assessment Timetable" and record the reason for withdrawal in the subject's original medical record. To ensure the safety of all subjects who withdrew early, the investigator should assess each subject and, if necessary, provide them with recommendations for any treatment and/or medical procedures that may be needed to maintain their health.

(4) Enrollment time

This clinical study is expected to start recruiting subjects in the second quarter of 2021, and complete the enrollment of subjects in the fourth quarter of 2021.

(5) The expected overall duration of the clinical trial and justification for its determination

The enrollment time of this clinical study is expected to be 6 months, and the follow-up time will be 12 months after the final second implant. The statistical analysis and writing of clinical trial report will take about 6 months, and the total duration will be about 26 months.

(6) Expected duration of participation of each subject

The follow-up time for each subject is 12 months, and the total expected duration of

participation in the study is 14 months.

The expected duration of participation and follow-up schedule all comply with the *Guidelines for Clinical Trials of Intraocular Lenses*, and refer to the content about clinical trials in ISO11979-7.

(7) Number of subjects required for the clinical trial

- Enrolled: 158 subjects
- Implanted: 142 subjects (284 eyes)
- Completed: At least 127 subjects available for evaluation (254 eyes)

6. Effectiveness Evaluation Method

(1) Explanation of effectiveness parameters

This study set 4 primary effectiveness endpoints [redacted] All effectiveness endpoints will be recorded in the corresponding follow-up (see Table 7-2 for the specific recording time), with Month 6 postoperative results being the most critical endpoint.

Primary effectiveness endpoints:

1) The percentage of eyes with BCDVA equal to or better than 0.3 logMAR

   According to China Monofocal IOL Guideline, effectiveness indicator: best corrected visual acuity. The primary evaluation indicator is the effective rate of the product at six months. Definition of effectiveness: the IOL implantation eye's best corrected visual acuity reaches 4.7 (standard logarithmic visual acuity chart).

   Therefore, we aim to study the percentage of eyes with BCDVA equal to or better than 0.3 logMAR.

2) Mean monocular and binocular Best Corrected Distance Visual Acuity (BCDVA)
3) Mean monocular and binocular Distance Corrected Intermediate Visual Acuity (DCIVA) (60 cm)
4) Mean monocular and binocular Distance Corrected Near Visual Acuity (DCNVA) (40 cm)

[redacted]

[redacted]

(2) Method and time selection for evaluating, recording and analyzing effectiveness parameters

Table 7-2 Method and time selection for evaluating, recording and analyzing effectiveness parameters

Effectiveness endpoints	Method for evaluating, recording and analyzing	Time selection
Primary Effectiveness Endpoints		
The percentage of eyes with BCDVA equal or better than 0.3 LogMAR	"Tumbling E ETDRS VA Charts" or "Chinese Standard Logarithmic VA Charts" will be used in this study for distance, intermediate and near VA test. Final direction on VA Charts will be provided in the "Operations Manual" provided to the site. For both DCIVA and DCNVA, the intermediate and near visual acuity is measured under the premise of the best correction of distance visual acuity.	1 week (7~14 days) after surgery, 1 month (30~60 days) after surgery 3 months (90~120 days) after surgery, 6 months (180~210 days) after surgery 12 months after surgery (360~390 days)
Mean monocular and binocular Best Corrected Distance Visual Acuity (BCDVA)		Monocular BCDVA: 1 week (7~14 days) after surgery, 1 month (30~60 days) after surgery 3 months (90~120 days) after surgery, 6 months (180~210 days) after surgery 12 months after surgery (360~390 days) Binocular BCDVA: 6 months (180~210 days) after surgery, 12 months (360~390 days) after surgery
Mean monocular and binocular Distance Corrected Intermediate Visual Acuity (DCIVA) （DCIVA）（60cm）		Monocular DCIVA: 1 month (30~60 days) after surgery, 3 months (90~120 days) after surgery 6 months (180~210 days) after surgery, 12 months (360~390 days) after surgery Binocular DCIVA: 6 months (180~210 days) after surgery, 12 months (360~390 days) after surgery

Mean monocular and binocular Distance Corrected Near Visual Acuity (DCNVA) (40 cm)		Monocular DCNVA: 1 month (30~60 days) after surgery, 3 months (90~120 days) after surgery 6 months (180~210 days) after surgery, 12 months (360~390 days) after surgery Binocular DCNVA: 6 months (180~210 days) after surgery, 12 months (360~390 days) after surgery

[redacted]

[redacted]

Protocol version number: V 2. 0
Protocol version date: Nov 5, 2020

7. Safety Evaluation Method

(1) Explanation of safety parameters

This study sets 3 primary safety endpoints [redacted]. All safety endpoints will be recorded in the corresponding follow-up (see Table 7-3 for the specific recording time), with the Month 6 and Month 12 results being the most critical endpoints.

Primary safety endpoints:

1) Evaluate the rates of ocular adverse events
2) Evaluate the rates of secondary surgical interventions (SSIs)
3) Estimate rates of severe and most bothersome visual disturbances as reported by the subjects using a questionnaire (QUVID)

[redacted]

(2) Method and time selection for evaluating, recording and analyzing safety parameters

Table 7-3 Method and time selection for evaluating, recording and analyzing safety parameters

Safety endpoints	Method for evaluating, recording and analyzing	Time selection
Primary Safety Endpoints		
Evaluate the rates of ocular adverse events	Assess and record all adverse events observed or reported, the ocular related AEs are primary safety endpoint.	Each visit
Evaluate the rates of secondary surgical interventions (SSIs)	Assess and record all secondary surgical interventions (excluding posterior capsulotomy)	Each postoperative visit
Estimate rates of severe and most bothersome visual disturbances as reported by the subjects using a questionnaire (QUVID)	See the attachment for the preoperative and postoperative QUVID questionnaire.	Preoperative screening 6 months (180~210 days) after surgery 12 months after surgery (360~390 days)

[redacted]

	elastic layer wrinkles	
Grade 3	Severe	Corneal center opacity, with invisible pupil borders and obvious posterior elastic layer wrinkles

Note: This classification refers to the *Guidelines for Clinical Trials of Soft Contact Lenses* (No. 51 of 2018) [4].

Each visit

Anterior chamber inflammation-graded using the following method:

Level 0	None	No anterior chamber planktonic cells or aqueous flare
Grade 1	Faint	Slight anterior chamber imflammation
Grade 2	Moderate	Iris and lens details clear
Grade 3	Marked	Iris and lens details hazy
Grade 4	Intense	Fibrin or plastic aqueous

Note: No relevant regulations or standards have been found to describe the grading criteria for anterior chamber inflammation. The above classification methods refer to the evaluation classification of aqueous flare in the reference [5].

Each visit

Hypopyon-graded using the following method:

Yes	With hypopyon
No	Without hypopyon

Note: This classification only records the presence or absence of anterior chamber empyema. (No reference standard)

Each visit

Endophthalmitis-graded using the following method:

Yes	With endophthalmitis
No	Without endophthalmitis

Note: This classification only records the presence or absence of endophthalmitis. (No reference standard)

<table>
<tr><td></td><td>Intraocular lens decentration
Examine the IOL with a slit lamp, and subjectively assess whether the IOL has changed position and decentration has occurred since the last visit. If IOL decentration has occurred, please record the size of the decentration in millimeters and in increments of 0.50 mm.
Note: IOL decentration is not cumulative. Only record changes since the last visit.
(This assessment method refer to Alcon PanOptix US IDE Study)</td><td>Each postoperative visit</td></tr>
<tr><td></td><td>Intraocular lens tilt
Examine the IOL with a slit lamp, and subjectively assess whether the IOL has tilted since the last visit. If IOL tilt occurs, please record the degree of tilt in increments of 1°.
(This assessment method refer to Alcon PanOptix US IDE Study)</td><td>Each postoperative visit</td></tr>
<tr><td></td><td>Intraocular lens dislocation-graded using the following method:<table><tr><td>Yes</td><td>With intraocular lens dislocation</td></tr><tr><td>No</td><td>Without intraocular lens dislocation</td></tr></table>Note: This classification only records the presence or absence of intraocular lens dislocation. (No reference standard)</td><td>Each postoperative visit</td></tr>
<tr><td></td><td>Intraocular lens opacity-graded using the following method:<table><tr><td>Yes</td><td>With intraocular lens opacity</td></tr><tr><td>No</td><td>Without intraocular lens opacity</td></tr></table>Note: This classification only records the presence or absence of intraocular lens opacity. (No reference standard)</td><td>Each postoperative visit</td></tr>
<tr><td>To observe the subject's posterior capsule opacity and whether to undergo laser posterior capsulotomy</td><td>Examine with a slit lamp, and assess the presence of PCO. If PCO exists, classify using the following method:<table><tr><td>Clinically Non-</td><td>Early development of PCO, including fibrosis and</td></tr></table></td><td>1 month (30~60 days) after surgery
3 months (90~120 days) after surgery
6 months (180~210 days) after</td></tr>
</table>

<table>
<tr>
<td></td>
<td>
<table>
<tr><td>significant</td><td>proliferation of lens epithelial cells, observable by slit-lamp biomicroscopy. Causes no apparent decrease in VA subjectively (e.g., glare) or objectively (e.g., decrease in visual acuity).</td></tr>
<tr><td>Clinically Significant</td><td>Increased PCO with early subjective and objective VA changes but not require posterior capsulotomy.</td></tr>
<tr><td>Clinically Significant Requiring YAG</td><td>Clinically significant PCO adversely affecting subjects' visual acuity and requiring posterior capsulotomy.</td></tr>
</table>
Note: For posterior capsulotomy assessment, indicate whether a posterior capsulotomy was performed since the last visit. If performed, report the date of the procedure and the size of the capsulotomy (largest diameter in mm).
This classification method refers to the routine evaluation standards for Alcon's internal clinical studies. (This assessment method refer to Alcon PanOptix US IDE Study)
</td>
<td>surgery
12 months after surgery (360~390 days)</td>
</tr>
<tr>
<td>Dilated fundus examination, pay attention to whether there is cystoid macular edema, retinal detachment, etc.</td>
<td>Perform dilated fundus examination, assess and record the vitreous body, retina, macula, optic nerve and cup-to-disk ratio.</td>
<td>Preoperative screening
1 week (7~14 days) after surgery
1 month (30~60 days) after surgery
6 months (180~210 days) after surgery
12 months after surgery (360~390 days)</td>
</tr>
<tr>
<td>Intraocular pressure</td>
<td>Use equipment commonly used by the investigator to measure IOP.
Note: The intraocular pressure measurement equipment must be calibrated according to the manufacturer's instructions.
The IOP of each subject should be measured with the same type of equipment at all follow-ups. The recording unit of the measurement result is mmHg.</td>
<td>All visits except the day of surgery</td>
</tr>
</table>

<table>
<tr><td>OCT examination to clarify the condition of the macular retina</td><td>Perform mydriatic or non-mydriatic OCT examination, assess and record the condition of the macular retina, and observe whether there is cystoid macular edema. Use the following method to record:<table><tr><td>No</td><td>Without cystoid macular edema</td></tr><tr><td>Yes</td><td>With cystoid macular edema</td></tr></table>If there is cystoid macular edema, it is necessary to describe the specific conditions such as the height of the edema; if there are other macular lesions, a description should be provided.
Note: This classification method is formulated in accordance with the requirements of the Guidelines for Clinical Trials of Intraocular Lenses.</td><td>Preoperative screening
1 month (30~60 days) after surgery</td></tr>
<tr><td>Corneal endothelial cell count</td><td>Use equipment commonly used by the investigator to measure and record corneal endothelial cell counts. The corneal endothelial cell count of each subject should be measured with the same type of equipment at all follow-ups. The recording unit of the measurement result is (cells)/mm^2.</td><td>Preoperative screening
3 months (90~120 days) after surgery
6 months (180~210 days) after surgery
12 months after surgery (360~390 days)</td></tr>
<tr><td>Device deficiencies</td><td>Assess and record all device deficiencies reported or observed since the last visit. (for specifics, refer to Section 13 Provisions on the Reporting of Adverse Events and Device Deficiencies)</td><td>Each visit except preoperative visit (Visit 0)</td></tr>
<tr><td>Evaluate the rates of adverse events</td><td>Assess and record all adverse events observed or reported, including events accompanied by changes in drug dosage since the last visit. (for specifics, refer to Section 13 Provisions on the Reporting of Adverse Events and Device Deficiencies)</td><td>Each visit</td></tr>
<tr><td colspan="3">Safety evaluation indicators:</td></tr>
<tr><td>Symptoms, signs, complications</td><td>Assess and record the observed symptoms, signs, and complications. If it meets the product complaint and/or AE criteria, it should be reported as required by the protocol.</td><td>Each visit</td></tr>
</table>

(II) Trial Process

1. Trial Flowchart

The subject will participate in 11 hospital visits, as shown in Figure 7-1, Table 7-4 and Table 7-5 below.

