a Novartis company

Clinical Trial Protocol

# Clinical Investigation of AcrySof® IQ PanOptix™ IOL Model TFNT00

| | |
|---|---|
| Protocol Number: | ILH297-C001 / NCT03280108 |
| Sponsor Name & Address: | Alcon Research, Ltd. and its affiliates ("Alcon")<br>6201 South Freeway<br>Fort Worth, Texas 76134-2099 |
| Project Name / Number: | PanOptix Trifocal IOL / A01875 |
| Test Article(s) / Product(s): | AcrySof IQ PanOptix<br>IOL Model TFNT00 |
| Release Date: | Refer to e-signature date |
| Investigator Agreement: | I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practices (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements. |

Principal Investigator:

_____ _____

Signature Date

Principal Investigator Name: _____

Principal Investigator Address: _____

_____

# 1 PROTOCOL SYNOPSIS

| | |
|---|---|
| Financial Disclosure for US FDA Submission Required? | Yes |
| Test Alticle(s) / Product(s): | The AclySofIQ PanOptix Intraocular lens (IOL) Model TFNT00 is a single-piece ultraviolet and blue light filtering foldable multifocal IOL. The biconvex optic is 6.0 mm in diameter and the lens has an overall diameter of 13.0 mm. The trifocal optic diffractive strncture is in the central 4.5 mm p01tion of the anterior surface of the optical zone and divides the incoming light to create a +2.17 D intelmediate and a +3.25 D near add power (IOL plane) in addition to the distance focus. The anterior surface is designed with 0.IO µm of negative spherical abenation to compensate for the positive spherical abe1rntion of the average human cornea.<br><br>The AclySofIQ PanOptix IOL is indicated for prima1y implantation in the capsular bag in the posterior chamber for the visual conection of aphakia in adult subjects with less than I diopter of pre-existing corneal astigmatism in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by also providing improved inte1mediate and near visual acuity compared to a monofocal IOL. |
| Objective(s): | Effectiveness:<br>The ***co-primary effectivenessobjectives*** are to:<br>• Demonstrate non-inferiority of Ac1ySof IQ PanOptix IOL Model TFNT00 compared to the concun ent control AcrySof Monofocal IOL Model SN60AT in mean photopic monocular best con ected distance visual acuity (4 m) for the first operative eye at Month 6 (Visit 4A).<br>• Demonstrate superiority of Ac1ySof IQ PanOpt ix IOL Model TFNT00 compared to the concun ent control Ac1ySof Monofocal IOL Model SN60AT in mean photopic monocular distance conected visual acuity at near (40 cm) for the first operative eye at Month 6 (Visit4A).<br>The ***secondary effectiveness objectives*** are to:<br>• First seconda1y: Demonstrate superior ity of Ac1y Sof **IQ** PanOptix IOL Model TFNT0O compared to the concun ent control Ac1ySofMonofocal IOL Model SN60AT in mean photopic monocular distance conected visual acuity at intermediate (66 cm) for the first operative eye at Month 6 (Visit 4A). |

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| | • Second seconda1y:Demonstrate superiority of AcrySof IQ PanOptix IOL Model TFNT00 compared to the concun ent control Ac1ySof Monofocal IOL Model SN60AT in proportion of subjects who respond "Never" to Q1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at Month 6 (Visit 4A).<br>Safety:<br>The ***co-primarysafety objectives*** are to<br>• Estimate the cumulative rate of secondary surgical interventions (SSis) related to the optical properties of the IOL for the first operative eye up to Month 6 (Visit 4A).<br>• Evaluate the mean binocular contrast sensitivity with and without glare for photopic and mesopic conditions at Month 6 (Visit 4A).<br><br>The ***secondary safety objective*** is to estimate rates of severe and most bothersome (separately) visual disturbances as rep01ted by the subjects using a questionnaire (QUVID) at Month 6 (Visit 4A).<br><br>The ***third safety objective*** is to evaluate rates of cumulative and persistent Adverse Events in first operative eyes at Month 6 (Visit 4A) in comparison to ISO 11979-7 Safety and Perfo1mance Endpoint (SPE) grid rates. |
| Clinical Trial Design: | This study is a prospective, multicenter, non-randomized, vision assessor-masked, parallel-group confirmatory trial. |
| No. of Subjects: | Required: 113 subjects bilaterally implanted with the AcrySof IQ PanOptix IOL Model TFNT00 and 113 subjects bilaterallyimplanted with the concunent control AcrySof Monofocal IOL Model SN60AT.<br><br>Planned: Approximately 125 subjects bilaterally implanted with the AcrySofI Q PanOptix IOL Model TFNT00 and 125 subjects bilaterally implanted with the concunent control AcrySof Monofocal IOL Model SN60AT to achieve the required numbers assuming a dropout rate of 10%, approximately, at 6 months post implantation. |
| Region(s): | United States |
| Clinical Trial Duration: | a. Total expected duration of the clinical investigation: 13 months<br>b. Expected duration of each subject'sparticipation:~7 months<br>c. Planned follow up dmation: 6-months post second eye implantation<br>d. Estimated time needed to select the number of subjects(ie, emollment period): 6 months |

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| Clinical Trial Population: | Adults subjects, 22 years of age or older, who require bilateral cataract extraction. | |
| Treatments: | ***Test Article:*** | AcrySof IQ PanOptix IOL Model TFNT00 |
| | Administration: | Routine small incision cataract surgery with IOL implantation. |
| | General Description: | A range of commonly utilized spherical powers (15 to 26.5 D) will be available. |
| | Duration of Treatment: | Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the cataract subject. |
| | ***Control Article:*** | AcrySof Monofocal IOL Model SN60AT |
| | Administration: | Routine small incision cataract surgery with IOL implantation. |
| | General Description: | A range of commonly utilized spherical powers (15 to 26.5 D) will be available. |
| | Duration of Treatment: | Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the cataract subject. |
| Inclusion & Exclusion Criteria: | Details can be found in Section 10 Subject Population | |
| Effectiveness Assessments | [redacted]<br>Distance Visual Acuity (VA)<br>• Monocular [redacted] and best corrected distance VA (4 m)<br>• Binocular and best corrected distance VA (4 m)<br>Intermediate Visual [redacted] cm<br>• Monocular- and distance corrected intermediate VA (66 cm)<br>• Binocular- and distance corrected intermediate VA (66 cm)<br>Near Visual Acuity<br>• Monocular and distance corrected near VA (40 cm)<br>• Binocular and distance corrected near VA (40 cm)<br>• Monocular mesopic distance corrected near VA (40 cm)<br>• [redacted]<br>IOLSAT questionnaire for spectacle need<br>[redacted] | |

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|---|---|
| Safety Assessments | • Adverse events (AEs) including secondary surgical intervention (SSI)<br>• Device deficiencies (DD)<br>• Surgical problems<br>• Intraocular pressure (IOP)<br>• Slit lamp examination<br>• IOL observations<br>• IOL position change<br>• Subjective posterior capsule opacification (PCO)<br>• Posterior capsulotomy<br>• Fundus visualization<br>• Dilated fundus examination<br>• Binocular contrast sensitivity<br>Photopic without glare<br>Photopic with glare<br>Mesopic without glare<br>Mesopic with glare<br>• [redacted]<br>• QUVID questionnaire for visual disturbances |
| [redacted] | |
| Planned Analyses: | Analyses relating to key endpoints are described below. See Section 15 Analysis Plan for additional details.<br><br>To account for multiplicity, the effectiveness hypotheses will be tested in sequence: 2 co-primaries, followed by first secondary followed by second secondaiy. The primary effectiveness objective is considered met only if both co-primary hypotheses are met. The type I enor for the non-inferiority test is 5% (I-sided) and for the superiority test is 2.5% (1-sided). Each of the secondaiy hypotheses will be tested at 2.5% (I -sided).<br><br>The statistical hypotheses in supp01i of the co-primaiy effectiveness objectives are:<br><br>• AcrySofIQ PanOptix IOL is non-inferior to AcrySof Monofocal IOL in mean photopic monocular best c01Tected distance visual acuity (BCDVA) for the first operative eye at Month 6.<br>• AcrySofIQ PanOptix IOL is superior to AcrySofMonofocal IOL in mean photopic monocular distance conected visual acuity at near (40 cm) for the first operative eye at Month 6.<br><br>he statistical hypotheses in supp01i of the secondaiy effectiveness bjectives are:<br><br>• AcrySofIQ PanOptix IOL is superior to AcrySof Monofocal IOL in mean photopic monocular distance conected visual acuity at |

| | |
|---|---|
| | inte rmediate (66 cm) for the first operative eye at Month 6.<br>• Ac1ySofIQ PanOptix IOL is superior to Ac1ySof Monofocal IOL in the propmtion of subjects who respond " Never" to Question 1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at Month 6.<br><br>Analysis of each co-prima1yeffectiveness endpoint and the first seconda1y endpoint (at Visit 4A) will be based on a mixed effects model. Two models will be fit to the first co-prima1y endpoint (BCDVA), 1 with a random effect for site and another with random effects for site and for treatment by site interaction. Both will include a fixed effect for treatment. The 2 models will be compared using Bayesian Infmmation Cliterion (BIC) and the model with lower BIC will be the chosen model to estimate the Least Squares Means (LSMEANS) difference in means (Ac1ySof IQ PanOptix IOL minus Ac1ySof Monofocal IOL) and the associated confidence intervals for all 3 aforementioned endpoints. The non-inferiority hypothesis will be deemed suppmted if the upper 95% confidence limit is less than the non-inferiority margin of 0.1 logMAR. Superiority hypotheses will be deemed suppmted if the upper 97.5% confidence limit is less than 0.0 logMAR.<br><br>The second secondary effectiveness endpoint will be analyzed by estimating the Mantel-Haenszel common difference of propmt ions (Ac1ySofIQ PanOptix IOL minus Ac1ySofMonofocal IOL) along with the con esponding confidence interval with site as a stratification variable. Superiority will be declared if the lower 97.5% confidence limit exceeds 0<br><br>The co-primaiy safety objectives are to<br>• Estimate the cumulative rate of secondary smgical interventions related to the optical prope1ties of the IOL for first operative eyes up to Month 6<br>• Evaluate the mean binocular contrast sensitivity with and without glai·e for photopic and mesopic conditions at Month 6.<br>The secondaiy safety objective is to<br>• Estimate rates of severe and most bothersome (separately) visual disturbances as repo1ted by the subjects using a questionnaire (QUVID) at Month 6.<br>The third safety objective is to<br>• Evaluate rates of cumulative and persistent adverse events in first operative eyes at Month 6 in compai·ison to the ISO 11979-7 SPE grid rates.<br><br>Analysis for the co-prima1yand secondaiy safety objectives will involve presenting point estimates (rates or means, depending on type of endpoint) and the con esponding confidence intervals for difference between IOL groups.<br><br>Descriptive statistics for adverse events will be |

<table>
<tr><td></td><td>first and all eyes. Incidence rates observed in each treatment arm (for first operative eyes, and for all eyes) will be compared to the cumulative and persistent adverse event SPE (safety and performance endpoint) rates based on 1-sided exact binomial calculation.<br><br>QUVID outcomes will be summarized using standard descriptive measures.</td></tr>
<tr><td>Sample Size Justification</td><td>Approximately 250 subjects will be bilaterally implanted with either the AcrySof IQ PanOptix IOL Model TFNT00 or the AcrySof Monofocal IOL Model SN60AT in a 1:1 ratio in order to ensure that at least 113 eligible subjects complete the study in the test group and the control group. This assumes a drop-out rate of 10%, approximately.<br><br>Power calculations for the effectiveness objectives are summarized in the table below:
<table>
<tr><th></th><th>Margin</th><th>Expected Difference</th><th>Std. dev</th><th>Type I error (1-sided)</th><th>Power</th></tr>
<tr><td>Non- Inferiority</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>BCDVA (4 m)</td><td>0.1</td><td>0.0</td><td>0.18</td><td>5%</td><td>99%</td></tr>
<tr><td>Superiority</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>DCNVA (40 cm)</td><td></td><td>0.1</td><td>0.18</td><td>2.5%</td><td>98%</td></tr>
<tr><td>DCIVA (66 cm)</td><td></td><td>0.1</td><td>0.18</td><td>2.5%</td><td>98%</td></tr>
<tr><td>Spectacle Wear</td><td></td><td>20%</td><td></td><td>2.5%</td><td>83%</td></tr>
</table>
All expected differences for tests of superiority favor the test lens. Estimates of VA endpoints reported in logMAR.<br><br>Adverse Events: For any event where a 0 incidence is observed in 113 first-operative eyes in the AcrySof IQ PanOptix IOL test group, the upper exact binomial 95% confidence limit is less than 3%. Thus, with 95% confidence, the true adverse event rate is less than 3%.<br><br>[redacted]<br><br>See section 15 for additional details.</td></tr>
</table>

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# List of Tables



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# 3 ABBREVIATIONS

| Abbreviation | Definition |
|---|---|
| AAS | All implanted analysis set |
| [redacted] | [redacted] |
| ADE | Adverse device effect |
| AE | Adverse event |
| ASADE | Anticipated serious adverse device effect |
| BAS | Best case analysis set |
| BCDVA | Best corrected distance visual acuity |
| BIC | Bayesian Information Criterion |
| CFR | Code of Federal Regulations |
| cm | Centimeter |
| CM | Clinical Manager |
| cpd | Cycles per degree |
| CRF | Case report form |
| CSM | Clinical site management |
| D | Diopter |
| DCDVA | Distance corrected distance visual acuity |
| DCIVA | Distance corrected intermediate visual acuity |
| DCNVA | Distance corrected near visual acuity |
| DD | Device deficiency |
| DFU | Directions for use |
| eCRF | Electronic case report form |
| EDC | Electronic data capture |
| FA | Fluorescein angiography |
| [redacted] | [redacted] |
| GCP | Good Clinical Practice |
| GPCMS | Global Product Complaint Management System |
| IB | Investigator's brochure |
| ICH | International Conference on Harmonization |
| IEC | Independent ethics committee |
| IOL | Intraocular lens |
| IOLSAT | Intraocular Lens Satisfaction questionnaire |
| IOP | Intraocular pressure |
| IRB | Institutional review board |
| ISO | International Organization for Standardization |
| IP | Investigational product |
| MOP | Manual of procedures |
| LASIK | Laser-assisted in-situ keratomileusis |
| LCSM | Lead Clinical Site Manager |
| LCVA | Low contrast visual acuity |
| LSMEANS | Least squares means |
| logMAR | Logarithm of minimum angle of resolution |

| | |
|---|---|
| m | Meter |
| µm | Micrometer |
| MedDRA® | Medical Dictionary for Regulatory Activities |
| mm | Millimeter |
| mmHg | Millimeters of mercury |
| nm | Nanometer |
| Nd:YAG | Neodymium-doped yttrium aluminium garnet |
| OCT | Optical coherence tomography |
| PCO | Posterior capsule opacification |
| PI | Principal Investigator |
| QUVID | Questionnaire for Visual Disturbances |
| RD | Retinal detachment |
| SADE | Serious adverse device effect |
| SAE | Serious adverse event |
| SAS | Safety analysis set |
| SOP | Standard operating procedures |
| SPE | Safety and Performance Endpoint |
| SS | Safety set |
| SSI | Secondary surgical intervention |
| SUN | Standardization of Uveitis Nomenclature |
| [redacted] | [redacted] |
| UNSV | Unscheduled visit |
| US | United States |
| USADE | Unanticipated serious adverse device effect |
| VA | Visual acuity |
| YAG | Yttrium aluminum garnet |

