Statistical Analysis Plan

Clinical Investigation of the TECNIS® Next-Generation Intraocular Lenses

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STATISTICAL ANALYSIS PLAN

CLINICAL INVESTIGATION OF THE TECNIS® NEXT-GENERATION INTRAOCULAR LENSES

PROTOCOL NUMBER: SUR-CAT-652-1001

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STATISTICAL ANALYSIS PLAN CHANGE HISTORY

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
1.0	N/A	N/A	Original	N/A
2.0	7.3 & 7.4	7	Change defocus and contrast sensitivity from binocular to monocular testing for 1-month postoperative visit Change defocus and contrast sensitivity from monocular to binocular testing for 6-month postoperative visit	Fix typo to match protocol testing
	Footer	All	Update Footer	Change to version 2.0 in footer

1 INTRODUCTION

This document summarizes the statistical methods to be implemented during the analysis of data for the TECNIS® Next-Generation IOLs, Models ZFR00 and ZYR00, clinical study (Protocol SUR-CAT-652-1001). This study will be a prospective, multicenter, subject/evaluator-masked, bilateral, randomized, clinical trial conducted at up to 14 sites. The two test lenses, TECNIS Model ZFR00 and Model ZYR00 IOLs, will be compared to the control lens, TECNIS Multifocal IOL, Model ZLB00, separately. Subjects are to be implanted with the same IOL in both eyes, the ZFR00 IOL, the ZYR00 IOL or the multifocal control IOL. Up to 260 subjects will be enrolled to achieve approximately 220 randomized and bilaterally-implanted subjects, resulting in approximately 195 evaluable subjects (65 in each IOL group) at 1 and 6 months.

The primary effectiveness endpoints for this study are mean (LogMAR) monocular, photopic, distance corrected intermediate visual acuity (DCIVA) at 66 cm. The primary safety endpoints are adverse event rates versus ISO 11979-7:2006/ Amd.1:2012(E) Safety and Performance Endpoint (SPE)[1] rates.

Other effectiveness endpoints include mean monocular and binocular diopters of defocus, monocular and binocular uncorrected and best corrected distance, uncorrected intermediate, uncorrected and distance corrected near, monocular and binocular 10% low-contrast distance corrected visual acuities, and questionnaire responses.

Additional safety endpoints include the proportion of first implanted eyes achieving 20/40 or better monocular photopic best corrected distance visual acuity vs. the ISO SPE rate, optical/visual symptoms, medical/lens findings, monocular and binocular best corrected distance contrast sensitivity and visual symptoms via PRO instrument.

The key study timeframe will be the 1-month postoperative visit, although data will be reviewed at other time points as well.

2 ANALYSIS POPULATIONS

2.1 ANALYSIS POPULATIONS

The analysis population will be the safety population, which includes all eyes implanted with either a test or control IOL(s) and with data available at the time of analysis (i.e., no data imputation). For bilateral testing and subject-based questionnaires, only subjects binocularly implanted with the same test lens or the same control lens will be included. If an eye or a subject is discontinued during the study, any available data prior to the study exit will be included in the analyses.

The primary analysis will be based on first-eye or binocular outcomes (as appropriate per effectiveness endpoints), unless stated otherwise. However, select data such as

medical/lens complications and adverse events will also be reported separately for second eyes. Binocular data will be reported for those who are implanted with the same IOL (test or control) in both eyes.

The two test lens, TECNIS Model ZFR00 and Model ZYR00 IOLs, will be compared to the TECNIS multifocal control IOL, Model ZLB00, separately and independently. All endpoint comparison analysis to the control lens will present in two separate tables as follows:

- ZFR00 vs. control
- ZYR00 vs. control

2.2 VISIT WINDOWS

Subject visits are Preoperative for both eyes; Operative, 1 day and 1 week for each eye; and 1 month and 6 months for both eyes together. The exact number of days for each interval is described in the protocol. The number of eyes with missing visits or data outside of the visit interval will be reported.