Figure 7-1 Study design flowchart

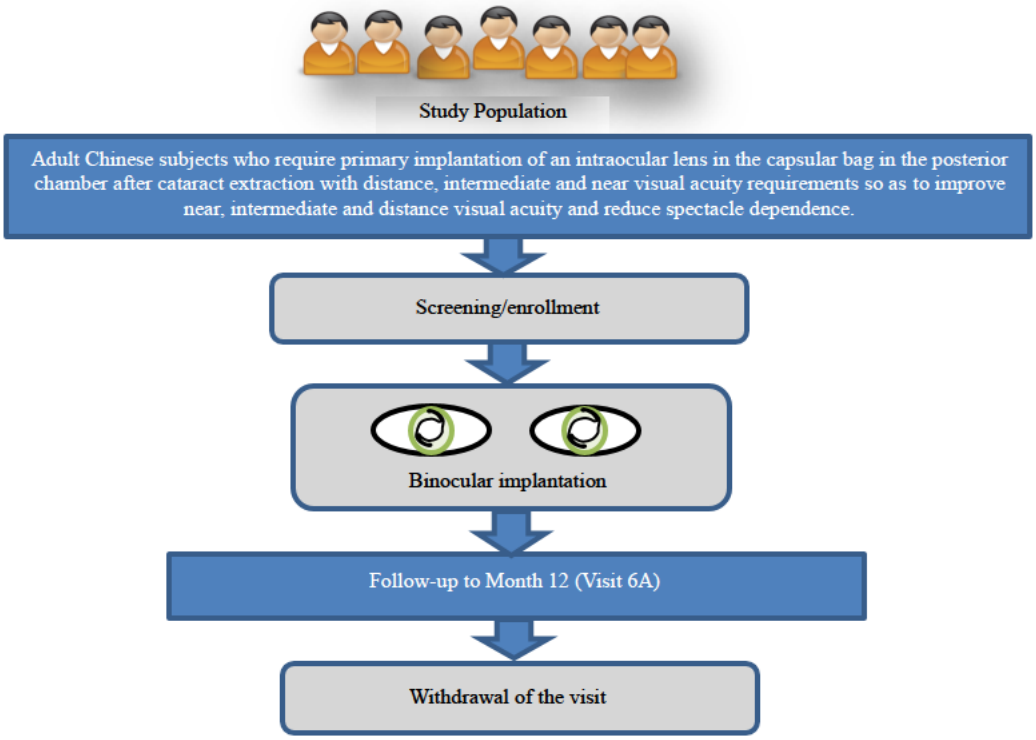


Table 7-4 Study follow-up

Calculated based on the time of IOL implantation	First eye	Second eye
Day -28 to Day 0	Visit 0 (binocular screening)	
Surgery (IOL implantation)	Visit 00 (0 day)	Visit 00A*(0 day)
1-2 days after surgery	Visit 1 (1 day)	Visit 1A (1 day)
7-14 days after surgery	Visit 2 (1 week)	Visit 2A (1 week)
30-60 days after the second eye surgery	Visit 3A (1 month)	
90-120 days after the second eye surgery	Visit 4A (3 months)	
180-210 days after the second eye surgery	Visit 5A (6 months)	
360-390 days after the second eye surgery	Visit 6A (12 months)	

*Implantation in the second eye must be performed 7-28 days after implantation in the first eye.

Table 7-5 SCHEDULE OF VISITS

Visit	Visit 0 Pre-op	Visit 00: OP [1]	Visit 1	Visit 2	Visit 00A: OP [2]	Visit 1A	Visit 2A	Visit 3A	Visit 4A	Visit 5A	Visit 6A	Early Exit
Eye	**Both eyes**	**First eye**	**First eye**	**First eye**	**Second eye**	**Second eye**	**Second eye**	**Both eyes**	**Both eyes**	**Both eyes**	**Both eyes**	**Not applicable**
Number of days	**Day -28-Day 0**	**Surgery**	**Day 1-2**	**Day 7-14**	**Surgery**	**Day 1-2**	**Day 7-14**	**Day 30-60**	**Day 90-120**	**Day 180-210**	**Day 360-390**	**Not applicable**
Informed consent	X											
Demographics	X											
Medical history	X											
Concomitant medication	X	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]
Inclusion/exclusion	X	X			X							
Urine pregnancy test [3]	X										X	X
Anterior chamber depth*	X											
Axial length*	X											
Corneal curvature*	X											
Target (expected) residual refractive error (spherical and cylindrical)*	X											
[redacted]												
QUVID questionnaire	X									X	X	X
[redacted]												
Corneal endothelial cell	X								X	X	X	

Visit	Visit 0 Pre-op	Visit 00: OP [1]	Visit 1	Visit 2	Visit 00A: OP [2]	Visit 1A	Visit 2A	Visit 3A	Visit 4A	Visit 5A	Visit 6A	Early Exit
Eye	**Both eyes**	**First eye**	**First eye**	**First eye**	**Second eye**	**Second eye**	**Second eye**	**Both eyes**	**Both eyes**	**Both eyes**	**Both eyes**	**Not applicable**
Number of days	**Day -28-Day 0**	**Surgery**	**Day 1-2**	**Day 7-14**	**Surgery**	**Day 1-2**	**Day 7-14**	**Day 30-60**	**Day 90-120**	**Day 180-210**	**Day 360-390**	**Not applicable**
count												
Distance visual acuity												
[redacted]												
• Best corrected distance visual acuity	X[5]			X			X	X	X	X[5]	X[5]	X[5]
Intermediate visual acuity at 60 cm												
[redacted]												
• Distance corrected intermediate visual acuity								X	X	X[5]	X[5]	
Near visual acuity at 40 cm												
[redacted]												
• Distance corrected near								X	X	X[5]	X[5]	

Visit	Visit 0 Pre-op	Visit 00: OP [1]	Visit 1	Visit 2	Visit 00A: OP [2]	Visit 1A	Visit 2A	Visit 3A	Visit 4A	Visit 5A	Visit 6A	Early Exit
Eye	**Both eyes**	**First eye**	**First eye**	**First eye**	**Second eye**	**Second eye**	**Second eye**	**Both eyes**	**Both eyes**	**Both eyes**	**Both eyes**	**Not applicable**
Number of days	**Day -28-Day 0**	**Surgery**	**Day 1-2**	**Day 7-14**	**Surgery**	**Day 1-2**	**Day 7-14**	**Day 30-60**	**Day 90-120**	**Day 180-210**	**Day 360-390**	**Not applicable**
visual acuity												
Slit lamp examination*	X		X	X		X	X	X	X	X	X	X
Dilated fundus examination*	X			X			X	X		X	X	X
Intraocular pressure*	X		X	X		X	X	X	X	X	X	X
Operative eye		X			X							
Intraocular lens information		X			X							
Incision position		X			X							
Final incision size		X			X							
Problems during surgery		X			X							
Other surgical procedures		X			X							
Subjective observation of PCO								X	X	X	X	X
Posterior capsulotomy								X	X	X	X	X
IOL observations			X	X		X	X	X	X	X	X	X
IOL position change (decentration/tilt)			X	X		X	X	X	X	X	X	X

Visit	Visit 0 Pre-op	Visit 00: OP [1]	Visit 1	Visit 2	Visit 00A: OP [2]	Visit 1A	Visit 2A	Visit 3A	Visit 4A	Visit 5A	Visit 6A	Early Exitl
Eye	**Both eyes**	**First eye**	**First eye**	**First eye**	**Second eye**	**Second eye**	**Secon d eye**	**Both eyes**	**Both eyes**	**Both eyes**	**Both eyes**	**Not applicable**
Number of days	**Day -28-Day 0**	**Surgery**	**Day 1-2**	**Day 7-14**	**Surgery**	**Day 1-2**	**Day 7-14**	**Day 30-60**	**Day 90-120**	**Day 180-210**	**Day 360-390**	**Not applicable**
Posterior segment OCT examination	X							X				
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X
Secondary surgical interventions			X	X		X	X	X	X	X	X	X
Device deficiencies		X	X	X	X	X	X	X	X	X	X	X

1 Visit 00 (1st eye surgery) must be performed within 28 calendar days from Pre-Operative Visit (Visit 0).

2 Visit 00A (2nd eye surgery) must be performed within 7 to 28 calendar days after Visit 00 (1st eye surgery).

3 In women of childbearing potential only.

4 Only recorded in the source documents.

5 Monocular (bilaterally) and binocular testing.

* If the subject has undergone these routine standard diagnosis and treatment assessments within 30 days before signing the informed consent, there is no need to repeat the measurement, and the results of these inspections can be used directly (based on the judgment of the investigator).

(1) Process for assessment of subjects' basic conditions:

1) Informed consent, screening and numbering of subjects

The investigator will evaluate potential study candidates based on eligibility criteria. Candidates must sign an informed consent form before conducting any study-related screening examinations that are beyond the usual standard diagnosis and treatment procedures. Routine standard diagnosis and treatment assessments (such as slit lamp examination, dilated fundus examination, bio-measurement, IOL calculation, and IOP measurement, etc.) performed on all subjects due to cataract surgery are not considered as specific study assessments.

Note: If the subject has undergone these routine standard diagnosis and treatment assessments within 30 days before signing the informed consent, there is no need to repeat the measurement, and the results of these inspections can be used directly (based on the judgment of the investigator).

Signing the informed consent form indicates that the subject is enrolled in the study. Enter the subject into the electronic data capture (EDC) system to generate a subject number.

Complete the research process and assessments according to the protocol. Verify whether the subject meets all the inclusion criteria. If the subject does not meet the inclusion criteria, it will be deemed as a subject screening failure and the subject will be notified that he/she does not meet the criteria for participating in the study.

Note: Subjects who fail the inclusion criteria shall not be subjected to secondary screening (that is, if a subject does not meet the research criteria, he/she will still be ineligible to participate in the study).

Subjects who meet the inclusion criteria may not meet the criteria for intraocular lens implantation. If these situations occur, see the section "Table 7-6 Subject Status after Reasons for Non-implantation" below. This section will clearly indicate how to follow up such subjects during the study.