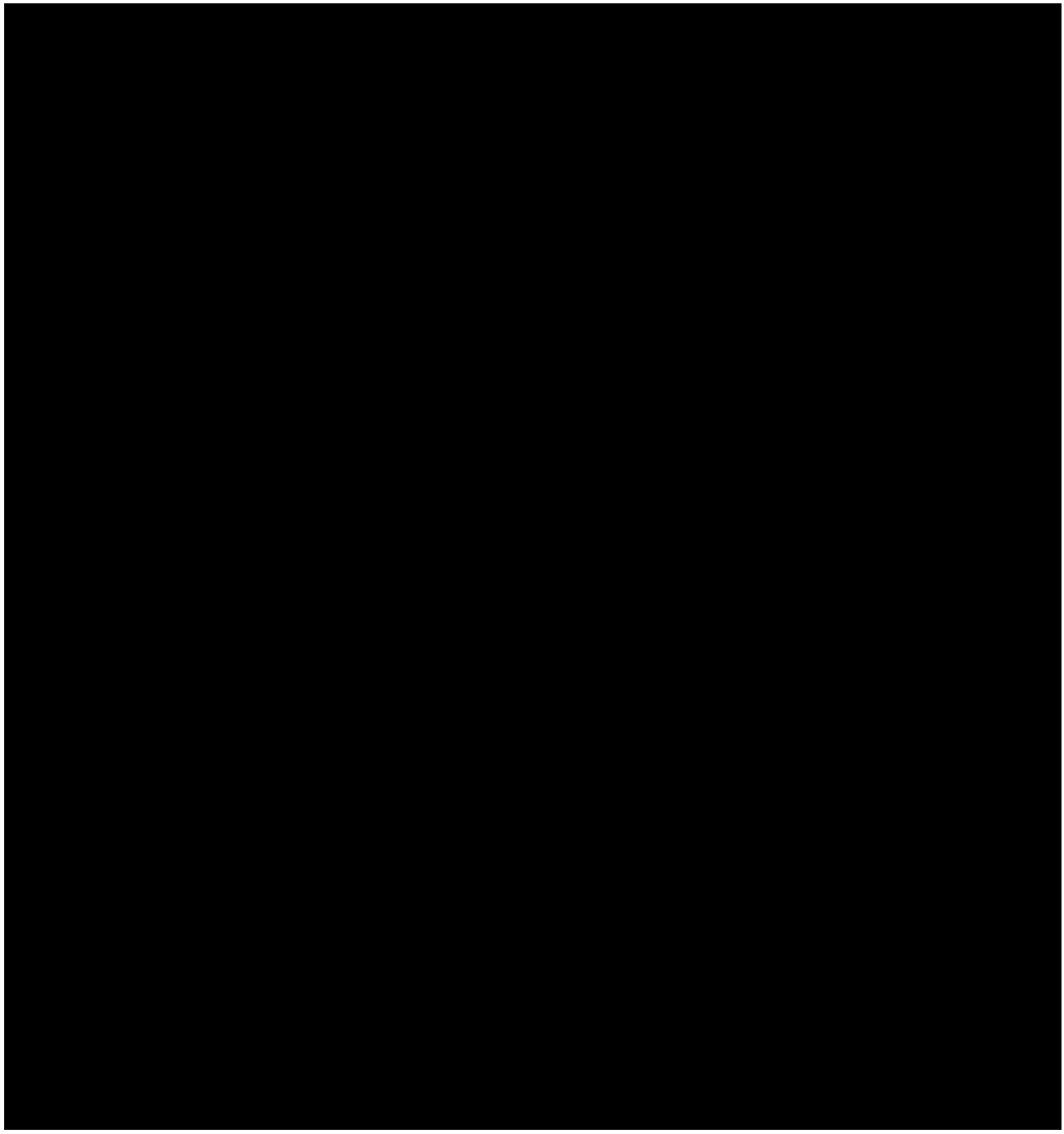
# 4 GLOSSARY OF TERMS

| | |
|---|---|
| Adverse Device Effect (ADE) | Adverse event related to the use of an investigational medical device or comparator, if applicable.<br>*Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the investigational medical device or comparator, if applicable.* |
| Adverse Event (AE) | Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.<br>*Note: For subjects, this definition includes events related to the investigational medical device, the comparator, or the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.* |
| Anticipated Serious Adverse Device Effect (ASADE) | Serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the risk analysis. |
| Assessment | A procedure used to generate data required by the study. |
| Device Deficiency | Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance.<br>*Note: This definition includes malfunctions, misuse or use errors, and inadequate labeling.* |
| Performance (Clinical) | Behavior of a medical device or response of the subject to that medical device in relation to its intended use, when correctly applied to appropriate subjects. |
| Malfunction | Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan. |
| Nonserious Adverse Event | Adverse event that does not meet the criteria for a serious adverse event. |
| Period | A minor subdivision of the study timeline; divides phases into smaller functional segments such as screening, baseline, operative, postoperative, etc. |
| Rhegmatogenous RD | Rhegmatogenous Retinal Detachment |
| Cumulative Adverse Events | Total number of Adverse Events that have occurred at any time up to a specified time point, postoperatively. |
| Persistent Serious | Adverse events present at the conclusion of the clinical investigation. |

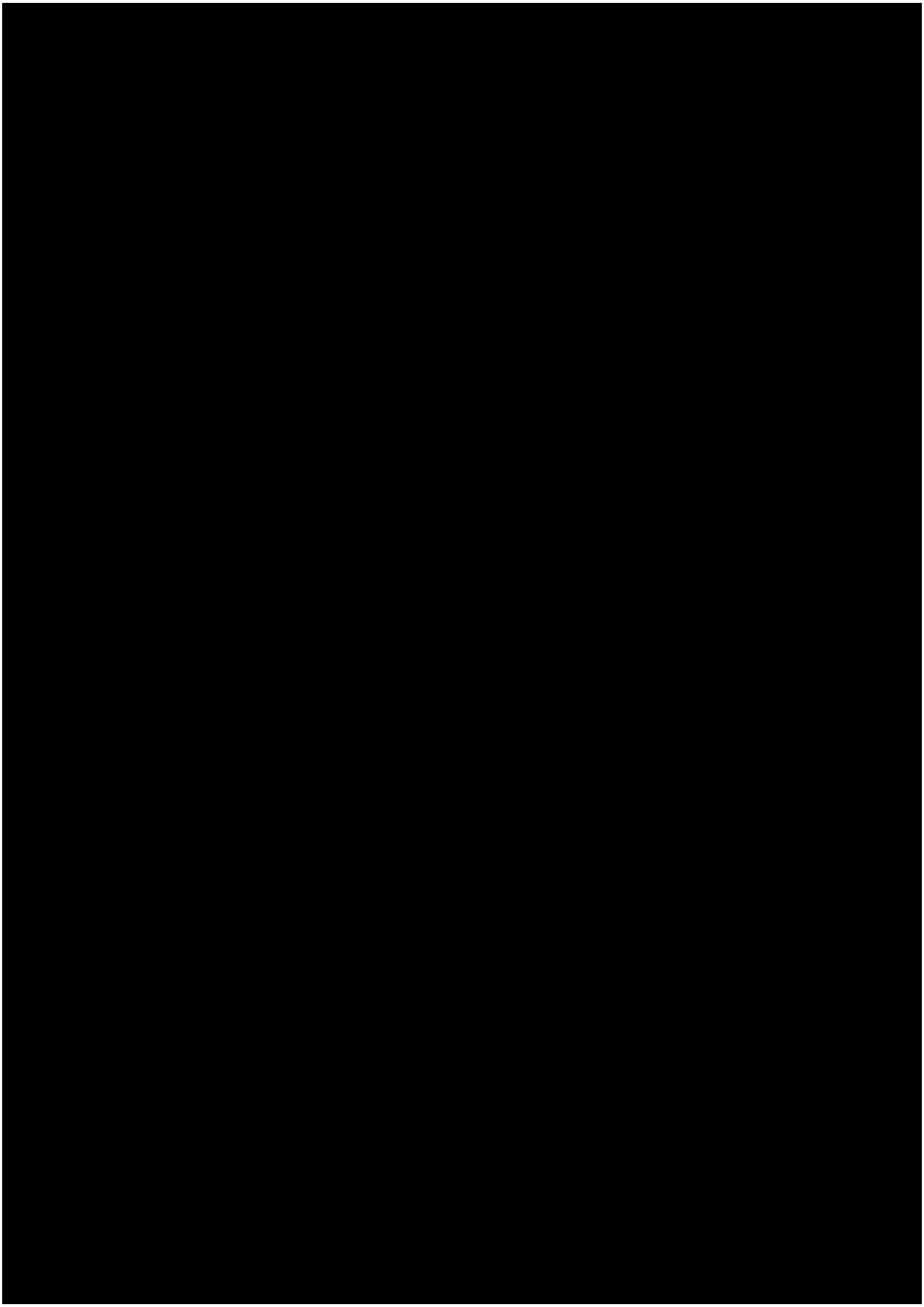
| | |
|---|---|
| Ad verse Even ts | |
| Serio us Ad verse Device Effect (SADE) | Ad verse device effect that has resulted in any of the consequences characteristic of a serious adverse event. |
| Serious Adverse Event (SAE) | Adverse event that led to any of the following:<br>• Death.<br>• Aserious deterioration in health that either resulted in:<br>a) a life-threatening illness or injmy.<br>*Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.*<br>b) pe1manent impaitment to a body structure or a bod y fu nction.<br>c) in-pat ient hospitaliza tion or pro lon ged ho spitalization .<br>*Note: Plan ned hospitalization for a pre-existing condition,or a procedure required by the clinical investigation plan, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalizationare AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether " hospitalization" occurred, the event should be considered serious.*<br>d) a medical or smgical intervention to prevent a) or b). This includes any ocular secondary smgical intervention excluding posterior capsulotomy.<br>e) any indirect haim as a consequence of incon ect diagnostic test results when used within manufacturer's instruc tions for use.<br>• Fetal disu-ess , fe tal death , or a con genit al abn o1m ali ty or bitth defect. |
| Subject Number | A number assigned to each subject who emolls in the study. When combined with the site number, a unique identifier is created for each subject in the study. |
| Unanticipated Serious Adverse Device Effect (USADE) | Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk analysis. |

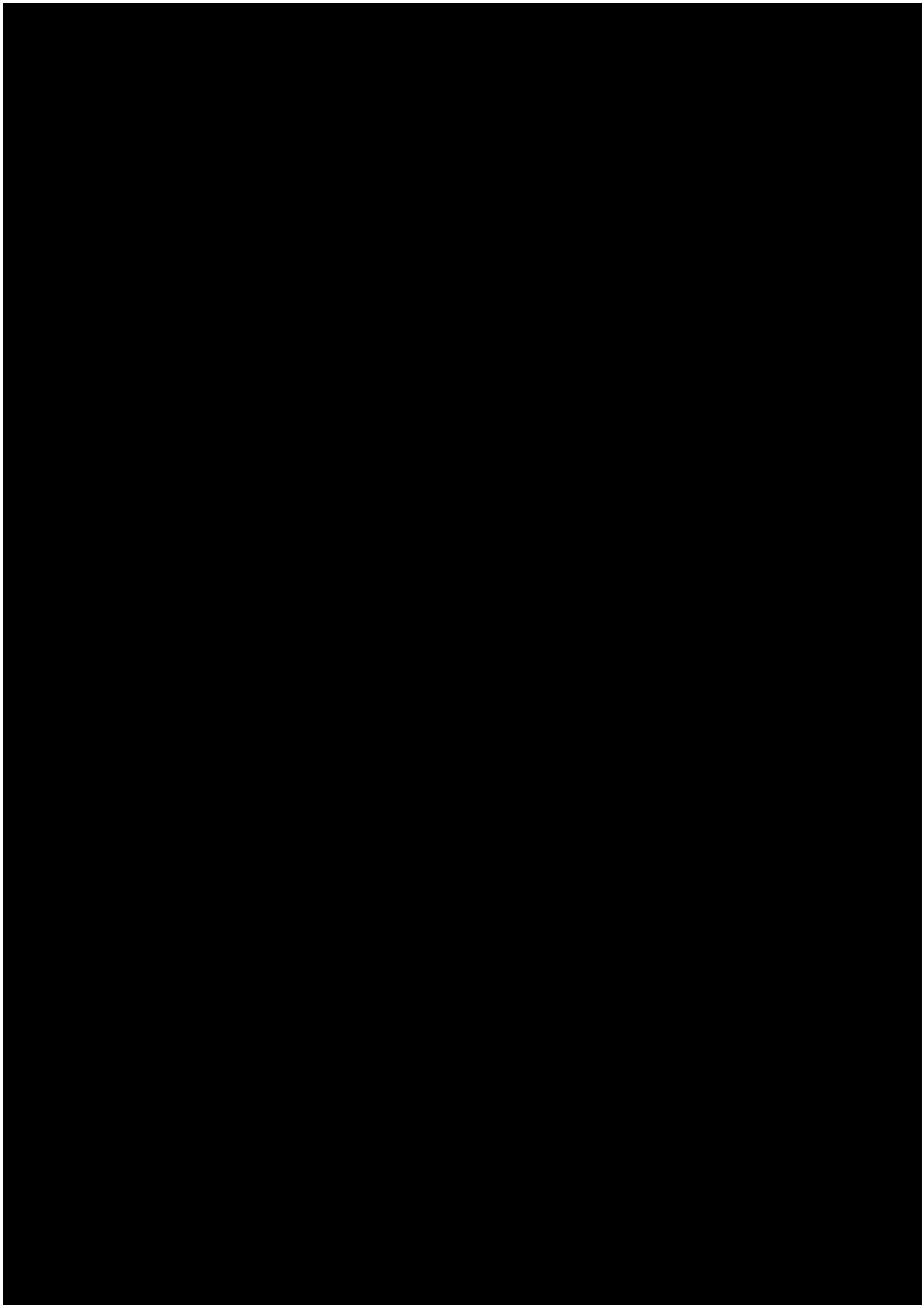
# 5 AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by the Sponsor and must be approved by the Institutional Review Board (IRB)/ Independent Ethics Committee (IEC) prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.