2.3 DATA CONVENTIONS

Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min.) and maximum (Max.) as appropriate for continuous variables. For categorical data, the frequency and proportion will be computed.

For continuous variables, statistical tests assuming normality will generally be used. However, the data will be reviewed to evaluate whether the normality assumption is appropriate. If it is found not to be appropriate, either an appropriate transformation of the data (i.e., logarithmic) may be used or the corresponding non-parametric tests may be used. Deviations from the proposed statistical guidelines will be substantiated by sound statistical rationale.

Unless otherwise indicated, alpha will be set to 0.05.

For visual acuity data, letter scores will be converted to LogMAR[2] prior to analysis. Formulas used for visual acuity analyses are included in Appendix II. For refractive data, all values will be converted to plus cylinder with sphere adjusted for infinity[3]. Formulas used for refractive data are also included in Appendix II.

2.4 RANDOMIZATION

Subjects are to be implanted with the same IOL in both eyes, the ZFR00 IOL, the ZYR00 IOL or the ZLB00 control IOL, according to a randomization schedule. JJV will use a centralized electronic randomization system.

If a surgeon implants the wrong study lens, i.e., other than the one on the randomization schedule, the subject's study data will be analyzed according to the actual lens received; however, the number of these events will be reported.

3 ACCOUNTABILITY/DEMOGRAPHICS

3.1 ACCOUNTABILITY

The number of enrolled subjects will be tabulated by site for first and second eyes. Subject accountability will be summarized as a frequency distribution by scheduled visits. A frequency table by IOL will be generated, showing the number of available eyes (those in interval and outside of the interval) and the number of missing (e.g., discontinued, missed visit, etc.) and active subjects.

3.2 DEMOGRAPHICS

Subject demographic data including age, sex, race, and eye color will be presented by IOL group. Age will be determined at the time of the preoperative visit and will be categorized by less than 60, 60 to 69, 70 to 79, and equal to or older than 80 years old. In addition, age will be summarized with descriptive statistics. The frequency distributions of sex, race, and iris color will also be tabulated.

Comparisons between IOL groups will be performed using Fisher's exact test for demographic categorical data. The null hypothesis is that there is no difference in the proportion with specific responses between IOL groups, whereas the alternative hypothesis is that there is a difference in at least one proportion between IOL groups. For comparisons between IOL groups for mean age, the two-sample t-test will be used. The null hypothesis is that there is no difference in mean values between IOL groups, whereas the alternative hypothesis is that there is a difference in mean values between IOL groups. Two-sided testing with an alpha level of 0.05 will be used for all demographic variables.

4 OPERATIVE PARAMETERS

Operative parameters related to surgical complications or procedures for first and second eyes will be reported for each IOL model. The frequency and proportion of eyes with selected responses will be tabulated. Statistical comparisons between IOL groups will be performed as described above for demographic data. Two-sided testing with an alpha level of 0.05 will be used for these operative parameters.

5 POSTOPERATIVE ANALYSES – PRIMARY EFFECTIVENESS ENDPOINTS

5.1 MODEL ZFR00: MONOCULAR DISTANCE CORRECTED INTERMEDIATE VISUAL ACUITY (DCIVA) AT 66 CM

The primary effectiveness endpoint for the Model ZFR00 IOL is mean (LogMAR), first-eye, monocular, photopic, distance corrected intermediate visual acuity (66 cm) at 1 month postoperative. The mean, SD, median, minimum, maximum and 95% C.I. will be reported by IOL group. Results will be reported by lens group for first eyes using one-sided, two-sample t-tests with an alpha level of 0.025. Note that a lower LogMAR value is a better acuity and a higher LogMAR value is a poorer acuity. The null hypothesis is that the mean monocular DCIVA LogMAR value for the Model ZFR00 eyes is worse than or equal to that for control eyes. The alternate hypothesis is that the mean monocular DCIVA LogMAR value for Model ZFR00 eyes is better than that for control eyes.