2) Demographics

During the preoperative visit (Visit 0), record the demographic data of the subjects, including age, gender and nationality.

3) Medical history

The medical history includes ocular and non-ocular diseases.

During the screening/preoperative visit (Visit 0), record the subject's medical history as follows:

- All ocular and non-ocular specific diseases* (chronic, intermittent or recurrent) that have occurred or recovered within 30 days prior to the signing of the informed consent.

*Specific diseases are defined as the history of non-ocular diseases recorded on the CRF.

- Any previous history of eye surgery, including laser surgery.

4) Concomitant medications

Concomitant medications can be divided into ocular and non-ocular medications. Both must be reported according to the following requirements:

During the screening/preoperative visit (Visit 0), record all ocular and non-ocular medications (prescription or over-the-counter drugs, including vitamins and herbal preparations) received within 30 days before the signing of informed consent. Record the diseases related to drug treatment, the start and end dates of drug treatment, and the route of administration. If necessary, update the concomitant medications (for example, new drug treatment, end date of drug treatment) at each study visit. Record this information in the source documents.

Enter the concomitant medication information into the EDC as follows:

- Medical history in the CRF
  - Medicines related to medical history
- Adverse events in the CRF
  - Drugs for AE treatment

Drugs routinely used during cataract surgery:

Record all routine surgical medications (including preoperative, intraoperative, and immediate postoperative medications) and all household medications (that is, the medications that the subjects take home for their own use) in the source documents of each subject. This information is not collected in the EDC.

Drugs non-routinely used during cataract surgery:

Record drugs non-routinely used during cataract surgery (for example, medications provided due to adverse events (AE)) in the EDC. Note: All medications must be recorded in the source documents.

5) Inclusion/exclusion

The enrollment criteria are divided into eye-related and non-eye-related. Check the enrollment criteria as follows.

During the screening/preoperative visit (Visit 0), according to the inclusion criteria and exclusion criteria in the protocol, verify whether the subject meets all the enrollment criteria. If the subject does not meet the inclusion criteria, it will be deemed as a subject screening failure and the subject will be notified that he/she does not meet the criteria for participating in the study. If the subject meets all the enrollment criteria and is willing to continue to participate in the study, determine the first surgical eye and continue to arrange the first surgical eye visit (Visit 00).

Note: The first surgical eye is defined as the eye with poorer best corrected distance visual acuity (BCDVA). If the BCDVA is the same in both eyes, identify the right eye (OD) as the first operative eye.

6) Urine pregnancy test

For women of childbearing age, a urine pregnancy test is required.

Note: If the subject is at least 1 year after menopause or more than 6 weeks after sterilization, urine pregnancy test is not required.

If pregnant, the subject fails the screening. If not pregnant, the subject continues to participate in the study.

Subjects who become pregnant during the study will terminate the study. Data will be excluded from the effectiveness analysis because pregnancy may change refractive and visual acuity results. The investigator should fill out the pregnancy report form and report it according to the serious adverse event reporting procedure. If applicable, the investigator should follow up until delivery/termination of pregnancy. Pregnancy should be documented in the medical history section of eCRF.

7) Reasons for non-implantation of IOL and the corresponding subject follow-up procedures

Subjects may discontinue the trial due to special circumstances during the operation. For specific criteria, see the reason for discontinuation (intraoperative) in the protocol above. Subject may continue to participate in the study or discontinue the study according to Table 7-6 below, depending on the circumstances. In addition, if attempts to implant the lens fail twice or more, the subject can abort the study. Table 7-6 below also applies to these situations.

Table 7-6 Subject Status after Reasons for Non-implantation

Eye	Special cases	Status/follow-up
First eye	• Reason for non-implantation • IOL did not touch the eye	Subject discontinuation
	• Reason for non-implantation • IOL did touch the eye • Non-implantation of IOL • IOL removed before surgery in the second eye • Finally implant another suitable non-study lens per standard of care	• The subject can continue to participate in the study • First eye: o **No** effectiveness assessment is performed o **Monocular** safety assessment at postoperative visits • Second eye: no more implantation of the study IOL

	• Reason for non-implantation • IOL did not touch the eye	• The subject can continue to participate in the study for the first eye • First surgical eye: **Monocular** safety and effectiveness assessment at postoperative visits • Do not perform binocular assessments or any other assessments on the second eye.
Second eye	• Reason for non-implantation • IOL did touch the eye • Non-implantation of IOL or IOL be removed later • Finally implant another suitable non-study lens per standard of care	• The subject can continue to participate in the study • First surgical eye: ○ **Monocular** safety and effectiveness assessment at postoperative visits • Second surgical eye: Safety assessment at postoperative visits • Do not perform binocular assessments

**Note:* Implanting a study lens when a reason for discontinuation during surgery is observed is a protocol deviation, and should not occur. If an exclusion occurs after the IOL is already implanted, the surgeon should use his best judgement for the safety of the subject to leave the study IOL implanted or to replace with a non-study IOL.

(2) Process for assessment of subjects' eye conditions:

1) Eye bio-measurement

Use the standard optical biometer of the site (ie IOL Master biometer and/or LenStar biometer, Corneal Topography biometer etc.) for bio-measurement. And record the following measurement results in the EDC: anterior chamber depth (ACD) and axial length (AL).

Save the results printed by the biometer as source documents.

2) Corneal curvature measurement

Use an optical biometer (ie IOL Master biometer and/or LenStar biometer, Corneal Topography biometer, etc.) to measure corneal curvature. Record the curvature (D) and axis position of the flat meridian (K_1) and the steep meridian (K_2) in the EDC.

3) IOL diopter calculation-target (expected) residual refractive diopter (spherical and cylindrical powers)

Formula:

It is recommended that investigators use the most experienced new-generation intraocular lens calculation formula (for example, SRK/T formula, Haigis formula) in their daily work, and use the Barrett Universal II formula for comparison and verification.

A constant (SRK/T formula):

PanOptix's recommended A constant (SRK/T) is 119.1 (recommended on the box). It is recommended that investigators use the optimized A constants of previously used AcrySof IQ (SN60WF) and AcrySof IQ ReSTOR +3.0 D (SN6AD1) to calculate the optimized A constant of PanOptix for the first time. Refer to the following table:

The investigator uses the optimized A constant of previous IOLs	Optimized A constant corresponding to PanOptix
AcrySof IQ（SN60WF）	+0.16 based on the optimized A constant of SN60WF
AcrySof IQ ReSTOR +3.0 D（SN6AD1）	+0.1 based on the optimized A constant of SN6AD1

Constant of Haigis formula:

According to the investigator's previous experience using SN60WF and SN6AD1, if there is no self-optimized Haigis formula constant, it is recommended to use: a_0 =1.42, a_1 = 0.40, and a_2 = 0.10; if the investigator has his/her own optimized Haigis formula constant, please refer to the following table to calculate the optimized A constant when PanOptix is used for the first time.

The investigator uses the optimized Haigis formula constants of previous IOLs	Optimized Haigis formula constant corresponding to PanOptix
AcrySof IQ（SN60WF）	a_0 is +0.07 based on the optimized constant of SN60WF, and the values of a_1 and a_2 remain unchanged
AcrySof IQ ReSTOR +3.0 D（SN6AD1）	a_0 is +0.07 based on the optimized constant of SN6AD1, and the values of a_1 and a_2 remain unchanged

Surgically induced astigmatism:

For surgically induced astigmatism (SIA), refer to the investigator's previous empirical values. If the investigator does not know his/her SIA, Alcon recommends using a vector SIA value ≈ 0.10 for incisions ≤ 2.5 mm.

Target (expected) residual refractive diopter:

The minimum intraocular lens power with the smallest target (predicted) residual refractive diopter and closest to emmetropia (SE 0.00 D) should be selected for the subject. Ensure that the target (expected) residual diopter is within the range of ±0.50 D.

Record the IOL power and IOL model selected for each subject.

Note: The IOL diopter calculated by the subject must be within the range of +6.0 to +34.0 D.

[redacted]

[redacted]

5) Questionnaire

The questionnaires include QUVID [redacted]

The Chinese study questionnaire will be provided so that the subjects can complete the study by themselves. Instruct the subject to fill out the questionnaires completely in the following order:

- QUVID
- [redacted]

Preoperative questionnaire: Provide the questionnaire after assessing and confirming the eligibility of the subjects. **Postoperative questionnaire:** Provide at Visits 5A and 6A after a simple greeting and before the following operations:

1. Any questionnaire regarding the health and/or visual acuity status of the subject, and
2. Any other assessments performed.

Even if the subjects request, no explanation is allowed. If the subjects need interpretation or explanation, it must not be provided, and it is recommended that they try their best to answer the questions.

After the subject completes the questionnaire, please review its completeness and the accurate completion of skipping different questions. Do not comment on the subjects' answers. If any question is left blank, instruct the subject to fill it out. If skipping different questions is not correctly completed, instruct the subject to review his/her answers again and fill in accordingly. Finally, review the strikethrough/correction of the questionnaire. If the subject corrects a mistake, instruct the subject to sign his/her name and indicate the date of change.

6) Corneal endothelial cell count

During the visit, each subject used the same instrument to measure the corneal endothelial cell count. The recording unit of the measurement result is: cells/mm^2.

Note: The equipment must be calibrated according to the instrument manufacturer's instructions.

7) Posterior segment OCT examination

The same instrument should be used for the fundus OCT examination of each subject during the visits. Perform mydriatic or non-mydriatic OCT examination, assess and record the

condition of the macular retina, and observe whether there is cystoid macular edema. Use the following method to record:

No	Without cystoid macular edema
Yes	If there is cystoid macular edema, please describe the specific conditions such as the height of the edema.

If there is cystoid macular edema, it is necessary to describe the specific conditions such as the height of the edema; if there are other macular lesions, a description should be provided.

Note: The equipment must be calibrated according to the instrument manufacturer's instructions.

[redacted]

The equipment used to measure visual acuity [redacted], assessment distance, lighting requirements, assessment management and scoring, please refer to the "Operation Manual".

Requirements for examination of visual acuity:

Measure VA [redacted] before measuring IOP, instilling mydriatic or anesthetic eye drops, or before any examination that requires eye contact.

1. Perform visual acuity measurement in accordance with the requirements of the “Operation Manual”.
2. Ask subjects to sit in front of the visual acuity chart to ensure that they are at an appropriate distance from the visual acuity chart, and the height of the line of sight is approximately aligned with the middle of the visual acuity chart.
3. Provide preliminary guidance to subjects.
    a. Inform subjects that their distance/intermediate/near/defocused visual acuity will be assessed.
    b. Explain that they should read slowly to best identify each letter when answering, and explain that they should not continue to read the next letter until they are clearly responded.
4. During the assessment, remind subjects to maintain an appropriate position and close the contralateral eye (if applicable). Also pay attention to squinting, excessive blinking, and head tilt. If these situations are found, correct the subject immediately. Do not point to the visual acuity chart or specific letters on the visual acuity chart. Do not comment on the accuracy of the answers. Encourage subjects to do their best to identify each letter, and encourage them to guess when necessary.

9) Slit lamp examination

Perform a slit lamp examination before IOP measurement and fundus examination. Observe corneal, anterior and posterior segment inflammation and intraocular lens performance under slit lamp (record corneal edema, corneal folds and

other related information; anterior and posterior segment inflammation, such as anterior chamber planktonic cells, aqueous flare, anterior chamber empyema and endophthalmitis manifestations; intraocular lens decentration, tilt, dislocation and opacity, etc.)