**Section 12.3: Unscheduled Visits**





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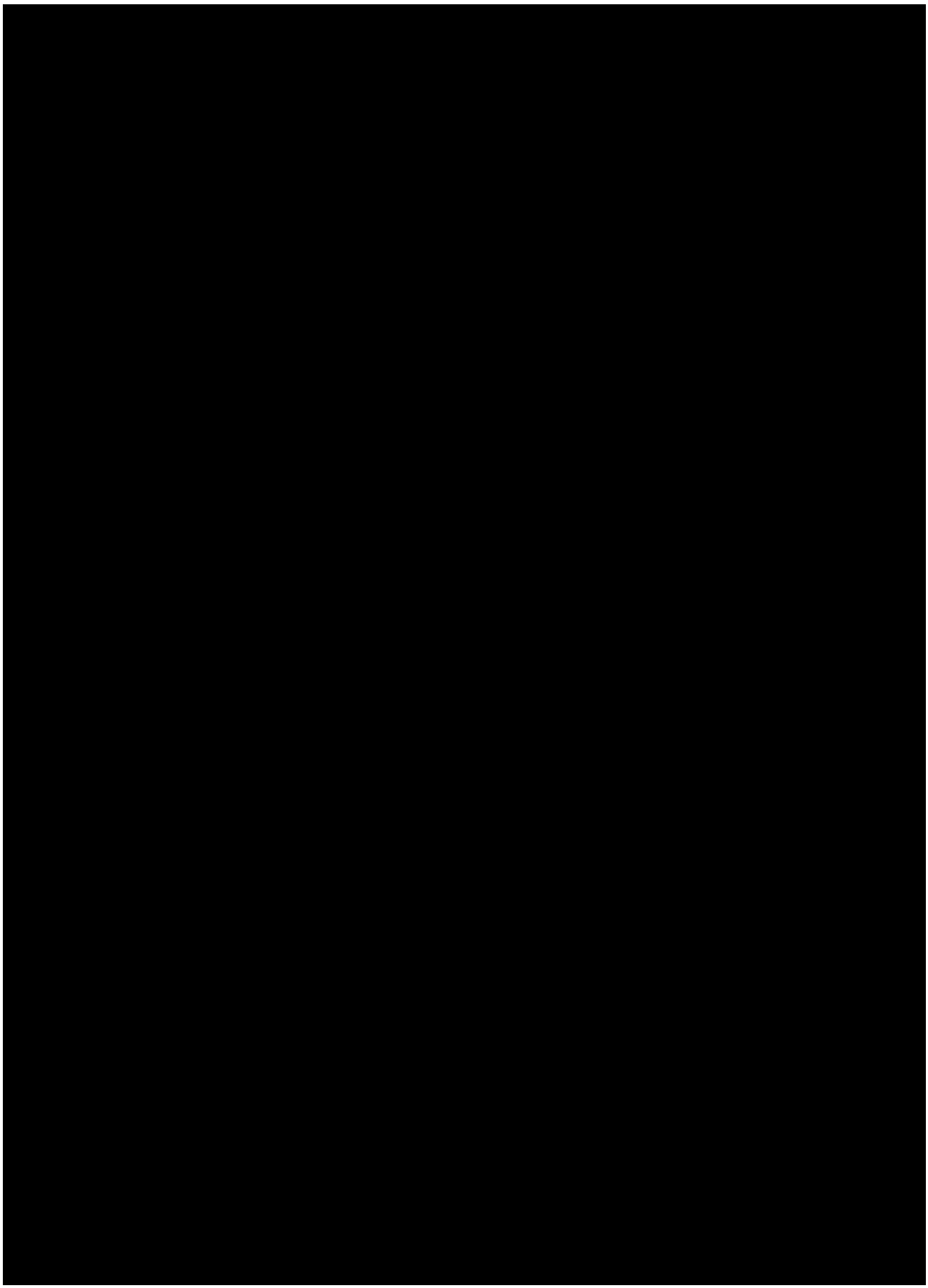


# 6 SCHEDULE OF VISITS

| | Visit 0 | Visit 00 | Visit 1 | Visit 2 | Visit 3 | Visit 00A | Visit 1A | Visit 2A | Visit 3A | Visit 4A* | | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Part 1 | Part 2 | |
| **Procedure/ Assessment** | **Screen (Day -30 to 0)** | **Implant 1** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Implant 2** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Day 120-180** (from 2nd eye) | | **N/A** |
| Informed Consent | X | | | | | | | | | | | |
| Demographics | X | | | | | | | | | | | |
| Medical History | X | | | | | | | | | | | |
| Concomitant Medications | X | X | X | X | X | X | X | X | X | X | X | X |
| Inclusion/Exclusion | X | X | | | | X | | | | | | |
| [redacted] | | | | | | | | | | | | |
| Urine Pregnancy Test | X | | | | | | | | | | | |
| Administer Treatment(s) | | X | | | | X | | | | | | |
| Device Deficiencies | | X | X | X | X | X | X | X | X | X | X | X |
| Adverse Events (Both Volunteered and Elicited) | X | X | X | X | X | X | X | X | X | X | X | X |
| [redacted] | | | | | | | | | | | | |

| | Visit 0 | Visit 00 | Visit 1 | Visit 2 | Visit 3 | Visit 00A | Visit 1A | Visit 2A | Visit 3A | Visit 4A* | | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Part 1 | Part 2 | |
| **Procedure/ Assessment** | **Screen (Day -30 to 0)** | **Implant 1** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Implant 2** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Day 120-180** (from 2nd eye) | | **N/A** |
| [redacted] | | | | | | | | | | | | |
| Photopic Best Corrected Distance Visual Acuity (4m) | X | | | X | X | | | X | X | X, Xb | | |
| Photopic Distance Corrected Intermediate Visual Acuity (66 cm) | | | | | X | | | | X | X, Xb | | |
| [redacted] | | | | | | | | | | | | |
| Photopic Distance Corrected Near Visual Acuity (40 cm) | | | | | X | | | | X | X, Xb | | |
| Distance Contrast Sensitivity – photopic | | | | | | | | | | Xb | | |

| | Visit 0 | Visit 00 | Visit 1 | Visit 2 | Visit 3 | Visit 00A | Visit 1A | Visit 2A | Visit 3A | Visit 4A* | | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Part 1 | Part 2 | |
| **Procedure/ Assessment** | **Screen (Day -30 to 0)** | **Implant 1** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Implant 2** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Day 120-180** (from 2nd eye) | | **N/A** |
| with glare | | | | | | | | | | | | |
| Distance Contrast Sensitivity – photopic without glare | | | | | | | | | | Xb | | |
| Distance Contrast Sensitivity – mesopic with glare | | | | | | | | | | Xb | | |
| Distance Contrast Sensitivity – mesopic without glare | | | | | | | | | | Xb | | |
| [redacted] | | | | | | | | | | | | |
| QUVID questionnaire for visual disturbances)† | Xb | | | | | | | | Xb | Xb | | Xb |
| IOLSAT questionnaire | Xb | | | | | | | | Xb | Xb | | |

| | Visit 0 | Visit 00 | Visit 1 | Visit 2 | Visit 3 | Visit 00A | Visit 1A | Visit 2A | Visit 3A | Visit 4A* | | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Part 1 | Part 2 | |
| **Procedure/ Assessment** | **Screen (Day -30 to 0)** | **Implant 1** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Implant 2** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Day 120-180** (from 2nd eye) | | **N/A** |
| for spectacle need | | | | | | | | | | | | |
| | | | | | | | | | | | | |
| Operative Eye | | X | | | | X | | | | | | |
| Surgical Problems | | X | | | | X | | | | | | |
| Other Procedures at Surgery | | X | | | | X | | | | | | |
| Incision Site | | X | | | | X | | | | | | |
| Final Incision Size | | X | | | | X | | | | | | |
| Lens Information | | X | | | | X | | | | | | |
| IOL Damage | | X | | | | X | | | | | | |
| Slit Lamp Examination | X | | X | X | X | | X | X | X | | X | X |
| Fundus Visualization | | | | | X | | | | X | | X | |
| Dilated Fundus Examination | X | | | | X | | | | X | | X | X |
| IOL Observations | | | X | X | X | | X | X | X | | X | X |
| Secondary Surgical Interventions | | | X | X | X | | X | X | X | | X | X |
| Subjective Posterior Capsule Opacification | | | X | X | X | | X | X | X | | X | X |
| Posterior Capsulotomy | | | X | X | X | | X | X | X | | X | X |
| Lens decentration and tilt | | | X | | X | | | X | X | | X | X |

| | Visit 0 | Visit 00 | Visit 1 | Visit 2 | Visit 3 | Visit 00A | Visit 1A | Visit 2A | Visit 3A | Visit 4A* | | USV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Part 1 | Part 2 | |
| **Procedure/ Assessment** | **Screen (Day -30 to 0)** | **Implant 1** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Implant 2** | **Day 1-2** | **Day 7-14** | **Day 30-60** | **Day 120-180** (from 2nd eye) | | **N/A** |
| Intraocular pressure | X | | X | X | X | | X | X | X | | X | X |

Xb - Binocular testing is performed on the study group subjects who are implanted bilaterally with the MIOL and on the control group subjects who are implanted bilaterally with the control IOL. The questionnaires will be completed in all subjects.

[redacted]

# 7 INTRODUCTION

## 7.1 Background

Monofocal IOLs are designed to replace the focusing power of the natural lens (typically after cataract surgery) by providing good visual function through a single, fixed, focal length; thus, generally correcting a subject's distance vision. However, many pseudophakic subjects implanted with monofocal IOLs ultimately require reading glasses to compensate for the loss of the ability to see clear at intermediate or near distances. Several IOL designs for treating presbyopia in pseudophakic subjects exist in modern day clinical practice, including the use of multifocal IOLs. Multifocal IOLs offer the subject an opportunity to overcome the loss of accommodation by providing multiple focal points. The majority of commercially available multifocal IOLs have 2 optical zones – one that provides distance vision and a second that provides near vision. The investigational AcrySof IQ PanOptix IOL Model TFNT00 test IOL (hereto referenced as TFNT00) improves on commercially available multifocal IOLs by creating an additional focal point for intermediate vision. The TFNT00 has a multifocal optical design that provides distance vision, near vision at approximately 40 cm and intermediate vision at approximately 60 cm. The control lens, the AcrySof Monofocal IOL Model SN60AT (hereto referenced as SN60AT) is a monofocal which provides distance vision only.

The purpose of this clinical study is to compare the visual outcomes of this multifocal IOL against that of a monofocal lens, the AcrySof Monofocal IOL Model SN60AT, in order to demonstrate comparable distance vision and superior near and intermediate vision.

## 7.2 Clinical Trial Design

This study is a prospective, multicenter, non-randomized, vision assessor-masked, parallel-group confirmatory trial. It compares an investigational trifocal IOL and a commercially available monofocal IOL. [redacted] (Note that neither laser nor any other types of refractive procedures are allowed at any time in the clinical trial.) The study will include adults (≥22 years of age) who require bilateral cataract extraction. Potential subjects will be screened for enrollment into the trial. Those qualifying will attend a total of 10 visits (7 visits occur postoperatively) over a 7 month period.

This study is not randomized. Because the test and control IOL designs offer different risks and benefits, trial subjects will be allowed to select the lens model that best fits his or her lifestyle. After careful consideration and consultation, the subject will be allowed at the time of consent to select the lens model that will be bilaterally implanted. Post consent, the electronic data capture (EDC) system will assign the subject number. To mitigate the risk of bias, the assessor

will be masked for all vision assessments. The subject will be provided with his/her permanent implant card at the time of implant.

Standard clinical trial methods that minimize bias in multicenter studies will be used such as standardized test procedures, commonInvestigator training, and common inclusion/exclusion criteria.

No interim analysis of the data will be conducted. Final data analysis will be conducted at study completion.

An overview of the study design is depicted in Table7-1.

**Table 7-1 Study Design**

| Time From Implantation | First Eye | Second Eye |
|---|---|---|
| -30 to 0 days pre-operatively | Visit 0 (monocular [First and Second eye] and binocular) | |
| Operative (IOL implantation) | Visit 00 | Visit 00A* |
| 1 - 2 days post-operatively | Visit 1 (monocular) | Visit IA (monocular) |
| 7 - 14 days post-operatively | Visit 2 (monocular) | Visit 2A (monocular) |
| 30 - 60 days post-operatively | Visit 3 (monocular) | Visit 3A (monocular) |
| 120 - 180 days post-operatively (after Second eye implantation) | Visit 4A" (monocular [First and Second eye] and binocular) | |

*NOTE: IOL implantation in the second eye is intended to occur between 7 and 30 days after IOL implantation in the first eye.

[redacted]

# 8 CLINICAL TRIAL OBJECTIVES

## 8.1 Primary Objective

The ***co-primary effectiveness objectives*** are to:

- Demonstrate non-inferiority of Ac1ySofI Q PanOptix IOL Model TFNT00 compared to the concmTent contro l Ac1yS of Monofocal IOL Model SN60AT in mean photopic monocular best coITected dis tance vis ual acuity (4 m) for the first operative eye at Month 6 (Visit 4A).

- Demonstrate superiority of AcrySof IQ PanOptix IOL Model TFNT00 compared to the concunent control AcrySof Monofocal IOL Model SN60AT in mean photopic monocular distance conected visual acuity at near (40 cm) for the first operative eye at Month 6 (Visit 4A).

The ***co-primary safety objectives*** are to

- Estimate the cumulative rate of secondary surgical interventions (SSis) related to the optical properties of the IOL for first operative eye up to Month 6 (Visit 4A).
- Evaluate the mean binocular contrast sensitivity with and without glare for photopic and mesopic conditions at Month 6 (Visit 4A).

## 8.2 Secondary Objectives

The ***secondary effectiveness objectives*** are to:

- First secondary: Demonstrate superiority of AcrySof IQ PanOptix IOL Model TFNT00 compared to the concunent control AcrySof Monofocal IOL Model SN60AT in mean photopic monocular distance conected visual acuity at intermediate (66 cm) for the first operative eye at Month 6 (Visit 4A).
- Second secondary: Demonstrate superiority of Acry Sof IQ PanOptix IOL Model TFNT00 compar·ed to the concurrent control AcrySofMonofocal IOL Model SN60AT in proportion of subjects who respond "Never" to Q1 of the IOLSATquestionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at Month 6 (Visit 4A).

The ***secondary safety objective*** is to:

- The ***secondary safety objective*** is to estimate rates of severe and most bothersome (separ·ately) visual disturbances as reported by the subjects using a questionnaire (QUVID) at Month 6 (Visit 4A).

## 8.3 Other Objectives

The ***third safety objective*** is to evaluate rates of cumulative and persistent Adverse Events in first operative eyes at 6 months (Visit 4A) in comparison to ISO 11979-7 SPE grid rates.

## 8.4 Study Endpoints

### 8.4.1 Effectiveness Endpoints

Primary, secondary, [redacted] effectiveness endpoints ar·e listed be lo w.

Primary Effectiveness

- Mean photopic monocular best corrected distance visual acuity (4 m)
- Mean photopic monocular distance corrected visual acuity at near (40 cm)

Secondary Effectiveness

- Mean photopic monocular distance conected visual acuity at intermediate (66 cm)
- Proportion of subjects who respond " Never" to Q1 of the IOLSAT questionnaire

[redacted]

[redacted]

### 8.4.2 Safety Endpoints

Primaiy Safety *(6* months)

- Cumulative rate of secondary surgical inte1ventions (SSis) related to the optical prope1ties of the IOL
- Mean photopic *without* glare binocular distance contrast sensitivity
- Mean photopic *with* glare binocular distance contrast sensitivity
- Mean mesopic *without* glare binocular distance contrast sensitivity
- Mean mesopic *with* glare binocular distance contrast sensitivity

Secondaiy Safety *(6* months)

Rates of severe and most bothersome (separately) visual disturbances as rep01ted by the subjects using a questionnaire (QUVID).

Third Safety *(6* months)

- Cumulative and persistent rates of adverse events in first operative eyes and all eyes at 6 months.