H_o: $\mu_c - \mu_t \leq 0$ (ZFR00 is worse than (higher LogMAR) or equal to control)
H_1: $\mu_c - \mu_t > 0$ (ZFR00 is better (lower LogMAR) than control)
where
μ_t = mean LogMAR DCIVA for Model ZFR00 lens
μ_c = mean LogMAR DCIVA for control lens
Reject the null hypothesis if one-sided p-value ≤ 0.025.

The success criterion is a statistically significantly lower mean LogMAR DCIVA score for the Model ZFR00 investigational lens compared to the control lens ($p \leq 0.025$).

5.2 MODEL ZYR00: MONOCULAR DISTANCE CORRECTED INTERMEDIATE VISUAL ACUITY (DCIVA) AT 66 CM

The primary effectiveness endpoint for the Model ZYR00 IOL is mean (LogMAR), first-eye, monocular, photopic, distance corrected intermediate visual acuity (66 cm) at 1 month postoperative. Analysis for the Model ZYR00 will be similar to the Model ZHR00 described above. The mean, SD, median, minimum, maximum and 95% C.I. will be reported by IOL group. Results will be reported by lens group for first eyes using one-sided, two-sample t-tests with an alpha level of 0.025. Note that a lower LogMAR value is a better acuity and a higher LogMAR value is a poorer acuity. The null hypothesis is that the mean monocular DCIVA LogMAR value for the Model ZYR00 eyes is worse than or equal to that for control eyes. The alternate hypothesis is that the mean monocular DCIVA LogMAR value for Model ZYR00 eyes is better than that for control eyes.

H_o: $\mu_c - \mu_t \leq 0$ (ZYR00 is worse than (higher LogMAR) or equal to control)
H_1: $\mu_c - \mu_t > 0$ (ZYR00 is better (lower LogMAR) than control)
where

μ_t = mean LogMAR DCIVA for Model ZYR00 lens
μ_c = mean LogMAR DCIVA for control lens
Reject the null hypothesis if one-sided p-value ≤ 0.025.

The success criterion is a statistically significantly lower mean LogMAR DCNVA score for the Model ZYR00 investigational lens compared to the control lens ($p \leq 0.025$).

6 POSTOPERATIVE ANALYSES - PRIMARY SAFETY ENDPOINTS

6.1 MODEL ZFR00: RATES OF ADVERSE EVENTS VS. ISO SPE RATES

The primary Model ZFR00 safety endpoint for this study is the rate of adverse events vs. ISO SPE rates at 1 month postoperative. The frequency and proportion of first eyes and second eyes with these events will be reported over time by IOL group. Statistical comparisons to ISO SPE rates will be based on first-eye data; adverse event rates for Model ZFR00 lens first eyes will be compared to the ISO SPE rates using a one-sided, exact test based on the binomial distribution. The null hypothesis is that the AE rate for Model ZFR00 investigational lens eyes is lower than or equal to the ISO SPE values, and the alternative hypothesis is that the AE rate for study eyes is higher than the ISO SPE values.

H_o: $p_t \leq p_i$
H_1: $p_t > p_i$

where
p_t = proportion of Model ZFR00 investigational lens eyes with the AE
p_i = proportion of eyes reported in ISO SPE rates with the AE

Reject the null hypothesis if one-sided p-value < 0.05.

6.2 MODEL ZYR00: RATES OF ADVERSE EVENTS VS. ISO SPE RATES

The primary Model ZYR00 safety endpoint for this study is the rate of adverse events vs. ISO SPE rates at 1 month. The frequency and proportion of first eyes and second eyes with these events will be reported over time by IOL group. Statistical comparisons to ISO SPE rates will be based on first-eye data; adverse event rates for Model ZYR00 lens first eyes will be compared to the ISO SPE rates using a one-sided, exact test based on the binomial distribution. The null hypothesis is that the AE rate for Model ZYR00 investigational lens eyes is lower than or equal to the ISO SPE values, and the alternative hypothesis is that the AE rate for study eyes is higher than the ISO SPE values.