Record all baseline clinical observation results. Continue to record the observation results during the postoperative visits until resolved.

10) Dilated fundus examination

Perform a dilated fundus examination (indirect or direct ophthalmoscopy). Assess the vitreous body, retina, macula, choroid, optic nerve, and cup-to-disk ratio. Record all baseline clinical observation results. And record the observation results until resolved.

If fundus observations were not observed at Screening/Preoperative Visit (Visit 0), it may become apparent under the microscope prior to surgery. In these instances, document the findings and update the Screening/Preoperative Visit (Visit 0) fundus exam panel in EDC. Observations made under the microscope during surgery or at the conclusion of surgery must be captured as AEs (ie, iatrogenic events, operative complications, etc.). Additionally, pathologic conditions observed after surgery must be documented and may be reported as a Screening/Preoperative Visit (Visit 0) finding.

11) Intraocular pressure

The IOP of each subject will be measured with the same instrument during each visit. The recording unit of the measurement result is mmHg.

Note: The equipment must be calibrated according to the instrument manufacturer's instructions.

12) Subjective PCO Including Posterior Capsulotomy

During the slit lamp examination, assess the presence of PCO. If PCO exists, grade as clinically non-significant, clinically significant or clinically significant requiring YAG according to Table 7-3 Method and time selection for evaluating, recording and analyzing safety endpoints above.

13) IOL observation

During the slit lamp examination, observe and record the IOL conditions, including dislocation, opacity, etc.

14) IOL position change (decentration/tilt)

Examine the IOL via the slit lamp and subjectively assess whether the lens has changed position and tilted, since the last visit. If the IOL decentration has occurred, the size of the decentration shall be recorded in millimeters (0.50 mm increments). If the IOL has tilted, record the degree of tilt (in 1° increments).

Note: Tilt and deviation are not accumulated. Only record changes since the last visit.

(3) Surgery-related assessment

1) Operative eye

In the EDC, record the first and second surgical eyes as OD or OS.

Regardless of the investigative site's standard operating procedure, the 1 st operative eye must be selected as described here: the first surgical eye is defined as the eye with the worst BCDVA at the screening visit. If the BCDVA is the same in both eyes, identify the right eye (OD) as the first operative eye.

2) IOL information, model, power, serial number

For each successful lens implantation, retain the IOL adhesive label which documents the lens model, lens power and unique serial number in the subject's source documents.

For each aborted lens implantation, assess the lens for device deficiency. If a defect is found, report the deficiencies as an adverse event or device defect in the protocol. In the subject's source documents, note the reason for the failed implantation and retain the IOL adhesive label (which documents the lens model, lens power and unique serial number).

Study staff must document the implanted lens model and serial number in EDC.

3) Incision position and final incision size

Perform routine phacoemulsification cataract surgery according to the investigator's standard procedure. According to the IOL DFU and study protocol, implant the IOL into the assigned subject. It is recommended that investigators have at least two IOLs of the same model and required power in the operating room during surgery.

The following standard information should be recorded in the original medical record:

- Incision size
- Incision position
- IOL injector and cartridge utilized
- OVD(s) utilized
- Surgical complications or other procedures
- Medications used
- Phacoemulsification and/or femtosecond laser used

4) Problems during surgery

Document whether any problems arose during surgery.

Problems include anterior capsular tear, poorly dilated pupils during surgery, and the lens loop stuck in the ciliary sulcus. Evaluate whether the problem meets the definition of an AE and report accordingly. Refer to the "Adverse Events and Device

Deficiencies" section of the protocol for definitions and reporting requirements.

Note: If problems arise during surgery, prior to implanting the IOL determine whether the lens should be implanted. Please refer to the "Reason for Discontinuation (Intraoperative)" section of the protocol for the criteria for not implanting the IOL for the study.

5) Record other surgical procedures

In cataract surgery, record whether any additional surgery (for example, anterior vitrectomy, capsular tension ring) is performed. Valuate whether the surgery meets the definition of AE and report accordingly. Refer to the "Adverse Events and Device Deficiencies" section of the protocol for definitions and reporting requirements.

Note: If other surgical procedures are performed, prior to implanting the IOL determine whether the lens should be implanted as recommended in the product DFU. Please refer to the "Reason for Discontinuation (Intraoperative)" section of the protocol for the criteria for not implanting the IOL for the study.

(4) Adverse events and device deficiencies

1) Adverse events

The collection of AEs starts when the subject signs the informed consent form. AEs may be ocular or non-ocular (eg, seasonal allergies, hip replacement surgery).

2) Device deficiencies

Refer to the "Adverse Events and Device Deficiencies" section of the protocol for the reporting requirements related to deficient devices. Return the product to the study sponsor as described below.

Unless otherwise arranged by the sponsor, products involving device deficiencies should be returned to the study sponsor for investigation.

2. Specification for Device Use

The study product is a regular commercially available product, and the method of use is shown in the product instructions. Throughout the research process, the investigator or designated personnel should keep a record of the IOL implanted in each subject.

(III) Monitoring Plan

The monitors appointed by the sponsor should formulate a complete and applicable monitoring plan according to the requirements of the trial, and conduct trial quality monitoring according to the monitoring plan.

1. Site's qualification confirmation visit

Before selecting investigators to participate in the study, a qualification visit is required. The purpose of the visit is to confirm that the investigator/site has sufficient staff (including the designated research coordinator) and facilities for conducting the study in accordance with the requirements of the trial protocol. The relevant personnel of the trial fully understand the protocol, process, responsibilities, and clinical trial-related regulations.

2. Study initiation visit

Before the site recruits subjects, a site initiation visit should be implemented. The purpose of the visit is to confirm that the site is still eligible to participate in the study and to review the responsibilities of and research requirements for the investigator/site. Site training should be implemented, including but not limited to:

(1) Clinical trial protocol and data collection procedure

(2) Monitoring requirements

(3) Ethical requirements

(4) Informed consent procedures

(5) Review of the site's records

3. Regular monitoring visits

The designated study monitors entrusted by the sponsor should pay regular monitoring visits to the site during the research process. The purpose of the visit is to confirm the compliance with the trial protocol, review the regulatory documents, keep accurate and complete records, and compare the source documents with the completed CRF for considerations of completeness and consistency. Determine the timetable for the initial monitoring visit to the site as soon as possible after 1 to 2 subjects are recruited for the study. The frequency of follow-up visits is determined by the recruitment rate and the performance of the site (the performance of the site is determined according to previous monitoring visits). Special assessments conducted during monitoring visits include:

(1) Continued acceptability of the site

(2) Compliance with the protocol

(3) Ethical approval status

(4) Use of approved informed consent form

(5) Adequacy of source documents

(6) Complete and accurate CRFs

(7) Adverse event reports

(8) Protocol deviations

(9) Site's records

If it is determined during the monitoring visit that the site has major non-compliance issues (including compliance with the trial protocol or applicable regulatory requirements), these issues should be discussed with the investigator and research coordinator, and guidance on how the site can comply should be given. If non-compliance is still found during follow-up monitoring visits, the site should be considered to stop participating in this study.

4. Site closure visit

A closure visit should be conducted at the end of the last follow-up visit at each site. Purpose of the visit:

(1) Check all unresolved data queries

(2) Recheck the requirements for research record keeping

(3) Arrange to return all study-related materials to the sponsor

(4) Recheck the final ethical requirements for the study

VIII. Statistical Considerations

(1) Statistical Design, Methods and Analysis Procedures

1. Statistical design

This clinical study is a prospective, single-arm, multi-center, post-marketing clinical study.

2. Statistical methods and procedures

Continuous variables will be summarized using sample size, mean, standard deviation (SD), median, minimum, and maximum, and confidence intervals (CIs) or confidence limits (if applicable). The count and percentage classification variables for each category will be summarized; any deviations in the analysis plan will be updated as part of the protocol revisions during the research process or will be detailed in the clinical study report.

2.1 Subject evaluability

The final subject evaluability must be determined prior to locking the database, depending on the protocol deviation and evaluability plan (DEP).

2.2 Analysis data sets

(1) Safety analysis set: This analysis set includes all subjects who have tried the implantation of IOL (successfully implanted or aborted after IOL contact with the eye).

(2) Full analysis set: The full analysis set (FAS) includes all subjects who have had IOL successfully implanted in at least one eye and have undergone at least one postoperative effectiveness assessment (BCDVA, UCDVA).

(3) Per protocol set: The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that meet any key deviation or evaluability criteria identified in the DEP.

2.3 Demographics and baseline characteristics

Demographics and baseline characteristics will be summarized using FAS and PP. Demographics include age and gender. Baseline characteristics include anterior chamber depth, axial length, corneal curvature (curvature (D) and axial position of flat meridian (K_1) and steep meridian (K_2), monocular BCDVA and binocular BCDVA. Counts and percentages will be used for categorical variables such as gender, age group (< 65 years; ≥ 65 years). The observed sample size, mean, standard deviation (SD), median, minimum, and maximum will be used to report continuous variables such as age.

2.4 Effectiveness analysis

This study defines 4 primary effectiveness endpoints [redacted] he primary effectiveness endpoints will be statistically discribed in the FAS and PP analysis sets.

[redacted]

(1) Analysis of the primary effectiveness endpoints

The primary effectiveness endpoints of this study include the following, with the Month 6 results as the most critical endpoints:

- Percentage of eyes with BCDVA equal to or better than 0.3 logMAR.
- Mean monocular and binocular Best Corrected Distance Visual Acuity (BCDVA)
- Mean monocular and binocular Distance Corrected Intermediate Visual Acuity (DCIVA) (60 cm)
- Mean monocular and binocular Distance Corrected Near Visual Acuity (DCNVA) (40 cm).