Other Safety

- Rates of all visual disturbances as reported by the subjects using the QUVID questionnaire at 1 and 6 months
- [redacted]
- IOP
- Slit lamp obse1vations
- Dilated fundus obse1vations
- Ability to evaluate the fundus
- Rates of ocular adverse events, including SSis related to the optical prope1ties, for either eye
- Adverse events
- Device deficiencies
- IOL observations

- IOL position change
- Subjective PCO
- Posterior capsulotomies
- Surgical problems

# 9 INVESTIGATIONAL PLAN

## 9.1 Outline of Clinical Trial

This is a prospective, non-randomized parallel-group confirmatory study in which unmasked subjects will be bilaterally implanted with either a test IOL (TFNT00) or a control IOL (SN60AT). To mitigate the risk of bias, the assessor will be masked for all vision assessments.

Subjects participating in the trial will attend a total of 10 visits study visits over a 7 month period. Of these 10 visits, 1 is preoperative, 2 are operative, and the remaining 7 are postoperative visits. Refer to Table 7-1 above for a study outline. Unscheduled visits (UNSV) may be attended if needed for medical attention.

Primary endpoint data will be collected at the final visit, Visit 4A (120-180 days post Second eye implantation). [redacted]

## 9.2 Study Design

This study is a prospective, multicenter, confirmatory trial comparing a trifocal IOL and a monofocal IOL following bilateral implantation. The study will include adults (≥ 22 years of age) who require bilateral cataract extraction. Potential subjects will be screened for enrollment into the trial. Those qualifying will attend a total of 10 visits (7 postoperative) over a 7 month period.

***Note:*** Month 6 (Visit 4A) will be completed over 2 days within a 2 week period. All visits must be completed within the specified visit window.

[redacted]

No interim analysis of the data will be conducted. Final data analysis will be conducted at study completion.

## 9.3 Rationale for Study Design

The purpose of this clinical study is to compare the visual outcomes of this multifocal IOL against that of a monofocal lens, the AcrySof Monofocal IOL Model SN60AT, in order to demonstrate comparable distance vision and superior near and intermediate vision.

## 9.4 Procedures per Study Visit

Section 12 Clinical Trial Procedures contains procedures per study visit.

## 9.5 Known and Potential Risks

Complications may occur on the surgery day or throughout the postoperative period. As with any type of intraocular surgery, there is a possibility of complications due to anesthesia, drug reactions, and surgical problems. The surgical procedure can exacerbate a pre-existing ocular condition. Possible problems during surgery include corneal endothelial touch, detached Descemet's membrane, iris damage, iris prolapse, iris trauma, iris incarceration, zonular rupture, vitreous loss, capsulorhexis tear, capsular rupture, uncontrollable intraocular pressure, hyphema, and retinal damage. An IOP increase may occur from the surgical procedure, residual viscoelastic in the eye, or a steroid response to postoperative medications.

Additionally, potential postoperative adverse events include but are not limited to corneal stromal edema, cystoid macular edema, endophthalmitis, hypopyon, iritis, lens dislocation, membrane formation on the IOL, pupillary block, retinal detachment, cyclitic membrane, transient or persistent glaucoma, retinal tear, vitritis, iris touch, pupil ovalization, posterior synechiae, ocular inflammation, ocular discomfort or pain, inflammation, decreased vision, decreased contrast sensitivity, decreased color perception, visual disturbances, and corneal endothelial cell loss.

An IOL replacement or explantation may be appropriate in some cases of residual refractive error, ocular infection, subject dissatisfaction, or visual disturbances (eg, glare, halos, starbursts, hazy vision, blurred vision, double vision, visual distortions, and color distortions, etc.). An SSI (eg, IOL repositioning, replacement, or explantation) may be appropriate if the IOL position significantly differs from the intended placement. Alternatively, spectacles or contact lenses may be prescribed to resolve residual refractive error. Other secondary surgical interventions include, but are not limited to: IOL repositioning, refractive laser treatment, paracentesis, vitreous aspirations, iridectomy or laser iridotomy for pupillary block, wound leak repair, and retinal detachment repair.

A summary of known and potential risks and benefits to humans, as identified in the literature or through preclinical testing and/or prior clinical evaluations, for each investigational product can be found in the Investigator's Brochure (IB-0143) and the Directions for Use (AcrySof Monofocal IOL Model SN60AT).

### 9.5.1 Potential Benefits

The TFNT00 IOL is a single-piece, trifocal diffractive lens with a +3.25 D near ADD and +2.17 D intermediate ADD intended to provide vision to aphakic subjects at near, intermediate, and distance (García-Pérez 2017; Kohnen 2015; Lawless 2017) without the need, in many subjects, for additional correction with spectacles or contact lenses.

### 9.5.2 Risk Benefit Assessment

Based on the formal risk assessment, TFNT00 demonstrates a risk profile that is comparable to the FDA-approved ACRYSOF IQ ReSTOR +3.0 Add Power IOL (Model SN6AD1), [redacted] Furthermore, it was concluded that the benefits of increased intermediate vision while maintaining visual performance at near distance significantly outweigh the risks of suboptimal surgical outcomes [redacted] when the TFNT00 is used in cataract surgery. Potential risks following implantation of the TFNT00 include visual disturbances such as glare and halos which are known risks for multifocal IOLs. The benefits of improved near and intermediate vision (Garcia-Perez 2017), when weighed against the risks of visual disturbances, result in a benefit to risk profile that is favorable for the both the test and control IOLs.

# 10 SUBJECT POPULATION

The study population includes approximately 250 subjects (125 in each arm) to be bilaterally implanted at approximately 12 sites with a minimum of 20 subjects per site (approximately 10 in each arm).

Each site should contribute a minimum of 20 subjects but not more than 25% of the total study sample size.

Enrollment is anticipated to take approximately 6 months.

To participate in the clinical trial, subjects must be ≥ 22 years of age with no ocular pathology that could confound study outcomes, and must require clear cornea cataract extraction in both eyes. Additional entry criteria are listed below in Sections 10.1 through 10.3.

Check all entry criteria at baseline (Visit 0) and at both surgical visits (Visit 00, Visit 00A). If a subject is excluded prior to first eye surgery (IOL does not come in contact with the eye), the subject should be discontinued from participation in the study. Refer to Section 12.4 Discontinued Subjects for further details.

If a subject reschedules surgery, and this rescheduling results in preoperative/baseline assessments (Visit 0) falling outside of the -30 to 0 day window, assessments should be repeated, and inclusion/exclusion criteria re-verified. Subjects failing to pass entry criteria may not be re-screened.

## 10.1 Inclusion Criteria

Inclusion criteria must be met in both eyes.

1. Adults, 22 years of age or older at the time of surgery, diagnosed with bilateral cataracts with planned cataract removal by phacoemulsification with a clear cornea incision
2. Able to comprehend and willing to sign informed consent and complete all required postoperative follow-up procedures
3. BCDVA projected to be 0.2 logMAR or better
4. Calculated lens power within the available range
5. Preoperative keratometric astigmatism of less than 1.0 D in both operative eyes.
6. Clear intraocular media other than cataract in both eyes

## 10.2 Exclusion Criteria

Exclusion criteria must be met in both eyes.

1. Clinically significant corneal abnormalities including corneal dystrophy (eg, epithelial, stromal, or endothelial dystrophy), irregularity (including irregularity due to dry eye syndrome), inflammation or edema per the Investigator's expert medical opinion

   *Note:* conditions including, but not limited to: keratitis, keratoconjunctivitis, keratouveitis, keratopathy, or keratectasia should be excluded.

2. Previous corneal transplant;
3. Previous refractive surgery or refractive surgery procedures (including, but not limited to LASIK, astigmatic keratotomy, and limbal relaxing incisions)
4. History of or current retinal conditions or predisposition to retinal conditions, previous history of, or a predisposition to, retinal detachment or presence of diabetic retinopathy that the Investigator judges could confound outcomes

   *Note:* Conditions including but not limited to background of diabetic retinopathy, diabetic macular edema or proliferative diabetic retinopathy, macular degeneration).

5. Amblyopia
6. Rubella, congenital, traumatic, or complicated cataracts
7. Extremely shallow anterior chamber not due to swollen lens
8. History of or current anterior or posterior segment inflammation of any etiology, or any disease producing an inflammatory reaction in the eye (eg, iritis or uveitis)
9. Iris neovascularization
10. Glaucoma (uncontrolled or controlled with medication)
11. Optic nerve atrophy
12. Subjects with diagnosed degenerative eye disorders (e.g. macular degeneration or other retinal disorders)
13. Pregnancy or lactation
14. Any subject currently participating in another investigational drug or device study
15. Subjects who may reasonably be expected to require a SSI at any time during the study (other than YAG capsulotomy)
16. Subjects who are expected to require retinal laser treatment

17. Any disease or pathology, other than cataract, that (in the expert opinion of the Investigator) is expected to reduce the potential postoperative BCDVA to a level worse than 0.30 logMAR

    *Note:* Conditions including, but not limited to the following: amblyopia, clinically severe corneal dystrophy (eg, epithelial, stromal, or endothelial dystrophy), diabetic retinopathy, extremely shallow anterior chamber, not due to swollen cataract, microphthalmos, previous retinal detachment, previous corneal transplant, recurrent severe anterior or posterior segment inflammation of unknown etiology, iris neovascularization, uncontrolled glaucoma, aniridia, or optic nerve atrophy, or diagnosis of pseudoexfoliation.

18. [redacted]

## 10.3 Reasons not to implant a study IOL

Below is a list of criteria that when occurring prior to IOL implantation prevents the study or control lens from being implanted. This is true for both eyes. A subject discontinuing at the time of surgery will be considered an enrolled subject, not a screen failure.

1. Any other additional procedures during the phacoemulsification and IOL implant due to intraoperative complications that require further intervention (including but not limited to posterior capture rupture, with vitreous loss, zonular dehiscence that may make the IOL implant less stable, etc.)
2. Excessive iris mobility
3. Mechanical or surgical manipulation required to enlarge the pupil prior to or at IOL implantation
4. Zonular or capsule rupture
5. Significant anterior chamber bleeding
6. Unrecognized (pre-existing but discovered during surgery) ocular conditions or complications in which the IOL stability could be compromised, including zonular weakness
7. Bag-sulcus, sulcus-sulcus or unknown placement of the haptics
8. Any other capsulorhexis other than circular continuous capsulorhexis (eg, no anterior radial inconsistencies in the capsulorhexis such as anterior capsular tears or any areas of ‘can-opener’ capsulotomy)

# 11 TREATMENT

Upon signing informed consent, subjects are considered enrolled in the study. All subjects will be assigned a single subject identifier at the Screening Visit. The subject identifier consists of a combination of a 4 digit investigator number and a 5 digit subject number. The number is automatically generated sequentially by the EDC system. As an example: “4584.00001” (The investigator number and subject number are separated by a “.” character). This number will be used throughout the clinical trial.

## 11.1 Investigational Products

Throughout the clinical trial, the Investigator will be responsible for the accounting of all test and control articles and will ensure that the investigational products are used in accordance with the manufacturer’s IB or DFU.

**Test Article: AcrySof IQ PanOptix IOL Model TFNT00**

The TFNT00 IOL is not approved in the United States (US), and therefore considered investigational, but it is a CE marked device that is commercially available in other countries across the globe.

The lens is an ultraviolet and blue-light filtering foldable multifocal IOL of single-piece design with a central optic and 2 open-loop haptics. The optic is 6.0 mm in diameter and the lens has an overall diameter of 13.0 mm. The optic consists of a proprietary high refractive index hydrophobic acrylic material with a blue light filtering chromophore which filters light in a manner that approximates the human crystalline lens in the 400-475 nm blue light wavelength range (Boettner 1962). It is biconvex and consists of a soft acrylic material capable of being folded prior to insertion, allowing placement through an incision smaller than the optic diameter of the lens. After surgical insertion into the eye, the lens gently unfolds to its intended shape. The optic diffractive structure is in the central 4.5 mm portion of the optic zone and divides the incoming light to create a +2.17 D intermediate and a +3.25 D near add power. The anterior surface is designed with 0.10 µm of negative spherical aberration to compensate for the positive spherical aberration of the average human cornea.

More information on the test article can be found in IB-0143.

**Control Article: AcrySof Monofocal IOL Model SN60AT**

The SN60AT IOL is approved in the US and is a CE marked device approved for use and commercially available in other countries across the globe.

The lens is an ultraviolet and blue-light filtering foldable monofocal IOL of single-piece design with a central optic and 2 open-loop haptics. The optic is 6.0 mm in diameter and the lens has an

overall diameter of 13.0 mm. The optic consists of a proprietaiy high refractive index hydrophobic ac1ylic material with a blue light filtering chromophore which filters light in a manner that approximates the human c1ystalline lens in the 400-475 nm blue light wavelength range (Boettner 1962). It is biconvex and consists of a soft ac1ylic material capable of being folded prior to inse1tion, allowing placement through an incision smaller than the optic diameter of the lens. After surgical inse1tion into the eye, the lens gently unfolds to its intended shape.

More information on the control a1ticle can be found in the Package Inse1t/DFU.

Both test and control IOLs will be individually packaged and will have unique serial numbers. The IOLs packages will contain the following items:

- The IOL
- A subject registration card (Lens Implant Card)
- A subject identification card
- Adhesive labels containing the IOL inf01matio n and unique serial number
- A package inse1t co ntainin g directions for use

Both test and control IOLs will be available in a diopter range of 15.0 D-26.5 Din 0.5 D increments for this study.

## 11.2 Usage

Intraocular lenses are single-use implantable medical devices and ai·e intended for long te1m use over the lifetime of the pseudophakic subject. See Section 11.1 Investigational Products for details on each lens.

In order to implant the test and control articles, the surgeons participating in the study must be licensed ophthalmologists with cataract surge1y experience. Each surgeonwill use his/her standard of care to implant the lens following respective Package Inse1t/DFU/IB instructions for each device.

## 11.3 Accountability Procedures

Upon receipt of IP, the Investigator or delegate must conduct an invento1yof all IOLs by serial number, complete study specific confumation of receipt procedures, and retain any required documentation in the Investigator 's clinical study records. Throughout the study, the Investigator or delegate must maintain records of IP use for each subject. This record must be made available to the study monitor for the purpose of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded

along with an explanation. All IP sent to the Investigator must be accounted for by Study Sponsor personnel, and in no case be used in an unauthorized manner.

The Investigator is responsible for proper disposition of all unused IPs at the conclusion of the study, according to the instructions provided by the Sponsor.

## 11.4 Assessor Masking

The assessor associated with vision testing will be masked in this study. Site personnel performing [redacted], all VA assessments [redacted] and all contrast sensitivity assessments will remain masked with regard to treatment assignment until after the final database lock (Visit 4A).

***Note:*** Any unmasking of the masked assessor must be reported to Alcon.

Masked study personnel must avoid seeking information that may compromise masking. Unmasked study personnel must not disseminate information that is potentially unmasking to any masked personnel. A list of unmasked individuals can be found in Table 11-1 below.

**Table 11-1 Unmasked Individuals**

| Unmasked Individual | Extent of Unmasking | Rationale |
|---|---|---|
| Subject | Unmasked to IP selection | The test and control IOL designs offer different risks and benefits. The subject will select the lens model that best fits his or her lifestyle. |
| Investigator | Unmasked to IP selection | Investigator will be advising the subject on the different risks and benefits of the IP to help the subject select the lens model that best fits his or her lifestyle. |
| Site Personnel (not completing assessments noted in section 11.4) | Unmasked to IP selection | Site personnel involved with operative visits and data entry into EDC |
| Monitor | Unmasked to IP selection | Monitor will complete IP accountability and monitoring responsibilities |

# 12 CLI NIC AL TRIAL PROCEDURES

## 12.1 Clinical Trial Assessments

The following section outlines the assessments to be perfmmed in this clinical trial. Assessments are described in detail in the Manual of Procedures (hereto refened to as the MOP), and are outlined in tabular fmmat in Section 6 Schedule of Visits of this protocol.