H_o: $p_t \leq p_i$
H_1: $p_t > p_i$

where

p_t = proportion of Model ZYR00 investigational lens eyes with the AE
p_i = proportion of eyes reported in ISO SPE rates with the AE

Reject the null hypothesis if one-sided p-value < 0.05.

7 POSTOPERATIVE ANALYSIS: OTHER ENDPOINTS

7.1 OTHER INTERMEDIATE VISUAL ACUITY ENDPOINTS

For binocular UCIVA and DCIVA and monocular UCIVA, a superiority approach similar to DCIVA described above will be used.

In addition, the frequency and proportion achieving each line for all other intermediate endpoints will be reported over time by IOL group.

7.2 NEAR AND DISTANCE VISUAL ACUITY ENDPOINTS

For monocular photopic BCDVA, the frequency and proportion achieving each line will be reported over time by IOL group. The proportion of investigational lens eyes achieving 20/40 or better at 1 month and 6 months postoperative will be compared to the ISO SPE rate for posterior chamber IOLs (all first eyes) using a one-sided, exact test based on binomial distribution. The null hypothesis (based on the ISO guidance document) is that the proportion of investigational lens eyes achieving 20/40 or better BCDVA is greater than or equal to the ISO SPE values, and the alternative hypothesis is that the proportion of investigational lens eyes achieving 20/40 or better BCDVA is less than the ISO SPE values.

In addition, the mean LogMAR photopic BCDVA will be compared between lens groups for first eyes using a non-inferiority method. The null hypothesis is that the mean difference (control minus investigational lens) between the control and investigational IOLs is ≤-0.1 LogMAR (1 line) with the alternative hypothesis that the mean difference is >-0.1 LogMAR. A 90% confidence interval (CI) of a two-sample, two-sided, t-test will be used for evaluation. The success criteria for BCDVA is achieved if the lower limit of the 90% CI of the difference is greater than -0.1 LogMAR.

Other distance endpoints, monocular and binocular UCDVA and BCDVA with low contrast (10%), and binocular BCDVA, will be analyzed using the non-inferiority method described above. The frequency and proportion achieving each line will also be reported over time by IOL group.

Near endpoints include binocular and monocular photopic UCNVA and DCNVA will be analyzed using the non-inferiority method similar to photopic BCDVA described above. The frequency and proportion achieving each line will also be reported over time by IOL group.

7.3 DEFOCUS

Best-corrected distance defocus testing will be performed at the 1- and 6-month visits (monocular at 1 month and binocular at 6 months). The mean visual acuity at each diopter will be plotted. The defocus curve will be presented for monocular and binocular by IOL model. The diopters of defocus where the mean visual acuity of 20/32 or better is achieved will be derived by visual inspection of the defocus curve. In addition, defocus curves will also be stratified by pupil size (≤ 2.5 mm, > 2.5 mm to < 4.0 mm, and ≥ 4.0 mm) for each IOL model. For binocular defocus curve, the average of the two pupil sizes will be used for stratification.

7.4 CONTRAST SENSITIVITY

Contrast sensitivity testing will be performed at the 1- and 6-month visits (monocular at 1 month and binocular at 6 months). The contrast sensitivity score will be converted to log units prior to analysis (see conversion formula in Appendix II). The average of the two contrast sensitivity log scores will be used for the analysis. Analyses including mean, standard deviation, median, minimum, maximum and 90% confidence intervals will be presented by IOL group.

In addition, contrast sensitivity will also be stratified by pupil size (photopic condition using photopic pupil size ≤ 2.5 mm, > 2.5 mm to < 4.0 mm, and ≥ 4.0 mm; mesopic condition using mesopic pupil size ≤ 4.0 mm, > 4.0 mm to < 5.0 mm, and ≥ 5.0 mm) for each IOL model. For binocular testing, the average of the two pupil sizes will be used for stratification.