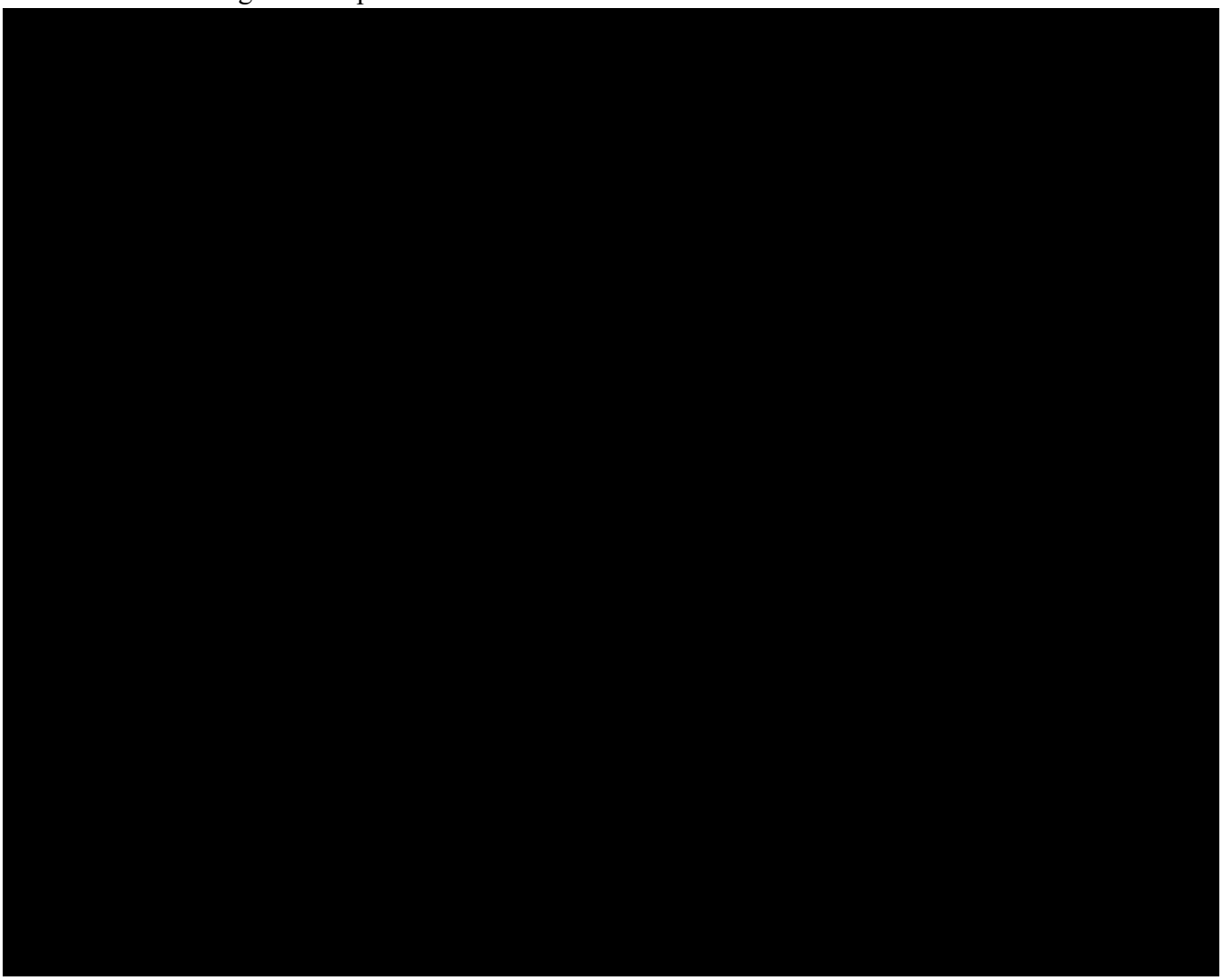
1) Statistical hypotheses and models

No inference is made about the primary effectiveness endpoints. Therefore, no hypotheses are made.

2) Analytical methods

All primary effectiveness endpoints will be descriptively statistically summarized. The percentage of eyes with BCDVA equal to or better than 0.3 logMAR will be used as a categorical variable for summary: 0.0 LogMAR and better, 0.1 LogMAR and better, 0.2 LogMAR and better, and 0.3 LogMAR and better, including counts and percentages. Monocular BCDVA, DCIVA and DCNVA are presented by the first eye, the second eye and all implanted eyes; binocular BCDVA, DCIVA and DCNVA are presented by subject, including sample size,

mean, median, standard deviation, maximum and minimum, and two-sided 90% confidence interval. Listings will be provided as needed.



2.5 Safety analysis

The primary safety endpoints of this study include:

The rates of ocular adverse events, the rates of secondary surgical interventions (SSIs), and ratesof severe and most bothersome visual disturbances as reported by the subjects using a questionnaire (QUVID)

All AEs that occur from the day when the subject signs the informed consent form to the subject‘s withdrawal from the study will be included in the report. Subjects who have had AEs after signing the informed consent form and before exposure to IP will be displayed in the form of a list; the AEs after exposure to IP will be summarized as follows:

1. All adverse events (combined serious and non-serious) form
    a. Ocular
    b. Non-ocular
2. Device/surgery-related adverse events form
    a. Ocular
    b. Non-ocular
3. All serious adverse events (including device/surgery-related adverse events) form
    a. Ocular
    b. Non-ocular
4. List of subjects with adverse events
    a. Non-serious ocular
    b. Non-serious non-ocular
    c. Serious ocular
    d. Serious non-ocular

The descriptive table of AEs (counts and percentages) will report the preferred terms provided in the Medical Dictionary for regulatory activities, and AEs that have caused discontinuation of the study should be identified.

The incidence of severe and most bothersome visual disturbances in the QUVID questionnaire survey will be presented as count, incidence, and two-sided 90% CI for incidence.

The intraocular pressure and its changes from baseline will be classified and summarized by observing the number, mean, median, standard deviation, minimum and maximum based on the surgical eye: IOP increases/decreases include > 30 mmHg, 21～30 mmHg, 11～20 mmHg and 6～10 mmHg, and the normal range is -5～5 mmHg. The baseline is defined as the last measurement taken before the IOL is implanted. A list of subjects' intraocular pressure and changes from baseline will be provided.

The OCT examination will use (no/with) cystoid macular edema to perform categorical variable statistics, and provide a list of the height of cystoid macular edema and a list of other macular lesions.

The results of slit lamp examination, fundus examination and IOL observation will be listed with descriptive statistics. Among them, count and percentage will be provided, and the changes in corneal endothelial count from baseline will be summarized. The number and percentage of eyes with IOL position changes (tilt≥ 1° and/or decentration ≥ 0.5 mm) will be

provided based on the surgical eye, and a list of eyes with IOL position changes will be provided.

The types of device deficiencies will be tabulated and a listing will be provided.

2.6 Interim analysis and report

This study plans to conduct an interim analysis of all data 6 months after all subjects have their second eye implanted.

(II) Calculation of Sample Size

1. Overall Sample Size

The study plans to recruit (signing of informed consent form) approximately 158 subjects at no more than 8 sites in China in order to include 142 subjects (284 eyes). It is expected that 127 subjects (254 eyes) will complete the study.

2. Number of Cases for the Clinical Trial of Each Disease and its Justification

1) Number of cases for the clinical trial of each disease

The study is a single-disease study, so the number of cases is the same as the total sample size.

2) Justification

According to the CSRs summarized in PanOptix DL Response for China registration, the ocular? SAE rate is 1.80%. A sample size of 127 subjects would ensure more than a 90% probability of observing at least one AE for any event that has a true incidence of 1.8% or greater.

Allowing for a 10% screening failure rate, approximately 158 subjects will be enrolled to obtain about 142 subjects who will undergo IOL implantation in both eyes. Assuming a further 10% dropout rate at Month 12 of follow-up, it is expected that 127 subjects (254 eyes) will complete the study.

3. In a multi-center clinical trial, the minimum and maximum number of subjects and reasons for each clinical trial institution and site-specific targets may vary based upon individual site capabilities. In order to control the central effect of the trial, in principle, the single-site enrollment should not exceed 1/3 of the total enrolled cases.

(III) Significance Level and Power of the Clinical Trial

In this study, there are no statistical hypotheses about the effectiveness and safety objectives, and the sample size is not calculated based on power.

(IV) Expected Dropout Rate

It is estimated that the screening failure rate is 10% and the dropout rate is 10%.

(V) Criteria for Qualified/Unqualified Clinical Trial Results

The trial is considered as successful as long as the data are true and credible.

(VI) Criteria for Terminating the Trial Based on Statistical Reasons and Justification

This trial will not be terminated based on statistical reasons.

(VII) Statistical Methods for All Data, as well as Processing Methods for Missing, Unused or Erroneous Data (Including Halfway Exit and Withdrawal) and Unreasonable Data

1. Data statistical methods

Descriptive statistics will be used, and lists provided when necessary.

2. Processing methods for missing, unused or erroneous data (including halfway exit and withdrawal) and unreasonable data

1) Processing of missing values: In this trial, missing values will not be processed.

2) Processing of unused or erroneous data: If the subject exits or withdraws from the trial halfway, the reason should be recorded and the missing data will not be processed. Before database locking, the data in the database should be cleaned up. If any erroneous data is found, the investigator will be questioned, and the data will be corrected according to the investigator's reply.

3) Processing of unreasonable data: Before database locking, the data in the database should be cleaned up. If any erroneous data is found, the investigator will be questioned, and the data will be corrected according to the investigator's reply.

(VIII) Procedures for Reporting Deviations from the Original Statistical Plan

The statistical analysis plan needs to be confirmed by the sponsor and the principal investigator, and finalized before the database is locked. Before finalization, the initial analysis plan can be modified according to the actual situation in the trial process. In principle, the main analysis principles, methods, and analysis sets will not be modified, and all modifications will be recorded.

(IX) Selection Criteria for the Subjects Included in the Analysis and Justification

The full analysis set (FAS) includes all subjects who have had IOL successfully implanted in at least one eye and have undergone at least one postoperative effectiveness assessment (BCDVA, UCDVA).

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

The safety analysis set includes all subjects who have tried the implantation of IOL (successfully implanted or aborted after IOL contact with the eye).

(X) Special Information Excluded from Hypothesis Verification and Justification (If Applicable)

Not applicable.

IX. Data Management

(I) Data Collection

The Electronic Data Capture (EDC) system is used to collect trial data. Before the system is officially launched, relevant users need to be trained and tested to ensure that the system meets the trial requirements. After the system is officially launched, the relevant personnel will be given the account number and password. The account is tied to the user's role and authority. The account information must be properly kept and the account information must not be disclosed to others or the corresponding rights shall be exercised on behalf of others.

The EDC will directly transmit data from the client to the server via the Internet. The investigator is responsible for the quality of the entered data, and should ensure the authenticity and completeness of the data. CRFs must be completed regularly in accordance with the clinical research visit plan. It is expected that all reported data will have corresponding entries in the source documents.

(II) Data Verification and Modification

When an investigator enters an abnormal data, the EDC system will issue a real-time warning to remind the investigator to check the data; the data administrator will perform logic check on the data stored on the server, and issue erroneous data through the EDC in the form of manual questioning. The investigator should answer the questions posted. The monitors should remind and assist the investigator to answer questions on a regular basis to ensure that every question is dealt with correctly. The system will record all questions and their corresponding answers.

(III) Database Locking

When all data are entered and submitted, and all queries are answered, the system enters the soft lock state. The statistician will generate a blind audit report based on the database. If it is confirmed that the data will no longer be modified, the sponsor, the person in charge of data management, and the person in charge of statistics need to sign the database locking form, and the data administrator will complete the database locking operation based on this form. The locked database cannot be modified again. If there are errors that affect the primary effectiveness indicators or safety indicators, the sponsor, the person in charge of data management, and the person in charge of statistics must confirm the unlocking modification and sign the database unlocking form. The data administrator will modify the erroneous data according to the reason for unlocking and carry out quality control. After the error is corrected, the sponsor, the person in charge of data management, and the person in charge of statistics need to sign the database locking form again.

(IV) Completed Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that the original data required to complete the CRF does exist and can be accessed for verification by the monitors at the site. All discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the Study Sponsor and are independent of study site staff.

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

At a minimum, source documents include the following information for each subject:

- Subject identification (name, sex, age)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of the research indicators required by the protocol
- Test article accountability records (if applicable)
- Documentation of AEs and other safety parameters (if applicable)
- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation, if applicable

It is required that the author of an entry in the source documents be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the CRF are consistent with the original source data.

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

(V) Data Review and Clarification

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

X. Feasibility Analysis

(I) Analysis of the Possibility of Success

PanOptix Intraocular Lens has been approved in many countries and regions, which meets the safety and effectiveness objectives of product design according to the obtained clinical application. The study design complies with the relevant guidelines, and it is a prospective, single-arm, multi-center, post-marketing clinical study. The study is designed based on the *Guidelines for Clinical Trials of Intraocular Lenses* (hereinafter referred to as the Guidelines), and refers to the content about clinical trials in ISO11979-7. The design is rigorous, and the method is scientific, and can reduce unnecessary biases. In summary, we expect that the study will confirm the safety and effectiveness of the product in the Chinese population.