## 12.2 Preoperative Visit (Visit 0)

**Visit 0: -30 to O D ays Prio r to V is it 00 , Bin oc ular Visit**

Below is a list of study procedures to be undert aken at Visit 0. It is recommended that procedures are performed in the order described below unless otherwise stated. All assessments must be documented in source documentation and case report fo rm s (if applicab le).

Data from the Investigator's previous routine cataract evaluation may be used [redacted] if the data 1) meet the requirements of this protocol and MOP, and 2) were collected less than 4 months before the preoperative examination for the study. All study specific testing not included in a routine cataract evaluation must be in the -30 to O day preoperative time period.

- Review non-study specific inclusion/exclusion criteria (eg, age, previous ocular history) to ensure that a potential subject meets all qualifications for participation in the study.
- For a potential subject meeting all entry criteria via pre-screening, invite him/her to palticipate in the study, and cany out the inform ed co nsent proce ss if he/she is interested. Refer to Section 16.2 Inform ed Consent Procedures.

  *Note:* Subjects must formally consent to the trial prior to any study specific testing.
- Document demographics, ocular and non-ocular medical histmy, ocular and non-ocular concomitant medications and pregnancy status (where applicable).
- Perform a urine pregnancy test, IF the subject is a woman of childbearing potential.
- [redacted]
- [redacted]
- [redacted]
- [redacted]

- [redacted]
- [redacted]
- [redacted]
- Perfmm tonometJ.y to measure IOP . [Both Eyes, Bilateral]
- Record any AEs. Refer to Section 13 Adverse Events and Device Deficiencies for fmther detail.
- [redacted]
- [redacted]
- Evaluate subject against all entJ.y c riteria . If s ubje ct fa il s cr it er i a screen fail the subject.
- [redacted]
- Proceedwithscheduling surge1y.
- Prior to the operative visit, perfo1m surgical planning using the following recommendations:

  If implanting the contJ.·ol lens , model SN60AT, use established formulae and associated constants for this commercialized lens.

  Note: Surgeons may use their personalized A-constant for model SN60AT.

  - [redacted]

  [redacted]

### 12.2.1 Operative Visit (Visit 00/00A)

**Visit 00: Day 0, Monocular First Eye**

**Visit 00A: 7-30 Days Post First Eye Implantation, Monocular Second Eye**

Below is a list of study procedures to be unde1taken at Visit 00 and Visit OOA. It is reco mmend ed that procedures are perf01med in the order described below unless othe1wise stated . Activities involving multiple delegated staff members may be perfmmed in parallel.

- All assessments must be documented in somce documentation and case repo1t f01ms (if applicable).

  *Note:* the Visit 00A window may overlap with other study visit windows (eg, Visit 3). In this case, both visits may be conducted on the same day at the discretion of the Investigator.

- In preparation for the operative visit, 1) confilm willingness to continue trial paiticipation, and 2) confnm scheduled surgical date and time.
- Prior to treatment, review inclusion/exclusion criteria and ensme the subject has been properly consented for participation in the trial.
- Documentany changes to oculai·and non-ocular concomitant medications.
- Record operative eye.
- Prepare subject for surgery in accordance to site specific operating procedures. [Operative Eye Only,Monocular]
- Perform surgery and implantation with the IOL chosen by the subject on the consent form [redacted] [Operative Eye Only, Monocular]
- Record incision site. [Operative Eye Only, Monocular]
- Measure and record final incision size. [Operative Eye Only, Monocular]
- Record any surgical problems, complications, or other procedures that occur during surge1y.Other procedures include those perfo1med outside of routine cataract surgery.

  *Note:* Other planned procedures at the time of surgery are exclusionaiy. [Operative Eye Only, Monocular]

- Record the lens information that is located on the IOL sticker or place sticker on the source document. Both successful and aborted (if applicable) test aiticle information should be recorded. [Operative Eye Only, Monocular]
- Record any adverse events including SSis.

  *Note:* Se ri o u s adverse events (SAEs) including SSis must be entered into EDC within 24 hours of the Investigator's knowledge. Refer to Section 13 Adverse Events and Device Deficiencies for further detail.

- Record any device deficiencies. Refer to Section 13 Adverse Events and Device Deficiencies for further detail.

### 12.2.2 1-Day Postoperative Visit (Visit 1/lA)

**Visit 1: 1-2 Days Post First Eye Implantation, Monocular First Eye**

**Visit 1A: 1-2 Days Post Second Eye Implantation, Monocular Second Eye**

Below is a list of study procedures to be undertaken at Visit 1 and Visit l A. It is recommended that procedures are perfo1med in the order described below unless othe1wise stated. All assessments must be documented in source documentation and case repmi forms (if applicable).

- Record changes in medical/ocular histmy and ocular and non-ocular concomitant medications.
- Perfmm slit lamp examination of the anterior segment. Include documentation ofI OL observations, if any. [Operative Eye Only, Monocular]
- [redacted]
- Obselve any IOL position changes (ie, tilt and decentration) occurring since the previous visit. [Operative Eye Only, Monocular]
- Assess subjective PCO, and record info1mation for any posterior capsulotomy that has occuned since surge1y, if applicable. [Operative Eye Only, Monocular]
- Perfmm tonomet:J.y to me as ure the IOP. [Operative Eye Only, Monocular]
- Record any AEs including SSis.

  *Note:* SAEs including SSis must be entered into EDC within 24 hours of the Investigator's knowledge. Refer to Section 13 Adverse Events and Device Deficiencies for fmiher detail.
- Record any device deficiencies. Refer to Section 13 Adverse Events and Device Deficiencies for fmther detail.

## 12.2.3 1-Week Postoperative Visit (Visit 2/2A)

**Visit 2: 7-14 Days Post First Eye Implantation, Monocular First Eye**

**Visit 2A: 7-14 Days Post Second Eye Implantation, Monocular Second Eye**

Below is a list of study procedures to be undetiaken at Visit 2 and Visit 2A. It is recommended that procedures are perfo1med in the order described below unless othe1wise stated. All assessments must be documented in source documentation and case repo11fo1ms (if applicable).

- Record changes in medical/ocular histo1y and ocular and non-ocular concomitant medications.
- [redacted]
- [redacted]

- [redacted]
- Perfo1m slit lamp examination of the anter ior seg ment. Include documentation of IOL observations , if any. [Operative Eye Only, Monocular]
- Grade cell and flare according to SUN system (refer to MOP for grading scheme). [Operative Eye Only, Monocular]
- Assess subjective PCO, and record inf01mation for any posterior capsulotomy that has occmTed since surge1y, if applicable. [Operative Eye Only, Monocular]
- Perf01m tonome tly to meas ure the IOP. [Operative Eye Only, Monocular]
- Record any AEs including SSls.

  *Note:* SAEs including SSis must be enteredinto EDC within 24 hours of the Investigator's knowledge. Refer to Section 13 Adverse Events and Device Deficiencies for fu1ther detail.
- Record any device deficiencies. Refer to Section 13 Adverse Events and Device Deficiencies for fmther detail.

### 12.2.4 1-Month Postoperative Visit (Visit 3/3A)

**Visit 3: 30-60 Days Post First Eye Implantation, Monocular First Eye**

**Visit 3A: 30-60 Days Post Second Eye Implantation, Monocular Second Eye**

Below is a list of study procedures to be unde1taken at Visit 3/3A. It is recommended that procedures are perf01med in the order described below unless othe1wise stated. All assessme nts must be documented in source documentation and case repo1t fo1ms (if applicable).

- Administer the QUVID and IOLSAT questionnaires.

  [redacted]
- Record changes in medical/ocular histo1y and ocular and non-ocular concomitant medications.
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

- [redacted]
- [redacted]
- Perfo1m slit lamp examinat ion of the anter ior segment. Include documentation ofI OL observations, if any. [Operative Eye Only, Monocular]
- Grade cell and flare according to SUN system (refer to MOP for grading scheme). [Operative Eye Only, Monocular]
- Observ e any IO L position changes (i.e., tilt and decentration) occuning since the previous visit. [Operative Eye Only, Monocular]
- Assess subjective PCO, and record inf01mation for any posterior capsulotomy that has occmTed since surgery, if applicable. [Operative Eye Only, Monocular]
- Perfo1m dilated fundus exam noting any issues with fundus visualization due to the lens optic. [Operative Eye Only, Monocular]
- Perfo1m tonometly to measure the IOP. [Operative Eye Only, Monocular]
- Record any AEs including SSis.

  *Note:* SAEs including SSis must be entered into EDC within 24 hours of the Investigator's knowledge. Refer to Section 13 Adverse Events and Device Deficiencies for further detail.
- Record any device deficiencies. Refer to Section 13 Adverse Events and Device Deficiencies for furth er detail.

### 12.2.5 6-Month Postoperative Visit (Visit 4A)

**Visit 4A: 120-180 Days Post Second Eye Implantation, Binocular**

Below is a list of study procedures to be undertaken at Visit 4A. Due to the number of assessments and expected duration of testing required for the final visit, this visit must be conducted over 2 days (Part 1 and Part 2). The 2 visits must occur no more than 2 weeks (14 days) apart from each other. Vision assessments must be performed in the order described to limit confounding effects. All assessments must be documented in source documentation and case repo1t fo1m s (if applicab le).

**Part 1**

- Record changes in med ical/oc ular histo1y and ocular and non-ocular concomitant medications.
- Administer the QUVID and IOLSAT questionnaires.

[redacted]

- Measure photopic pupil size at distance. [Both Eyes, Bilateral]
- [redacted]
- [redacted]
- Assess monocular and binocular best con ected distance (4 m) visual acuity. [Both Eyes, Bilateral and Binocular]
- Assess monocular and binocular distance co1Tected in te rmediate (66 cm) visual acuity. [Both Eyes, Bilateral and Binocular]
- Assess monocular and binocular distance co1Tected near (40 cm) visual acuity. [Both Eyes, Bilateral and Binocular]
- [redacted]
- [redacted]
- [redacted]
- Perform photopic without glare contrast sensitivity testing. [Both Eyes, Binocular]
- Perform photopic with glare contrast sensitivity testing. [Both Eyes, Binocular]

After patient mesopic lighting adaptation of at least 10 minutes, continue Part 1 testing by performing the following tests:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- Perform mesopic without glare contrast sensitivity testing. [Both Eyes, Binocular]
- Perform mesopic with glarecontrast sensitivity testing. [Both Eyes, Binocular]

**Part 2 (within 2 weeks of Part 1 testing)**

- Reco rd changes in medical/ocular histo1y and ocular and non-ocular concomitant medications.
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- Perfmm slit lamp examination of the anterior segment. Include documentation of IOL observations, if any. [Both Eyes, Bilateral]
- [redacted] [Operative Eye Only, Monocular]
- Obse1ve any IOL position changes (ie, tilt and decentration) occmTing since the prev ious visit. [Both Eyes, Bilateral]
- Assess subjective PCO, and record infmmation for any posterior capsulotomy that has occmTed since surge1y, if applicable. [Both Eyes, Bilateral]
- Perfo1m tonometty to measure the IOP. [Both Eyes, Bilateral]
- Perfmm dilated fundus exam noting any issues with fundus visualization due to the lens optic. [Both Eyes, Bilateral]
- Record any AEs including SSis.

  *Note:* Serious adverse events (SAEs) including SSis must be entered into EDC within 24 hours of the Investigator's knowledge. Refer to Section 13 Adverse Events and Device Deficiencies for further detail.
- Record any device deficiencies. Refer to Section 13 Adverse Events and Device Deficiencies for further detail.

## 12.3 Unscheduled Visits

An unscheduled visit (UNSV) is defined as follows:

- Ocular examination that is not standard of care and not required by the protocol; Examination conducted by the study staff; new findings, or a change to a previous finding was discovered; and Not site standardof care/routine.

An UNSV may or may not result in the capture of an adverse event. Likewise an adverse event may be captured without the report of an UNSV (eg, AE identified subsequent to study eye examination by non-study personnel).

The assessments captured at the UNSV are dictated by the Investigator per his/her medical judgment. The following assessments are recommended.

- [redacted]
- Concomitant medications
- Slit lamp exam including IOL position change
- Subjective PCO and posterior capsulotomy assessment
- Grade cell and flare according to SUN system (refer to MOP for grading scheme)
- Dilated fundus exam
- IOP
- Adverse events
- Device deficiencies

*Note:* Assessments are not limited to the above list.

If the subject is discontinued at the unscheduled visit, pe1f01m all Early Exit procedures. Refer to Section 6 Schedule of Visits. For safety pmposes, if an UNSV is required after the final study visit, document the visit. Refer to Section 13.6 Follow-Up of Subjects with Adverse Events for further detail.

## 12.4 Directions Related to Secondary Surgical Interventions

One of the co-primary safe ty object ives of the study is to estimate the rate of secondary surgical interventions (SSis) related to the optical prope1 1ie s of the IOL for first operative eye up to month 6 (Visit 4A). This section is intended to provide guidance on the documentation and procedures related to SSis in this investigation.

The main procedural steps in the decision process for SSis and notification to the Sponsor are detailed below.

1. The Investigator must detel mine whether an SSI is related to the optical prope1 ies of the IOL.

2. Any SSI (other than posterior capsulotomy laser treatment) perfo1med for any reason should be recorded as a serious adverse event and reported to the Sponsor within 24 hours of its occmTence.

Note: If the SSI is a lens exchange or repositioning, the subsequent study post-operative visits should be based on the date of this surge1y. Unscheduled Visit Case Report F01ms (CRFs) should be used for other post-operative follow-up visits, where applicable. If the study lens is exchanged and replaced with a non-study lens, the subject will be required to complete all original subsequent study visits through Visit 4A (6 months).

Evaluation of Need for a Seconda1y Surgical Intervention

- The need for consideration of an SSI includes one or more of the following:

  1. An Investigator assessment of subject's clinical outcome.

  2. A subject spontaneously complaining about visual symptoms to the investigational site personnel.

  3. Other reason(s) for an SSI, e.g., retained lens fragments.

The Investigator should perfo1m a thorough evaluation including diagnostic testing as needed and a subject interview to understand subject observations in detail to dete1mine if an SSI is the appropriate treatment for the subject's undesired outcome (e.g., blmTed vision, visual disturbances/disto1tions, or other reasons). Case management should be based on the Investigator's clinical assessment with consideration of the subject's postoperative_ , BCDVA, IOL stability after implantation, and any subjective complaints. Careful consideration of the potential risks and benefits associated with the SSI for the subject is required, and these should be discussed with the subject prior to electing to reposition or explant the IOL or othe1wise smgically intervene. For anyvisit in which an SSI is planned, [redacted]

**Guidance on determining whether the SSI cause is related to the co-primary safety endpoint**

The following causes are considered **unrelated** to the optical properties of the IOL:

- [redacted]

- [redacted]

- Surgical complications noted at the operative visit that may reasonably affect postoperative outcomes

- Pre-existing or newly developed ocular pathologies

- Corneal disorders (e.g., dry eye syndrome, edema, and corneal irregularities)

- Macular edema – confirmed by optical coherence tomography and/or fluorescein angiography

- Anisometropia (≥ 1 D difference in sphere or cylinder between contralateral eyes) due to cataractous lens in fellow eye rather than post-operative outcomes of the first eye

- Posterior capsular opacification

- Wearing corrective lenses with unsuitable prescription

The following are considered as **related** to the optical properties of the IOL:

- IOL repositioning or explantation/replacement

  a) IOL repositioning due to IOL instability (e.g., decentration and tilt)

  b) Subject intolerance of visual symptoms that are not expected to resolve if an SSI is not performed.

If the Investigator determines that an SSI is warranted and the reason is not defined above or if there is any uncertainty as to whether the SSI is related to the optical properties of the IOL or some other, unrelated factor(s), the Investigator should consult with the Medical Monitor. The Investigator should determine the most suitable SSI procedure for each case. Please note that limbal relaxing incisions and keratorefractive procedures to address residual refractive error are disallowed by the protocol. Subjects who undergo such procedures will be excluded from the best case analysis set, but will be evaluable for the safety and all implanted analysis sets.

Additional recommendations regarding Secondary Surgical Interventions

The following information is not intended to replace or limit the surgeon's decision-making process but rather to establish general guidance for time point and conditions for secondary surgical interventions.

1. IOL Repositioning

If IOL repositioning is required, it should be done in the early postoperative period before capsule fibrosis, preferably within the first 30 days following surgery. Repositioning should only be considered in cases when tilt or decentration, either due to instability or placement, is necessary to improve the visual outcomes of the subject.

2. IOL Explantation and Replacement

Should explantation of the investigational IOL (AcrySof® IQ PanOptix™ IOL Model TFNT00 ) or control IOL (AcrySof® Monofocal IOL Model SN60AT) and IOL replacement be necessary, it should be done in the early postoperative period in the case of inaccurate preoperative planning and/or surgical error. In the case where an investigational or control IOL is explanted, it should be replaced with another Alcon AcrySof® IOL.

In the case of an incorrect IOL power or residual refractive error, any SSI to replace the IOL should be considered if the placement of a different IOL power or IOL type is expected to improve the visual outcomes of the subject.

In the case where the subject complains of visual disturbances/distortions in the early postoperative period, the surgeon should remind the subject that these symptoms generally improve over time due to neural adaptation. Therefore, adequate time must be allowed for neural adaptation to occur. The medical judgment of the Investigator, consultation with the Medical Monitor and careful consideration of the potential benefits and risks of the SSI should be discussed with the subject. If the subject is intolerant of persistent visual disturbances/distortions and the Investigator identifies the primary cause as related to intrinsic IOL properties, lens replacement should be considered.

**Summary**

The Investigator must consider subject complaints and clinical outcome in his or her consideration of the need for a SSI, determine whether the cause of a needed SSI is due to optical properties of the IOL, and report findings to the Sponsor within defined timelines.

Note: Table 18-2 contains additional indications for secondary IOL interventions and their associated definitions. (Masket, 2017).

## 12.5 Missed Visits

If a subject misses a scheduled visit, reschedule the subject within the same visit period. Show diligence in trying to schedule the subject for all visits, and document all attempts to contact the subject in the subject's chart. In documentation, include dates, times, method of contact, etc.

If a subject is unable to return for the final study visit, complete the Exit Case Report Form with the appropriate reason for discontinuation. If attempts to contact the subject are unsuccessful,

document the date the subject is considered lost to follow-up. Complete the subject's Exit Case Report Form after the last window (Pa1t 2 of Visit 4A) closes, indicating the subject is lost to follow-up.

## 12.6 Discontinued Subjects

Discontinued subjects withdraw, or are withdrawn from the study after signing consent, and prior to completing all study visits. Subjects signing consent, but withdrawing shall be considered discontinued due to screen failure, and the failed entry cri terion documented (eg, inclusion criterion 2, exclusion criterion 5). Refer to Section 10 Subject Population.

Subjects may discontinue study participation at any time and for any reason. Subjects may be discontinued from the study at any time if in the medical opinion of the PI or designated, qualified medical personnel, continued pa1ticipation poses a health risk to the subject. Subject numbers from discontinued subjects will not be reissued. Discontinued subjectswill not be replaced.

## 12.7 7 Clinical Trial Termination

The Sponsor reserves the right to close the investigational site or terminate the study in its entirety at any time, for reasonable cause. The Investigator also may terminate the study at his/her site for reasonable cause. Reasons for the closure of an investigational site or termination of a study may include:

- The Investigator fails to comply with the protocol or GCP guidelines
- Safety concerns
- Inadequate recruitment of subjects by the Investigator

If the clinical study is prematurely terminated or suspended, the Sponsor will inform the Investigator and the regulat01y authorities (where applicable) of the termi nation/ suspe nsion and the reason(s) for the termi nation/suspe nsion. The Investigator should promptly notify the IEC/IRB of the termination or suspension and of the reasons.

If the Sponsor terminates the study for safety reasons, it will immediately notify the Investigator(s), and provide written instructions for study termination and applicable subject follow-up.

# 13 ADVERSE EVENTS AND DEVICE DEFICIENCIES

## 13.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test article). Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

**Figure 13–1 Categorization of All Adverse Events**

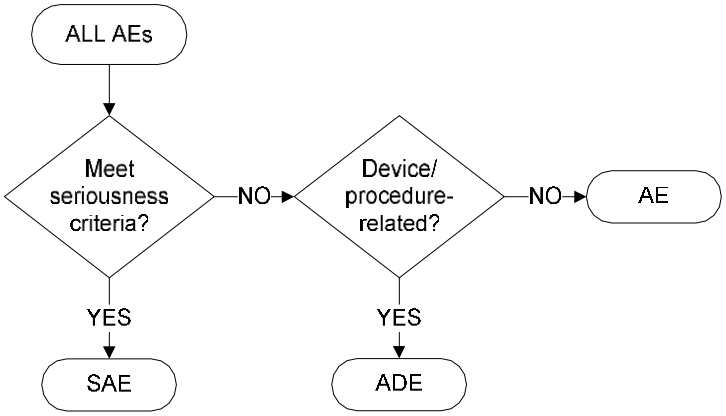
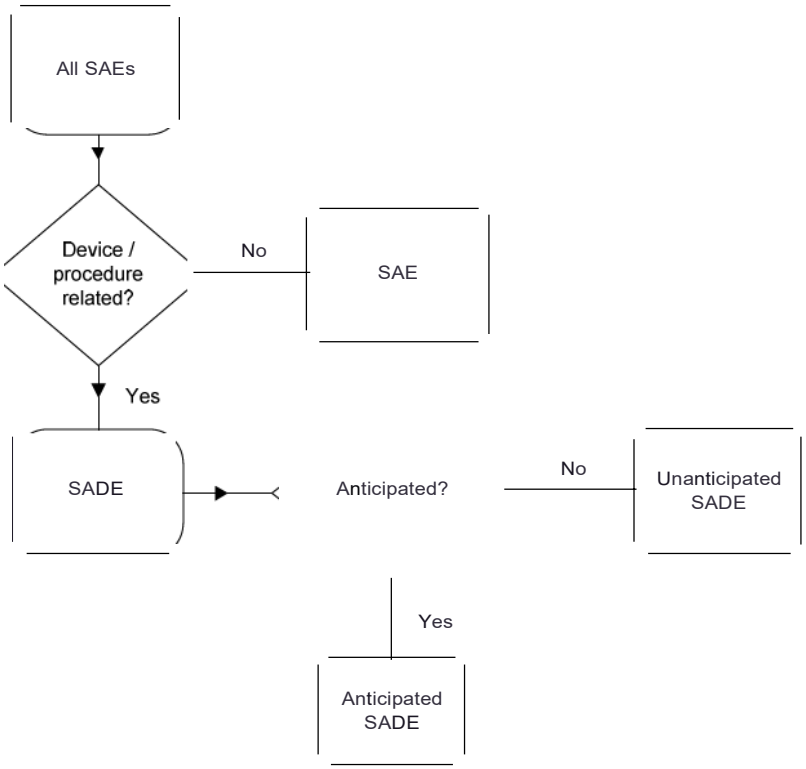


**Figure 13-2 Categorization of All Serious Adverse Events**




**Specific Events Relevant to this Protocol**

In addition to repo1ting all AEs (serious and non-serious) meeting the definitions, the Investigator must repmt any occmTence of the follo wing as an SAE:

***Cumulative Serious Adverse Events***

- Cystoid macular edema
- Hypopyon
- Endophthalmitis
- Lens dislocation from posterior chamber
- Pupillary block
- Retinal detachment
- Secondaly smgical intervention (excluding posterior capsulotomy)

***Per sis tent Serious Adverse Events***

- Corneal stromal edema
- Cystoid macular edema
- Iritis
- Raised IOP requiring treatment

This list is consistent with the categories provided in ISO 11979-7 SPE grid rates. A persistent AE is an AE that is present at the conclusion of a clinical investigation per ISO 11979-1 te1ms and definition s. Any other potentially sight-threatening event may also be considered serious based on the judgment of the Investigator and should be repo1ied appropriately as delineated in Section 13.3 Procedures for Recording and Reporting Deficiencies.

***Secondary Surgical Interventions (SSI)***

Secondary Surgical Interventions reporting will be sub-categorized using the following terminology: exchange, removal, and repositioning. Indications and associated definitions for these outcomes are provided in Section 18 Appendices, Table 18-2.

## 13.2 Monitoring for Adverse Events

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

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

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

## 13.3 Procedures for Recording and Reporting

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

In addition, aqueous cells and flare, corneal edema, raised IOP and superficial punctate keratitis are examples of early post-operative 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.

For each recorded event, the ADEs and SAEs documentation must include: date of occurence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the Investigator must document all device deficiencies reported or observed with test and control articles on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the Study Sponsor immediately as follows:

- ADEs or SAEs are documented on the *Serious Adverse Event and Adverse Device Effect* eCRF within 24 hours of the Investigator's or site's awareness.
- Device deficiencies are documented on the *Device Deficiency* eCRF within 24 hours of the Investigator's or site's awareness.

- A printed copy of the completed *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* eCRF must be included with product returns.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- Document all relevant information from Discharge Summary, Autopsy Report,
- Certificate of Death etc., if applicable, in narrative section of the *Serious Adverse Event and Adverse Device Effect* eCRF.
- UADEs must be reported to the IRB as soon as possible, but not later than 10 working days after the Investigator's or site's awareness.

  *Note:* Should the EDC system become non-operational, the site must complete the appropriate paper *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* Form. The completed form is faxed or emailed to the Study Sponsor at [redacted] or [redacted] according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for non-study marketed devices/products (ie, BSS, OVD, Delivery systems, etc.) will be considered and processed as spontaneous (following the post-market vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives may be contacted for any protocol related question and their contact information is provided in the Manual of Procedures that accompanies this protocol.

Further, depending upon the nature of the AE or device deficiency being reported, the Study Sponsor may request copies of applicable portions of the subject's medical records. The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

## Intensity and Causality Assessments

Where appropriate, the Investigator must assess the intensity (severity) of the AE based on medical judgment with consideration of any subjective symptom(s), as defined below:

### *Intensity (Severity)*

| | |
|---|---|
| Mild | An AE is mild if the subject is aware of but can easily tolerate the sign or symptom. |

| | |
|---|---|
| Moderate | An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities. |
| Severe | An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities. |

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

***Causality***

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

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

[redacted]

## 13.5 Return product analysis

Study Sponsor representatives and their contact information are provided in the MOP that accompanies this protocol.

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

### 13.6 Follow-Up of Subjects with Adverse Events

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

The Investigator should provide the study Sponsor with any new safety info1mation (which includes new AEs and changes to previously repmted AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ ongoing at time of subject exit from study, any additional info1mation received at follow-up should be documented in the eCRFs up to study completion(ie, database lock).

Any additional data received up to 6 months after subject discontinuation or exit must be documented and available upon the Study Sponsor's request. All complaints received after this tin1e period will be considered and processed as spontaneous (following the post-market vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

The Investigator should report complaints on non-Alcon products directly to the manufacturer as per the manufacturer's instiuctions or local regulato1y requirements.

### 13.7 Pregnancy in the Clinical Trial

Pregnancy is not repmtable as an AE; however, complications may be repmtable and will be decided on a case-by-case basis. An Alcon fo1m will be utilized to capture all pregnancy related info1mation until bi1th of the child.

## 14 DATA REVIEW AND HANDLING

### 14.1 Completion of Source Documents and Case Report Forms

The nature and locationof all source documents will be identified to ensure that original data required to complete the electi·onic case report fo1ms (eC RFs) exists and are accessible for verification by the monitor. It is required that the author of each entiy in the source documents be identifiable (eg, initials or signature and date). At a minimum, source documents should include the following info1mation for each subject:

- Subject identification (name, date of bi.1th or age , sex)
- Documentationof subjecteligibility
- Date of info1med consent
- Dates of visits
- Documentation that protocol-specificprocedures were perfo1med

- Results of study testing, as required by the protocol
- Test article accountability records
- Documentation of SAEs and other safety parameters (as 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

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

Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the eCRF are consistent with the original source data. Data reported on the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. Any change or correction to data reported on a source document shall be dated, initialed, and explained if necessary, and shall not obscure the original entry (i.e. an audit trail shall be maintained); this applies to both written and electronic changes and corrections. eCRFs shall be signed and dated by the Principal Investigator or his/her authorized designee(s).

## 14.2 Data Review and Clarifications

Upon completion of the eCRFs, targeted data will be reviewed by the assigned Sponsor global clinical site management (CSM) team for accuracy and completeness. The planned source document verification and overall monitoring activities for this study are outlined in a separate document, the Protocol Monitoring Plan. Corrections and/or any necessary additions to the data will be applied and if required, queries will be generated. Designated investigative staff is expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data are reflected in the subjects' source documentation.

Deviations from this protocol, regulatory requirements and GCP must be recorded. An explanation of the deviation should be included, as applicable. In addition, corrective and preventive action should be identified, implemented and documented within the study records. Prior to study start, a plan for data validation will be completed by Alcon clinical data management, and agreed upon by the study clinical manager (CM) and other team members.

Concomitant medications entered into the database will be coded using the WHO Drug Reference List. Operative medications will be detailed in site-specific surgical study protocols and will not be entered in the eCRFs; any deviation to the site's standard surgical protocol for the study will require entry into the eCRF. Medical history and adverse events will be coded using the medical dictionary for regulatory activities (MedDRA) terminology. In addition, standardized definitions

to allow for additional supportive characterization of AEs based on Postoperative Adverse Event Definitions for Intraocular Lenses are provided in the appendices, Table 18-1 (These are additional characterizations and are not intended to change the ISO defined events), and will be collected in eCRFs. Upon completion of the study and once the database is declared completed and accurate, the database will be locked and data will be available for data analysis. Any changes to the database after lock will be implemented upon agreement between the Sponsor's clinical trial management, medical safety clinical data management and biostatistics depa1iments, and will be completedfollowing the Sponsor's procedures for changes to a database after database lock.

# 15 ANALYSIS PLAN

## 15.1 Subject Evaluability

The final subject evaluability will be dete1mined prior to locking the database.