(II) Analysis of the Possibility of Failure

The main possibilities of failure include slower than expected enrollment speed and failure to complete the enrollment targets. Problems may arise during the research process, such as bias, poor compliance of subjects, inaccurate inspection data, and non-repeatability. Targeted preventive considerations for the above possibilities have been made in the "Measures to reduce and avoid bias" section above.

XI. Quality Control of the Clinical Trial

During the research process, the clinical monitors appointed by the sponsor will regularly pay on-site monitoring visits to the site to ensure that all the contents of the study protocol are strictly followed and the research materials are filled in correctly. All personnel participating in the study must receive unified training to unify the recording methods and judgment standards. The entire clinical trial process should be carried out under strict operation.

The investigator or authorized personnel should record various contents in the eCRF truthfully, thoroughly and carefully according to the CRF filling requirements, and ensure that the contents of the case report forms are complete, true and reliable. All observations and findings in the clinical study should be verified to ensure the reliability of the data and ensure that the conclusions in the clinical study are derived from the original data. There should be corresponding data management measures in the clinical research and data processing stages.

The original materials of this study, including the signed informed consent forms, research supplies distribution and use records (if applicable), relevant laboratory test reports, auxiliary examination reports, medical records and other related records, etc. They should be kept in the clinical trial institution of the hospital where each site is located for 10 years after the end of the clinical trial, and the sponsor should save the clinical trial data until the investigational medical device is no longer used.

XII. Ethical Issues of the Clinical Trial and Informed Consent

(I) Ethical considerations

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

(1) The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.

(2) Good Clinical Practice for Medical Devices (Decree No. 25 of the National Medical Administration and the National Health and Family Planning Commission of the People's Republic of China)

(3) SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.

(II) Approval of the trial protocol

Before clinical study initiation, this protocol, the informed consent form, any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by the ethics committee. The Investigator must provide documentation of the ethics committeeapproval to the Study Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, consent form amendment (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. A copy of the clinical investigator's brochure, PanOptix package insert, any periodic safety updates, and all other information required by local regulations and/or the ethics committee must be provided to the ethics committee. At the end of the study, the Investigator must notify the ethics committee about the study’s completion. The ethics committee also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the ethics committee on the progress of the study at intervals stipulated by the ethics committee.

(III) Informed Consent Process and Informed Consent Form Text

Voluntary informed consent must be obtained from each subject and this process must be completed prior to the subject proceeding to the specific procedure for the clinical study. The investigator must clearly document the process of obtaining informed consent. Specifically, the investigator or his/her authorized personnel must explain the clinical research process to each potential subject, and the subject must sign an approved informed consent form and date it to indicate voluntary consent. The subject should have the opportunity to raise questions to the investigator, and should also be able to ask other qualified personnel if required by local regulations. The investigator must provide the subject with a copy of the consent form, and the subject should be able to understand the content of the consent form. The consent form must comply with all applicable local laws and provide the subjects with information about the objectives, procedures, requirements, and restrictions of the study, all known risks and potential benefits related to IP and the study, compensation that the subjects can get, and existing

provisions on the protection of confidentiality of their personal health information. The subject must be informed of the voluntary nature of participating in the study, and must be provided with the contact information of the relevant personnel in case that the subject has questions or concerns during the study. The investigator must also inform the subject that the relevant authorities and personnel designated by the sponsor can access their records. The investigator must retain the original signed copy of the consent form (archived in the subject's medical record) and must provide a copy to each subject in accordance with local regulations.

The ethics committee must review and approve the informed consent form dedicated for this study. As long as new information that may affect the subject’s consent is obtained, the written informed consent form (and any other written information provided to study subjects) should be updated. Any such revisions or updates must be approved by the review ethics committee before being provided to study subjects.

The study will be registered at the website of
http://www.chictr.org.cnwww.clinicaltrials.gov.

XIII. Provisions on the Reporting of Adverse Events and Device Dfficiencies

(I) Adverse events and serious adverse events

1. Overview

Adverse event refer to adverse medical events occur during the process of clinical trial, no matter they are relevant to investigational medical devices or not.

Serious adverse event refer to events occurred during the process of clinical trial that cause death or serious deterioration of health condition, including fatal diseases or injuries, permanent deficiency of body structure or body functions, demands of hospitalization or extending the duration of hospital stays, demands of medical or surgical intervention so as to avoid causing permanent deficiency to body structure or body functions, and events leading to fetal distress, fetal death or congenital anomaly and congenital defect.

Note: Planned hospitalization for a pre-existing condition, without seriousdeterioration 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 seriouscriteria, the event is serious. When in doubt as to whether “hospitalization” occurred, the event should be considered serious.

Please refer to the figure below for the classification of adverse event and serious adverse event.

Figure 13-1 Classification of all adverse events

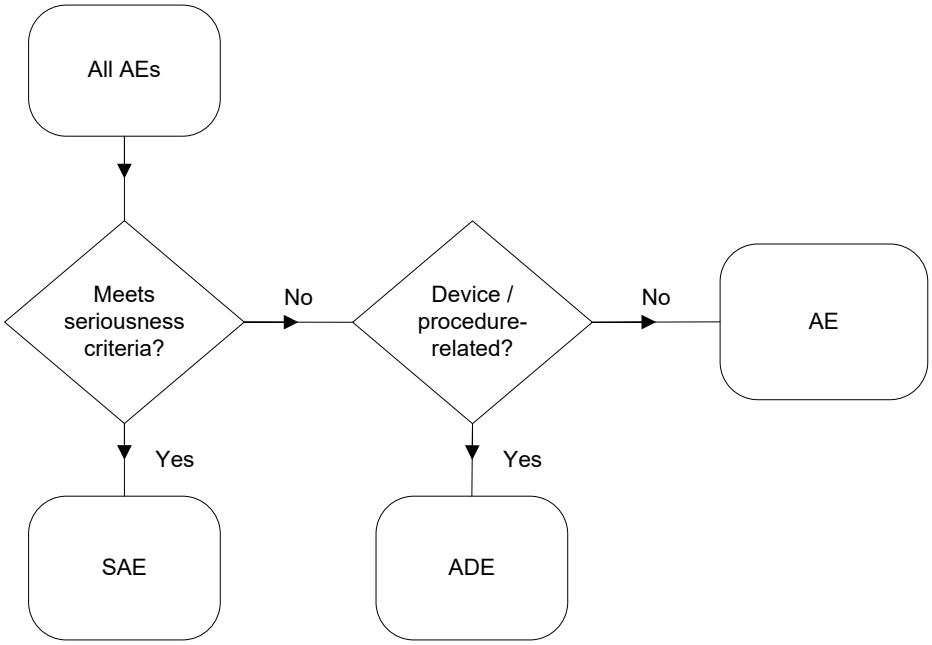
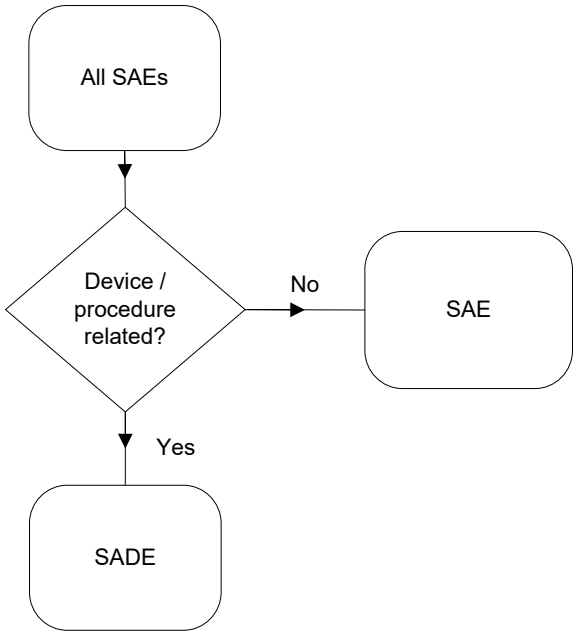


Figure 13-2 Classification of all serious adverse events



2. Specific Events Relevant to this Protocol

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

- Cystoid macular edema
- Hypopyon

- Endophthalmitis
- Lens dislocation
- Pupil block
- Retinal detachment
- Secondary surgical intervention (excluding posterior capsulotomy)

Any other potentially sight-threatening event may also be considered serious based on the judgment of the Investigator and must be reported appropriately as described in the reporting procedure below.

(II) Device deficiencies

Device deficiency refer to unreasonable risks of medical devices under normal use during the process of clinical trial that may endanger human health and life safety, such as labeling mistake, quality problem and malfunctions. In case of malfunctions or other efficiencies, the study device should be returned to the sponsor for further investigation.

The investigator should record all adverse events that occur during the clinical trial and device deficiencies found, analyze the cause with the sponsor, form a written analysis report, and put forward his/her opinions for continuing, suspending or terminating the trial. Then the opinions should be reported to the ethics committee for review through the medical device clinical trial management department of the clinical trial institution.

Examples of device deficiencies include the following:

1) Incompliance with product quality specification (for example, inaccurate IOL powers)
2) IOL defect
3) Broken IOL optic
4) Broken IOL haptic
5) Scratched IOL optic
6) Unsealed device packaging
7) Suspected product contamination
8) Lack of effectiveness

(III) Reporting procedures and contact person’s information

The collection of AEs starts from the signing of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (ie, before informed consent form is signed) are not considered AEs in the study and should be recorded. In addition, anterior chamber planktonic cells and flare, corneal edema, raised IOP, and superficial punctate keratitis are examples of early postoperative findings that are typically observed following ocular surgery. These are not considered AEs if they can be reasonably expected to resolve within a week and not result in any untoward long term visual outcome impact.

Each recorded event should include: date of occurrence, severity, treatment (if applicable),

outcome, and assessments of the severity and causality.

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

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

Changes in any protocol-specific ocular or systemic parameter evaluated during the study are to be reviewed by the Investigator. In addition, the subject's responses to any questionnaire utilized during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in a protocol-specific parameter or questionnaire response that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality. Subjects with adverse events should be followed up clinically until the adverse event has recovered (returned to a normal state or to a baseline state), or until the condition is stable, or there is a reasonable explanation.

If any **serious adverse event** occurs in the clinical study, no matter whether it is related to the test device, the Investigator should immediately take appropriate treatment measures to the subject, and at the same time, report in writing to the medical device clinical trial management department of the clinical trial institution to which it belongs. The sponsor will be notified in writing by the medical device clinical trial management department. The medical device clinical trial management department should report in writing to the corresponding ethics committee, the medical products administration departments and the competent health and family planning authority of the province, autonomous region, or municipality directly under Central Government where the clinical trial institution is located within 24 hours. For death events, the clinical trial institution and the investigator should provide all necessary materials to the ethics committee and the sponsor.

The sponsor should quickly investigate the serious adverse events that have occurred with the investigator, take necessary measures to ensure the safety and rights of the subjects, and report to the medical products administration department and the competent health and family planning authority at the same level within 5 working days after being informed. At the same time, the sponsor should notify other clinical trial institutions and investigators participating in the trial, and inform the ethics committees of the clinical trial institutions through their medical device clinical trial management department.

In addition, the Investigator must record all device deficiencies reported or observed in the study product in the device efficiency eCRF. The site must immediately submit all available information about SADE, SAE and device deficiencies to the study sponsor:

- All SAEs are documented on the Adverse Device Effect and Serious Adverse Event eCRF within 24 hours of the Investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reported within

10 calendar days after the investigator or research center is notified.