## 15.2 Analysis Data Sets

The All-Implanted Analysis Set (AAS) includes all eyes with successful IOL implantation with at least 1 post-operative visit and will be the prima1y analysis set for all effectiveness analyses [redacted]

The Best-Case Analysis Set (BAS) will be the primruy analysis set for c tntra s nd includes all eyes successfully implanted that had

- at least 1 post-operative visit;
- no preoperative ocular pathology;
- no macular degeneration detected at any time; and
- no major protocol deviations.

[redacted]

The Safety Analysis Set (SAS) will include all eyes with attempted IOL implantation (successful or ab01ied after contac t with the eye). The SAS will be the prima1y set for all safety analyses except contrnst sensitivity.

All monocular measures from eyes implanted with a non-study lens and binoculru· measures assessed in subjects with at least 1 non-study IOL implant will be excluded from all analysis sets. Treatment assignments for final analysis will be based on the lens implanted.

Although all sites are expected to contribute both test and control subjects, due to the non-randomized nature of the study it is possible that a site may emoll all subjects in 1 group. Such sites, and possibly additional sites with low emollment, will be combined into 1 pseudo site to

ensure that at least 2 subjects are in each treatment group to avoid estimation issues with the use of mixed effects models.

## 15.3 Demographics and Baseline Characteristics

Summary statistics will be provided for demographic and baseline characteristics by IOL group. Number and percentage will be presented for categorical variables and descliptive statistics including mean, standard deviation, minimum and maximum will be presented for continuous variables.

## 15.4 Performance Analyses

A total of 4 hypothesis tests will be conducted to address the co-primary and secondary effectiveness objectives of the study. To account for multiplicity, a sequential testing approach consisting of the 2 co-primary hypotheses, followed by the first secondary hypothesis, followed by the second secondary hypothesis will be employed. The primary effectiveness objective is considered met only if both co-primary hypotheses are met. The type I error for the non-inferiority test is 5% (1-sided) and for the superiority test is 2.5% (1-sided). Each of the secondary hypotheses will be tested at 2.5% (1-sided).

Analysis of the co-primary and first secondary endpoints will begin with a model selection step in an effort to select the most parsimonious model. Two mixed effects models, the first with a fixed effect for treatment and random effect for site, and the second with a fixed effect for treatment and random effects for site and treatment by site interaction, will be fit to the first co-primary endpoint (best corrected distance visual acuity). The 2 models will be compared using Bayesian information criterion (BIC) and the model with lower BIC will be employed for analysis of all 3 aforementioned endpoints.

### 15.4.1 Primary Performance

The co-primary effectiveness endpoints are:

- Mean photopic monocular best corrected distance visual acuity (4 m) for the first operative eye at Month 6
- Mean photopic monocular distance corrected visual acuity at near (40 cm) for the first operative eye at Month 6

#### 15.4.1.1 Statistical Hypotheses

The null and alternative hypotheses for the first co-primary analysis are:

$$H_0: \mu_{JFNTOO\_VA} - \mu_{SN60AT\_VA} \geq 1.1$$

$$H_A: \mu_{TFNTOO\_VA} - \mu_{SN60AT\_VA} < 1.1$$

Where , !).. refers to the non-inferiority margin, set at 0.10 logMAR, $\mu_{TFNTOO\_VA}$ and $\mu_{SN60AT\_VA}$, refer to the population mean monocular best conected distance visual acuity at 4 m for the test and control lenses respectively, in the first operative eye at Month 6.

The null and alternative hypotheses for the second co-primary analysis are:

$$H_o: \mu_{TFNTOO\_VA} \geq \mu_{SN60AT\_VA}$$

$$H_A: \mu_{TFNTOO\_VA} < \mu_{SN60AT\_VA}$$

Where , $\mu_{TFNTOO\_VA}$ and $\mu_{SN60AT\_VA}$ refer to the population mean monocular distance corrected visual acuity at near (40 cm) for the test and control lenses respectively, in the first operative eye at Month 6.

### 15.4.1.2 Analysis Methods

Least Squares Means (LSMEANS) from the mixed effects model chosen during the model selection step will be employed to estimate the difference in means (Clysofl Q PanOptix IOL Model TFNT00 minus Clysof Monofocal IOL Model SN60AT) and the associated confidence intervals for each co-primary endpoint.

The non-inferiority hypothesis (first co-primary) will be deemed supported if the upper 95% confidence limit is less than the non-inferiority margin of 0.10 logMAR.

The superiority hypothesis (second co-primary ) will be deemed supported if the upper 97.5% confidence limit is less than 0.0 logMAR.

The above analysis will be repeated for the second eyes [redacted]

An analysis with a mixed-effect model analysis of variance (ANOVA) accounting for correlation between the first and the second eye will be performed as a sensitivity analyses.

## 15.4.2 Secondary Performance

The secondary effectiveness endpoints are:

- First secondary: Mean photopic monocular distance corrected visual acuity at intermediate (66 cm) for the first operative eye at Month 6
- Second secondary: Proportion of subjects who respond "Never" to Question 1 of the IOLSAT questionnaire (Q1: Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at Month 6

### 15.4.2.1 Statistical Hypotheses

The null and alternative hypotheses for the first secondary analysis are:

$$H_0: \mu_{TFNT00\_VA} \geq \mu_{SN60AT\_VA}$$

$$H_A: \mu_{TFNT00\_VA} < \mu_{SN60AT\_VA}$$

Where $\mu_{TFNT00\_VA}$ and $\mu_{SN60AT\_VA}$ refer to the population mean monocular distance corrected visual acuity at intermediate (66 cm) for the test and control lenses respectively, in the first operative eye at Month 6.

The null and alternative hypotheses for the second secondary analysis are:

$$H_0: \pi_{TFNT00\_IOLSAT} \leq \pi_{SN60AT\_IOLSAT}$$

$$H_A: \pi_{TFNT00\_IOLSAT} > \pi_{SN60AT\_IOLSAT}$$

Where, $\pi_{TFNT00\_IOLSAT}$ and $\pi_{SN60AT\_IOLSAT}$ refer to the population proportion of subjects who respond "Never" to Question 1 of the IOLSAT questionnaire at Month 6 for the test and control lenses, respectively.

### 15.4.2.2 Analysis Methods

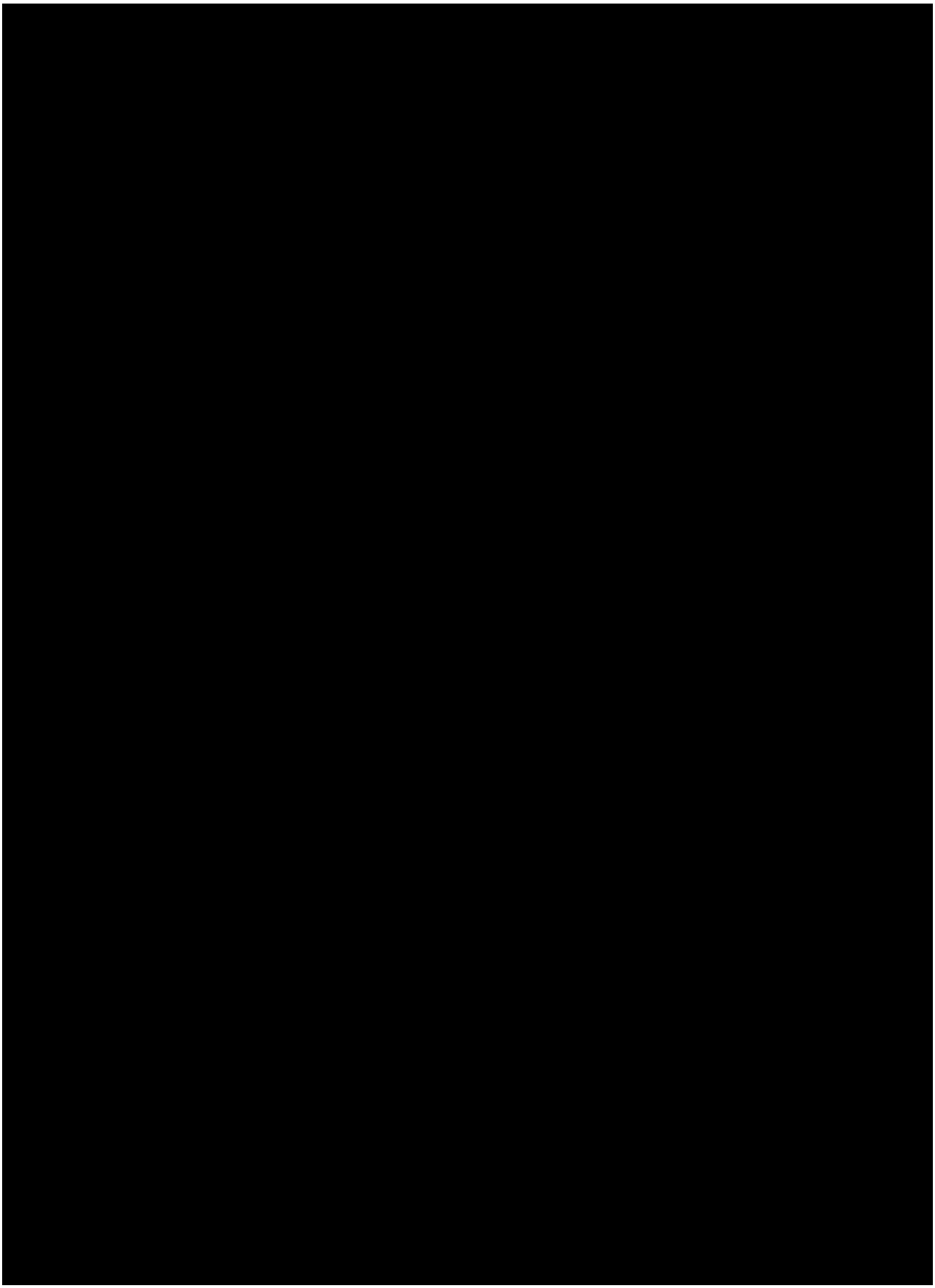
Least Squares Means (LSMEANS) from the mixed effects model chosen during the model selection step will be employed to estimate the difference in means (AcrySof IQ PanOptix IOL Model TFNT00 minus AcrySof Monofocal IOL Model SN60AT) and the associated confidence interval.

The first secondary superiority hypothesis will be deemed supported if the upper 97.5% confidence limit is less than 0.0 logMAR.

The above analysis will be repeated for the second eyes and will be considered supportive.

The second secondary endpoint will be analyzed by estimating the Mantel-Haenszel common difference of proportions (AcrySof IQ PanOptix IOL Model TFNT00 minus AcrySof Monofocal IOL Model SN60AT) along with the corresponding confidence interval with site as a stratification variable. The superiority hypothesis will be deemed supported if the lower 97.5% confidence limit of the confidence interval exceeds 0.

[redacted]



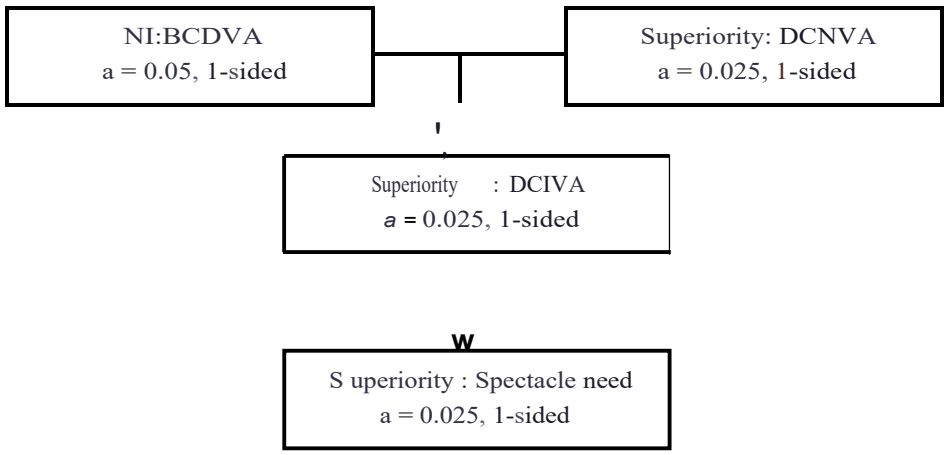
[redacted]

## 155 5 Handling of Missing Data

Sensitivity analyses are planned to assess the impact of missing data on the conclusions from the co-primaryeffectiveness analyses and the second co-primarysafety objective. Details are provided in the statistical analysis plan.

## 156 Multiplicity

To account for multiplicity, the effectiveness hypotheses will be tested in sequence, 2 co-primaries, followed by first secondaiy, followed by second secondary. The primary effectiveness objective is considered met only if both co-primaryhypotheses are met. The type I enor for the non-inferiority test is 5% (I-sided) and for the superiority test is 2.5% (I-sided). Each of the secondaiy hypotheses will be tested at 2.5% (I-sided).




## 157 Safety Analysis

The co-primary safety objectives are to:

- Estimate the cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL for first operative eye up to Month 6.
- Evaluate the mean binocular contrast sensitivity with and without glare for photopic and mesopic conditions at 6 months.

The secondary safety objective is to estimate rates of severe and most bothersome (separately) visual disturbances as reported by the subjects using a questionnaire (QUVID) at Month 6.

The third safety objective is to evaluate rates of cumulative and persistent Adverse Events in first eyes at month 6 in comparison to ISO 11979-7 SPE grid rates.

### 15.7.1 Analysis for Co-Primary Safety Objectives

#### 15.7.1.1 Secondary Surgical Interventions Related to Optical Properties of the IOL

Descriptive summaries (count, rate and 95% (two-sided) exact confidence interval) of secondary surgical interventions will be presented for each IOL group and the difference between the groups, separately for first operative eyes and all eyes in each of the following categories:

1. Related to IOL - due to optical properties
2. Related to IOL - not due to optical properties
3. Unrelated to IOL
4. Overall

A listing of all SSIs will be also be presented.

#### 15.7.1.2 Binocular Contrast Sensitivity

Analyses of log contrast sensitivity will be performed for each testing condition and spatial frequency. [redacted]

### 15.7.2 Analysis for Secondary Safety Objective

The secondary safety endpoint is rates of severe and most bothersome visual disturbances as reported by subjects using the QUVID questionnaire at Month 6. Descriptive summaries (rates

and 95% (two-sided) exact confidence intervals) of severe and most bothersome visual disturbances will be presented for each IOL group and the difference between the IOL groups.

### 15.7.3 Analysis for Third Safety Objective

The third safety endpoint is adverse events. Incidence rates observed for each IOL group will be compared to the cumulative and persistent adverse event Safety and Performance Endpoint rates in IS EN ISO 11979-7 SPE grid rates. An eye with multiple ocular adverse events of the same preferred term is only counted once toward the total of this preferred term. The Safety and Performance Endpoint rate is considered not exceeded if the lower exact binomial 95% confidence limit does not exceed the Safety and Performance Endpoint rate.

The frequencies of adverse events will be presented overall, and by subcategories of age (<65 years vs. ≥65 years) and investigative site, separately for cumulative and persistent adverse events. Additionally, frequencies and two-sided 95% confidence intervals will be reported for adverse events related to the IOL for each IOL group. Adverse events related to the IOL may also be referred to as adverse device effects.

[redacted]

## 15.8 Interim Analyses

Interim reports pertaining to the progress of this study will be submitted to the US FDA for review annually until study completion. There are no planned interim analyses of the endpoints.

## 15.9 Adaptive Study Design

Not applicable.