- Additional relevant information after initial reporting is to be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death, etc., if applicable, in narrative section of the Adverse Device Effect (for related AEs) and Serious Adverse Event eCRF.

The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory agencies or the ethics committee.

(IV)Severity and causality assessment

The Investigator should assess the severity of the AE as mild, moderate, or severe based on medical judgment with consideration of any subjective symptom(s), as defined below:

Severity

- Mild: An AE is mild if the subject is aware of but can easily tolerate the sign or symptom.
- Moderate: An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.
- Severe: An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

Causality

For every AE in the study, the Investigator must assess the causality (Related or Not Related to the medical device or test procedure). An assessment of causality will also be performed by the Study Sponsor utilizing the same definitions, as shown below:

- Related: An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.
- Not Related: An AE classified as not related may either be definitely unrelated or simply unlikely to be related (ie, there are other more likely causes for the AE).

The Study Sponsor will assess the AEs and may upgrade the Investigator's assessment of severity and/or causality. The Study Sponsor will notify the Investigator of any AEs that is upgraded from non-serious to serious or from unrelated to related.

XIV. Deviations from the Clinical Trial Protocol and Provisions on the Modification of the Clinical Trial Protocol

(I) Deviations from the clinical trial protocol

Definition: Events where the Investigator or the staff of the site fails to carry out the study in accordance with the clinical study protocol, corresponding laws, corresponding management regulations or research contracts.

The Investigator should strictly abide by the clinical trial protocol, and shall not deviate from the protocol or change the protocol substantially without the consent of the sponsor and the ethics committee, or without the approval of the National Medical Products Administration as stipulated. However, there are exceptions for emergency situations that require protection of the life or health of the subjects. Such approval should have written records and kept in the trial record file. Prior approval is usually impossible for situations that the Investigator cannot

anticipate and control (such as the subject's failure to undergo follow-up as planned), but the event itself is still considered a deviation.

After a deviation event occurs, the study staff should promptly report the above-mentioned research deviation to the sponsor. The study staff should report the handling of deviations from the trial in accordance with the requirements of the ethics committee.

(II) Revision of clinical trial protocol

All modifications made to the protocol must be approved by the sponsor and the Investigator, and submitted to the ethics committee for review and approval by the medical device clinical trial management department of the clinical trial institution. Amendments may require changes to informed consent and other study-related materials. If the informed consent form is revised, all subjects currently participating in the study must sign an approved and revised informed consent form (re-consent) in accordance with the requirements of the ethics committee.

When clinical trial institutions and investigators have changed compared with the original list, the list can be updated for each change without using a formal amendment, but the final report must provide the final list of all clinical trial institutions and investigators.

XV. Direct Access to Source Data and Documents

(I) Definition of source data and source documents

Source data refers to the original records of clinical findings, observations, and other activities in clinical trials and all the information in their approved copies, which can be used for clinical trial reconstruction and evaluation.

Source documents refer to printed documents, visual documents or electronic documents that contain source data.

(II) Provisions on direct access to source data and documents

The investigator should truthfully and accurately record and save the source data and source documents in the clinical trial process.

The clinical trial institution and the investigator should accept the sponsor’s monitoring and audits, and the ethics committee’s supervision, and provide all required trial-related records. Where the medical products administration and the competent health and family planning authority dispatch monitors to carry out inspections, the clinical trial institution and the investigator shall cooperate.

The original data of this trial will be preserved in accordance with the data preservation provisions required by the by the *Good Clinical Practice for Medical Devices* (Decree No. 25), that is, the clinical trial institution shall preserve the clinical trial data for 10 years after the end of the clinical trial. The sponsor should save the clinical trial data until the medical device is not used any more.

XVI. Finance and Insurance

Before the enrollment of subjects, the sponsor, the clinical trial institution and the investigator should reach a written agreement on the trial design, trial quality control, division of responsibilities in the trial, clinical trial-related expenses borne by the sponsor, and principles for the handling of harms that may occur in the trial.

This trial stipulates that the sponsor shall bear the cost of treatment and corresponding financial compensation for subjects who suffer injuries or deaths associated with the clinical trial, except for damages caused by the fault of the medical institution and its medical staff in the diagnosis and treatment activities. The sponsor has purchased medical device clinical trial liability insurance for this trial.

See the *Clinical Research Contract* for specific provisions.

XVII. Contents to Be Covered by the Clinical Trial Report

The investigator should verify or validate the safety and effectiveness of the investigational medical device in accordance with the design requirements of the clinical trial protocol, and complete the clinical trial report. The clinical trial report of a multi-center clinical trial should include the clinical trial summary of each sub-site.

For multi-center clinical trials, the clinical trial summary of each sub-site should at least include the clinical trial overview, general clinical data, information description of the investigational medical device, safety and effectiveness data sets, incidence and treatment of adverse events, and description of protocol deviations, with case report forms attached.

The clinical trial report complies with the relevant requirements of *Good Clinical Practice for Medical Devices*, and will be formulated by referring to the *Sample Medical Device Clinical Trial Report* and *Guidelines for Clinical Trials of Intraocular Lenses.*

XVIII. Confidentiality Principle

All data obtained in the clinical trial are subject to data protection. The investigator shall not disclose the subject’s name and other personal information (excluding date of birth/age and sex). It must be ensured that the CRF or other documents sent to the sponsor (such as copies of reports on special findings) do not contain names, but only the subject's study code (number, date of birth and/or random number).

Similarly, data storage for statistical evaluation can only be performed under the subject's study code. Only the investigator can identify the subject’s name/other personal details by the study code.

During the clinical trial, if the name of the subject needs to be identified due to medical reasons, all relevant personnel are obliged to keep it confidential.

The sponsor can publish anonymous research data to external investigators for future research directly related to the study objective, or future research beyond the scope of the current study objective. The informed consent form explains this point to the study subjects. Anonymity means that all identifiable information will be deleted from the data sets and all links to subjects in the study will be deleted. Data confidentiality can ensure the confidentiality of the subjects participating in the study, so that they cannot be identified by external investigators. The anonymized data sets will contain the records of all subjects in the current study, but the anonymization process may change the data sets in some way, so external investigators will be informed that they cannot copy some results of the study.

XIX. Agreement on Publication of Test Results

An interim analysis will be performed on all research data after the last subject completes the follow-up at Month 6 after surgery.

The final results of this study will be submitted by the sponsor to the National Medical Products Administration for **renewal of registration** approval. The sponsor has obtained the product registration certificate granted by the National Medical Products Administration. All sites can publish articles on their own research, but the data and results of their published articles must be consistent with the summary report of this trial and the sub-site summary reports, and the sponsor must be notified in writing.

XX. Responsibilities Assumed by Each Party

The responsibilities stipulated in the *Good Clinical Practice for Medical Devices* are as follows:

(I) Responsibilities of Sponsors

Article 38 The sponsor is responsible for initiating, applying for, organizing and monitoring clinical trials, and shall be responsible for the authenticity and reliability of clinical trials. The sponsor is usually a manufacturer of medical devices. If the sponsor is an overseas institution, it shall appoint an agent within the territory of China.

Article 39 The sponsor is responsible for organizing the formulation and modification of the Investigator's Brochure, clinical trial protocol, informed consent form, case report form, relevant standard operating procedures, and other relevant documents, and is responsible for organizing the implementation of the training necessary for clinical trials.

Article 40 The sponsor shall choose clinical trial institutions and investigators in qualified medical device clinical trial institutions according to the characteristics of the investigational medical device. Before the sponsor signs the clinical trial agreement with clinical trial institution, the latest Investigator's Brochure and other relevant documents shall be provided to the clinical trial institution and investigator for them to decide whether they can undertake the clinical trial or not.

Article 41 The Investigator's Brochure shall contain the following main contents:

(1) Basic information of the sponsor and investigator;

(2) Summary of the investigational medical device;

(3) Summary and evaluation supporting the intended use of the investigational medical device and justification for the clinical trial design;

(4) Declaration that the manufacturing of the investigational medical device meets the requirements of applicable quality management system of medical devices.

Article 42 The sponsor shall not exaggerate to publicize the mechanism and efficacy of the investigational medical device when organizing the formulation of the clinical trial protocol.

Article 43 In the process of clinical trials, the sponsor shall modify the Investigator's Brochure and relevant documents in a timely manner when obtaining important information that affects the clinical trial, and submit the modified documents to the ethics committee for review and approval through the medical device clinical trial management department of the clinical trial institution.

Article 44 The sponsor shall reach a written agreement with the clinical trial institution and investigator on the following issues:

(1) Implement clinical trials according to relevant laws and regulations and clinical trial protocol, and accept monitoring, audit and inspection;

(2) Comply with data recording and reporting procedures;

(3) Keep the basic documents related to the trial for no less than the statutory period, until the sponsor informs the clinical trial institution and investigator that the documents are no longer needed;

(4) The sponsor is responsible for providing investigational medical devices to clinical trial institutions and investigators after being approved by the ethics committee, and determining the transportation conditions, storage conditions, time of storage, validity period, etc.;

(5) Investigational medical devices shall be qualified and have special identification for easy recognition and with correct coding and marking with "for trial", and shall be properly packaged and stored in accordance with the requirements of the clinical trial protocol;

(6) The sponsor shall establish standard operating procedures related to the quality control of clinical trials, such as transportation, reception, storage, distribution, handling and recovery of medical devices used in the trials, which shall be followed by the clinical trial institutions and investigators.

Article 45 The sponsor is responsible for the safety of the investigational medical device in the clinical trial. When it is found that the safety of subjects may be affected or the implementation of the trial may change the approval of the ethics committee to continue the trial, the sponsor shall immediately notify all clinical trial institutions and investigators, and take corresponding measures.

Article 46 If deciding to suspend or terminate the clinical trial, the sponsor shall inform the medical device clinical trial management department of all clinical trial institutions within 5 days, and explain the reason in writing. The medical device clinical trial management department of clinical trial institutions should timely notify the corresponding investigators and ethics committees. Suspended clinical trials shall not be resumed without the consent of the ethics committee. After the completion of the clinical trial, the sponsor should inform the food and drug regulatory authority of the province, autonomous region, or municipality directly under Central Government where the sponsor is located.

Article 47 The sponsor shall ensure that all investigators who conduct the clinical trial strictly abide by the clinical trial protocol. If the sponsor finds that the clinical trial institution and investigator do not comply with relevant laws and regulations, the GCP and the clinical trial protocol, the case shall be pointed out and corrected; if the case is serious or persists without correction, the trial should be terminated and a report should be made to the medical products administration departments of the province, autonomous region, or municipality directly under the Central Government where the clinical trial institution is located and the National Medical Products Administration.

Article 48 The sponsor shall bear the cost of treatment and corresponding economic compensation for subjects that suffer injuries or deaths associated with the clinical trial, except for harms caused by the fault of the medical institution and its medical staff in the diagnosis and treatment activities.

Article 49 The sponsor shall assume the responsibility for the monitoring of clinical trials, and select qualified supervisors to perform the supervision responsibilities.

The number of monitors and times of monitoring depend on the complexity of the clinical trial and number of clinical trial institutions participating in the trial.

Article 50 The monitor shall have the relevant professional background such as clinical medicine, pharmacy, biomedical engineering and statistics, and shall have received necessary training, be familiar with the relevant regulations and the GCP, familiar with the non-clinical information of the investigational medical device and clinical information of similar products, the clinical trial protocol and related documents.

Article 51 The monitor shall comply with the standard operating procedures for monitoring the clinical trials of the investigational medical device formulated by the sponsor, supervise and urge the implementation of clinical trials in accordance with the clinical trial protocol. The specific responsibilities include:

(1) Confirming that the clinical trial institution has had appropriate conditions, including the staffing and training meet the requirements, the laboratory is fully equipped and working in good condition, it is expected that there will be a sufficient number of subjects, and the participating study staff is familiar with the test requirements.

(2) Monitoring whether the clinical trial institutions and investigators comply with relevant regulations, the GCP and the clinical trial protocol in the early, middle, and late stages of the trial.

(3) Confirming that each subject has signed the informed consent form before participating in the clinical trial, and knowing the inclusion of subjects and the progress of the trial; clearly and truthfully recording the follow-ups, tests and examinations that the investigator have not done, and whether mistakes and omissions have been corrected; confirming that subjects who are affected but have not ended the participation of clinical trial re-sign the modified informed consent form.

(4) Confirming that all case report forms are filled out correctly and consistent with the source data; all mistakes and omissions have been corrected or noted, and signed and dated by the investigator; the disease type, total number of cases, and the sex, age, therapeutic effect of all cases shall be confirmed and recorded.

(5) Confirming that cases where the subject withdraws from the clinical trial or does not comply with the requirements of the informed consent form are documented, and discussing the cases with the investigator.

(6) Confirming that all adverse events, complications, and other device efficiencies are documented, and that serious adverse events and device deficiencies that may lead to serious adverse events are reported and documented within the specified time limit.

(7) Monitoring the supply, use, maintenance as well as transportation, receiving, storage, distribution, handling and recovery of the investigational medical device.

(8) Supervising the regular maintenance and calibration of the equipment in the course of clinical trials.

(9) Ensuring that all the documents related to the clinical trial received by the investigators are the latest version.

(10) A written report shall be submitted to the sponsor after each monitoring. The report shall include the name of the monitor, the date, time, place and contents of monitoring, the name of the investigator, project completion status, existing problems, conclusions, and correction of mistakes and omissions.

Article 52 The sponsor may organize auditors dependent from the clinical trial who have relevant training and experiences to audit the progress of the clinical trial and assess whether the clinical trial meets the requirements of the clinical trial protocol so as to ensure the quality of the clinical trial.

Auditing can be a part of the routine clinical trial quality management work of the sponsor, and also can be used to assess the effectiveness of monitoring activities, or audit serious and repeated deviations from the clinical trial protocol, suspected fraud and other cases.

Article 53 The auditor shall formulate an audit plan and audit procedures according to the importance of the clinical trial, number of subjects, type and complexity of the clinical trial,

and the risk level for subjects.

Article 54 For serious adverse events and device deficiencies that may lead to serious adverse events, the sponsor shall report to the medical products administration department that the sponsor has filed to and the competent health and family planning authority at the same level within 5 working days after knowing them. At the same time, the sponsor shall notify other clinical trial institutions and investigators participating in the trial, and inform the ethics committees of the clinical trial institutions through their medical device clinical trial management department.

Article 55 If the sponsor uses electronic clinical databases or remote electronic clinical data systems, it shall ensure that the clinical data is controlled and truthful, and that complete validation documents are formed.

Article 56 For multi-center clinical trials, the sponsor shall ensure that the documents have been formulated before the clinical trial to clarify the division of responsibilities of coordinating investigators and other investigators.

Article 57 For multi-center clinical trials, the sponsor shall organize the formulation of standard operating procedures according to the clinical trial protocol, and organize the training of all investigators participating in the trial on the clinical trial protocol and the usage and maintenance of the investigational medical device to ensure the consistency of the implementation of the clinical trial protocol and the usage of the investigational medical device.

Article 58 In multi-center clinical trials, the sponsor shall ensure that the case report form is designed rigorously and reasonably and enables the coordinating investigators to obtain all data of the clinical trial institution of each sub-site.

(II) Responsibilities of Clinical Trial Institutions

Article 59 Before accepting a clinical trial, clinical trial institutions shall assess their relevant resources according to the characteristics of the investigational medical device to decide whether they should accept the clinical trial.

Article 60 Clinical trial institutions shall properly keep the records and essential documents of the clinical trial in accordance with the agreement with the sponsor.

Article 61 The investigator responsible for the clinical trial shall meet the following conditions:

(1) With relevant professional technical title and qualification, such as associate chief physician, associate professor, associate researcher, and other titles above associate senior;

(2) With the professional knowledge and experiences required for investigational medical devices, and having received the relevant training if necessary;

(3) Be familiar with the requirements of the sponsor and the documents and literature related to the clinical trial provided by the sponsor;

(4) Having the ability to coordinate, dominate and use the personnel and equipment for conducting the trial, and having the ability to deal with the adverse events and other associated

events of the investigational medical device;

(5) Be familiar with the relevant Chinese laws, regulations and the GCP.

Article 62 Before the clinical trial, the medical device clinical trial management department of clinical trial institutions shall cooperate with the sponsor to apply to the ethics committee, and submit relevant documents in accordance with relevant provisions.

Article 63 The investigator shall ensure that the relevant personnel participating in the trial are familiar with the principle, scope of application, product performance, operation method, requirements for installation and technical indicators of the investigational medical device, understand the pre-clinical research data and safety data of the investigational medical device, and master the prevention and emergency handling of possible risks that may arise from the clinical trial.

Article 64 The investigator shall ensure that all personnel participating in the clinical trial fully understand the clinical trial protocol, relevant provisions, the characteristics of the investigational medical device and the responsibilities related to the clinical trial, ensure that a sufficient number of subjects that meet the inclusion criteria of the clinical trial protocol will participate in the clinical trial, and ensure that there is enough time to safely implement and complete the clinical trial in accordance with the relevant provisions during the trial period agreed in the agreement.

Article 65 The investigator shall ensure that the investigational medical device will only be used by the subjects in this clinical trial, and no fee may be charged.

Article 66 The investigator shall strictly abide by the clinical trial protocol, and shall not deviate from the protocol or change the protocol substantially without the consent of the sponsor and the ethics committee, or without the approval of the National Medical Products Administration as stipulated. However, in case of an emergency such as immediate danger to the subject, which needs to be eliminated immediately, it may also be reported in writing afterwards.

Article 67 The investigator is responsible for recruiting subjects and talking to the subjects or their guardians. The investigator is also responsible for explaining the details related to the investigational medical device and the clinical trial, informing subjects of the possible benefits and known and foreseeable risks, and obtaining the informed consent form signed and dated by subjects or their guardians.

Article 68 The investigator and other personnel participating in the trial shall not force or induce subjects by unfair means to participate in the trial.

Article 69 When the investigator finds an unexpected adverse event of the investigational medical device in the clinical trial, he/she shall modify the relevant contents of the informed consent form together with the sponsor. After the modified informed consent form is reviewed and approved by the ethics committee according to the relevant work procedures, the affected subjects or their guardians shall re-sign and confirm the modified informed consent form.

Article 70 The investigator is responsible for making medical decisions related to the clinical trial. When any clinical trial-related adverse event occurs, the clinical trial institution and the investigator shall ensure that the subjects are provided with adequate and timely treatment and care. The investigator shall timely inform subjects in a timely manner when the subject has a concurrent disease requiring treatment and care.

Article 71 If serious adverse events occur in the clinical trial, the investigator shall take appropriate treatment measures for subjects immediately, and report in writing to the medical device clinical trial management department of the clinical trial institution which will notify the sponsor in writing. The medical device clinical trial management department should report in writing to the corresponding ethics committee, the medical products administration departments and the competent health and family planning authority of the province, autonomous region, or municipality directly under Central Government where the clinical trial institution is located within 24 hours. For death events, the clinical trial institution and the investigator should provide all necessary materials to the ethics committee and the sponsor.

Article 72 The investigator shall record all adverse events that occur during the clinical trial and device deficiencies found, analyze the cause with the sponsor, form a written analysis report, and put forward his/her opinions for continuing, suspending or terminating the trial. Then the opinions shall be reported to the ethics committee for review through the medical device clinical trial management department of the clinical trial institution.

Article 73 The investigator shall ensure that the clinical trial data will be recorded in the case report form accurately, completely, clearly and timely. The case report form shall be signed by the investigator, and any modification of data shall be signed and dated by the investigator. At the same time, the original records shall be kept, and the original records shall be clearly identifiable.

Article 74 The clinical trial institution and the investigator shall ensure that the data, documents and records formed in the clinical trial are true, accurate, clear and secure.

Article 75 The clinical trial institution and the investigator shall be subject to the sponsor's supervision, verification, and oversight by the ethics committee, and shall provide all necessary records related to the trial. Where the medical products administration department and the competent health and family planning authority dispatch monitors to carry out inspections, the clinical trial institution and the investigator shall cooperate.

Article 76 If the clinical trial institution and the investigator find that the risks overweight the potential benefits, or obtain results sufficient to determine the safety and effectiveness of the investigational medical device, which requires to suspend or terminate the clinical trial, the subjects shall be notified, and it shall be ensured that the subjects will receive appropriate treatment and follow-up. At the same time, the situation shall be reported in accordance with the provisions, and a written explanation shall be provided. If necessary, the situation shall be reported to the local medical products administration department of the province, autonomous region and municipality directly under the Central Government.

The investigator shall inform the subjects in time after receiving the notification to suspend or terminate the clinical trial from the sponsor or the ethics committee, and ensure that the subjects will receive appropriate treatment and follow-up.

Article 77 If the sponsor violates the relevant provisions or demands to change the trial data or conclusion, the clinical trial institution and the investigator shall report to medical products administration department of the province, autonomous region and municipality directly under the Central Government where the sponsor is located, or the National Medical Products Administration.

Article 78 At the end of the clinical trial, the investigator should ensure that all records and reports are completed. At the same time, the investigator shall also ensure that the number of received investigational medical devices is consistent with the number of used, obsolete or returned devices, and ensure that the remaining investigational medical devices are disposed of properly, recorded and archived.

Article 79 The investigator may authorize relevant personnel to recruit subjects, communicate with subjects, record clinical trial data and manage investigational medical devices according to the needs of the clinical trial. The investigator shall offer related training to the authorized personnel and form relevant documents.

XXI. References

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3. Ophthalmic implants – Intraocular lenses – Part 7: Clinical investigations of intraocular lenses for the correction of aphakia (ISO 11979-7: 2018).
4. Guidelines for Clinical Trials of Soft Contact Lenses No. 51 of 2018.
5. SUN Working group (2005) Standardization of uvieitis nomenclature for reporting clinical data. Results of the first international workshop. Am J Ophthalmol 140: 509-516.

Investigator’s statement

I agree:

1. I will carry out this clinical trial in strict accordance with the Declaration of Helsinki, China's current regulations, and the requirements of the trial protocol.

2. I will accurately record all required data in the case report form (CRF), and complete the clinical trial report on time.

3. The investigational medical device will only be used for this clinical trial. I will completely and accurately record the receiving and use of the investigational medical device in

the course of the clinical trial, and keep the records.

4. I will allow the monitors, auditors authorized or dispatched by the sponsor and the regulatory authority to monitor, audit, and inspect the clinical trial.

5. I will strictly perform the terms of clinical trial contract/agreements signed by all parties.

I have completely read the clinical trial protocol, including the above statement, and I agree to all contents above.