## 15.10 Sample Size Justification

Approximately 250 subjects will be bilaterally implanted with either the AcrySof IQ PanOptix IOL Model TFNT00 or the AcrySof Monofocal IOL Model SN60AT in a 1:1 ratio in order to ensure that at least 113 eligible subjects complete the study in the test group and the control group. This assumes a drop-out rate of 10%, approximately.

For co-primary and first secondary effectiveness objectives, the proposed sample size will provide ≥98% power for each of the hypotheses, with α=0.05, 1-sided for the non-inferiority test, and α=0.025, 1-sided, for superiority tests. For tests of superiority, assumptions include a difference of means of 0.1 logMAR between the groups for distance corrected visual acuity at intermediate (66 cm) and distance corrected visual acuity at near (40 cm) and a common standard deviation of 0.18 logMAR. For test of non-inferiority, assumptions include a difference in means of 0 between the groups for best corrected distance visual acuity (4 m), a non-inferiority margin of 0.1 logMAR and a common standard deviation of 0.18 logMAR. The standard deviation of 0.18 is based on the maximum variability of logMAR observed in study C-06-40 (Clinical Study Report: Clinical Investigation of ACRYSOF ReSTOR Aspheric +3.0 D Add Power IOL).

For the second secondary effectiveness objective, the proposed sample size will provide 83% power, with α=0.025, 1-sided, to detect a difference in proportion of 20%, assuming a ≥50% rate in the AcrySof IQ PanOptix IOL test group. The estimates of rates of spectacle need for the test and control lenses are inferred from studies ILH297-P002 and C-10-016, respectively, using a binocular [redacted] visual acuity threshold of 0.2 logMAR or better at near (40 cm) and distance (4 m) as a proxy measure.

Power calculations for the effectiveness objectives are summarized in the table below:

| | Margin | Expected Difference | Std. dev | Type I error (1-sided) | Power |
|---|---|---|---|---|---|
| Non- Inferiority | | | | | |
| BCDVA (4 m) | 0.1 | 0.0 | 0.18 | 5% | 99% |
| Superiority | | | | | |
| DCNVA (40 cm) | | 0.1 | 0.18 | 2.5% | 98% |
| DCIVA (66 cm) | | 0.1 | 0.18 | 2.5% | 98% |
| Spectacle need | | 20% | | 2.5% | 83% |

All expected differences for tests of superiority favor the test lens. Estimates for VA endpoints reported in logMAR.

Adverse Events: For any event where a 0 incidence is observed in 113 first-operative eyes in the AcrySof IQ PanOptix IOL test group, the upper exact binomial 95% confidence limit is less than 3%. Thus, with 95% confidence, the true adverse event rate is less than 3%.

# 16 ADMINISTRATIVE PROCEDURES

## 16.1 Regulatory and Ethical Compliance

This clinical trial will be conducted in accordance with the principles of the Declaration of Helsinki, and in compliance with ISO 14155:2011 Clinical investigation of medical devices for human subjects – Good clinical practice, Code of Federal Regulations (CFR), and laws and regulations of foreign countries, whichever affords greater protection to subjects. The

trial shall also be conducted in accordance with the Sponsor's Standard Operating Procedures (SOPs) and all other applicable regulations. The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that

all personnel involved in the conduct of the clinical trial are qualified to perform their assigned duties through relevant education, training, and experience.

## 16.2 Informed Consent Procedures

Voluntary informed consent will be obtained from every subject prior to the initiation of any screening or other clinical trial-related procedures. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or designee, will explain the clinical trial to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and will provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the clinical trial, along with any known risks

and potential benefits associated with the investigational product, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the clinical trial and will be provided with contact information for the appropriate individuals should questions or concerns arise during the clinical trial. The subject also will be told that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject.

## 16.3 Responsibilities of the Investigator and IRB/IEC

Before clinical trial initiation, this protocol, the informed consent form (and assent form, if applicable), any other written information provided to subject, and any advertisements planned for subject recruitment must be approved by an Institutional Review Board / Independent Ethics Committee (IRB/IEC). A master list of IRBs/IECs for this clinical trial can be found in the Trial

Master File. The Investigator must provide documentation of IRB/IEC approval to the Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, assent form (if any), all applicable recruiting materials, written information for subjects, and subject compensation programs. The IRB/IEC must be providedwith a copy of the Investigator's Brochure, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. At the end of the clinical trial or in the case of early termination, the Investigator will notify the IRB/IEC of the clinical trial's final status. Finally, the Investigator will report to the IRB/IEC on the progress of the clinical trial at intervals stipulated by the IRB/IEC.

### 16.3.1 Sponsor and Monitoring Responsibilities

The Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals. The clinical investigation will be monitored, following the Protocol Monitoring Plan, to ensure that: the rights and well-being of the subjects are protected; the reported data are accurate, complete, and verifiable from the source documents; the equipment used to assess variables in the clinical investigation is maintained and calibrated per manufacturer instructions and Sponsor requirements; the study is conducted in compliance with the current approved protocol (and amendment[s], if applicable), with current Good Clinical Practice (GCP), and with applicable regulatory requirements.

All investigative sites will have a site initiation. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone, written and fax correspondence. The assigned CSM will contact each site at appropriate intervals. The Lead Clinical Site Manager (LCSM) will determine the frequency of site visits. Closeout visits will take place after the last visit of the last subject.

## 16.4 Regulatory Documentation and Records Retention

Essential documents must be retained by the investigator in compliance with the medical device directive and its local transposition as well as other applicable national and international regulations. The Investigator(s)/institution(s) must comply with record retention stipulations outlined in the Clinical Study Agreement. Additionally the Investigator will be supplied with further instruction at study completion.

## 16.5 Clinical Trial Results

The Investigator will notify the accredited ethics committee of the end of the study as required by the ethics committee. The end of the study is defined as database lock. In case the study is ended prematurely, the Investigator will notify the accredited ethics committee, including the reasons for the premature termination. Within 1 year after the end of the study, the Investigator/sponsor will

submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited ethics committee as required.

## 16.6 Publication of the Clinical Trial

Any information other than that which is disclosed upon registration should not be discussed with persons outside the study. The protocol, study data, and information related to the study or to Alcon's products or research programs that is provided by Alcon (Confidential Information) is to be kept confidential, and not disclosed directly or indirectly to any third party other than those involved in the study who has a need to know.

All data and discoveries arising out of the study, patentable or non-patentable, shall be the sole property of Alcon, Inc. Alcon reserves the right of prior review of any publication or presentation of information related to the study. Alcon may use these data now and in the future for presentation or publication at Alcon's discretion or for submission to government regulatory agencies.

The existence of this clinical study is confidential and should not be discussed with persons outside of the study. You shall hold confidential, and not disclose directly or indirectly to any third party other than those persons involved in the study who have a need to know, the protocol, the data arising out of the study, and any other information related to the study or to Alcon's products or a research program that is provided by Alcon to you (the "Confidential Information"). All such persons must be instructed not to further disseminate this information to others. You shall not use the Confidential Information for any purpose other than the study.

The foregoing obligations of confidence and non-use assumed by you shall not apply to: (a) information which at the time of disclosure is in the public domain; (b) information which thereafter lawfully becomes part of the public domain other than through disclosure by or through you; (c) information which, as evidenced by your written records, was known by you prior to Alcon's disclosure; (d) information which is lawfully disclosed to you by a third party not under any obligation of confidence to Alcon; or (e) information which is required to be disclosed by law or government regulatory agency, provided reasonable advance notice of such disclosure is given to Alcon.

In signing this protocol, you agree to the release of the data from this study and acknowledge the above confidentiality and publication policy. The provisions of this Statement shall survive the completion of the study.

# 17 REFERENCES

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ISO 11979-9:2014 Ophthalmic implants – intraocular lenses – part 9: multifocal intraocular lenses

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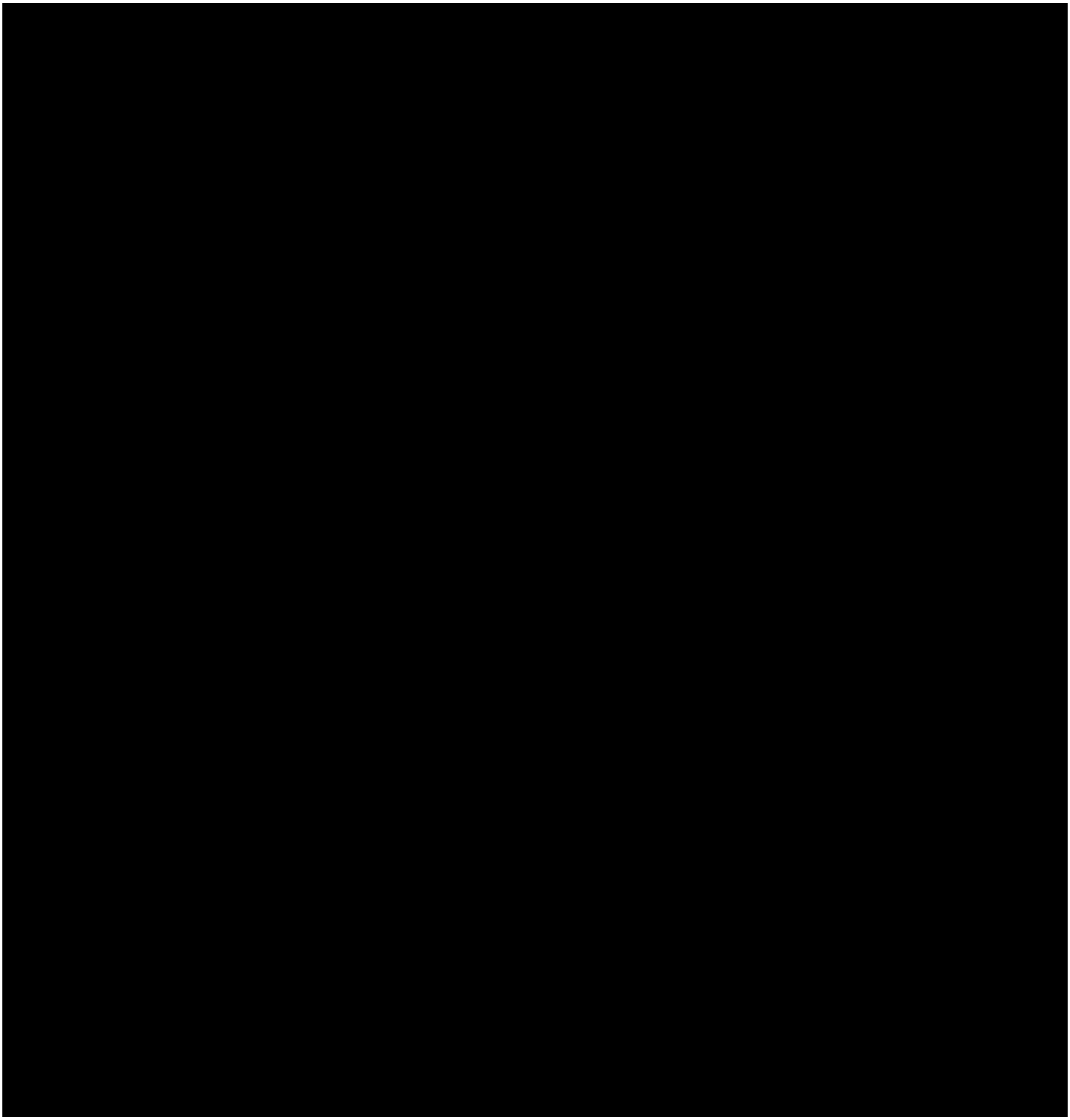

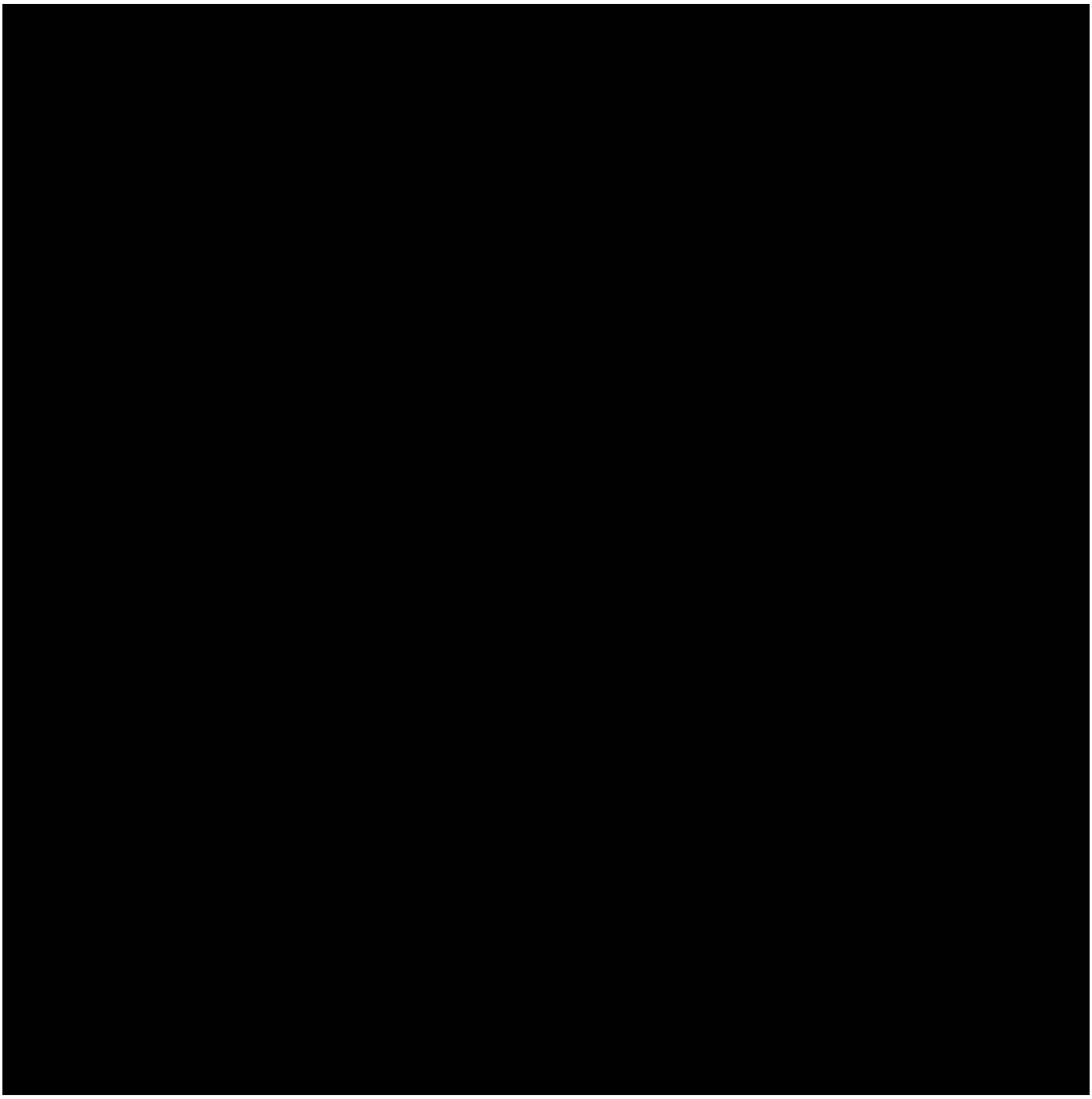

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