7.5 MANIFEST REFRACTION

Descriptive analysis of refractive sphere, cylinder and spherical equivalent (MRSE) will be reported by IOL groups for both eyes. Since refraction was performed at 4M, 0.25D will be subtracted from the sphere value. Refractive data will then be converted to plus cylinder notation.

MRSE is then calculated by the following formula: MRSE = sphere + ½ cylinder.

7.6 MEDICAL AND LENS FINDINGS

Rates of postoperative medical and lens findings will be tabulated with the frequency and proportion of eyes with these events reported over time by IOL group. As mentioned above in Section 6.1 and 6.2 Rates of Adverse Events, medical complication rates listed in ISO-11979 will be compared to the ISO SPE rates for test lens first eyes at 6 months using a one-sided, exact test based on the binomial distribution. The null hypothesis is that the study rate for test lens eyes is lower than or equal to the ISO rate, and the alternative hypothesis is that the rate for test lens eyes is greater than the ISO rate. For adverse events and other medical and lens findings, data will be reported for first eyes, and data for second eyes will be reported as supportive data.

7.7 NON-DIRECTED OPTICAL/VISUAL SYMPTOMS

The frequency and percentage of non-directed optical/visual symptoms will be reported over time by IOL groups for both eyes.

7.8 SUBJECT QUESTIONNAIRES FOR VISUAL SYMPTOMS, SPECTACLE INDEPENDENCE AND SATISFACTION

The questionnaire data will be reported for subjects who have received the same test lenses or same control lenses in both eyes. Subject questionnaire data for visual symptoms, spectacle independence, satisfaction and other questionnaire responses will be tabulated with the frequency and proportion for each response by IOL group. Comparison between IOL groups for categorical data will be performed using Fisher's exact test with the null hypothesis that there is no difference between responses and the alternative hypothesis that there is a difference between responses. Comparisons for ordinal data will be done using the Wilcoxon rank-sum test with the null hypothesis that there is no difference in scores between IOL groups and the alternative hypothesis that there is a difference in scores between IOL groups. Two-sided testing and an alpha of 0.05 will be used to evaluate questionnaire data.

8 SAMPLE SIZE CALCULATIONS

For the primary endpoint of distance corrected near visual acuity, there is 90% power to detect a 1-line or greater difference in mean visual acuity between the investigational lens groups and the control group (assume one-sided testing with an alpha of 0.025 and standard deviation of 1.6 lines) with 65 subjects in each lens group.

For contrast sensitivity, there is 80% power to detect a non-inferiority margin of 0.15 log units between the investigational lens groups and the control group (assume one-sided alpha=0.05 and standard deviation of 0.34) with 65 subjects in each lens group.

If the dropout rate is assumed at 10%, approximately 73 subjects will be implanted in each lens group to achieve a minimum of 65 subjects in each lens group at 1 and 6 months.

8.0 REFERENCES

1. ISO 11979-7:2006I. International Standard for Ophthalmic Implants – Intraocular Lenses – Part 7: Clinical Investigations, (2006). Amendment 1 to Annex B (2012).
2. Holladay, J.T., Visual Acuity Measurements, J. Cataract Refract. Surg. Vol 30, Feb, 2004
3. Holladay, J.T., Dudeja, D.R., Koch, D.D. Evaluating and Reporting Astigmatism for Individual and Aggregate Data, J. Cataract Refract. Surg. Vol. 24, Jan, 1998

APPENDIX I: TABLE LISTING

	First Eyes ZFR00	First Eyes ZYR00	First Eyes Control	Second Eyes ZFR00	Second Eyes ZYR00	Second Eyes Control	Subjects ZFR00	Subjects ZYR00	Subjects Control	Comments
ENROLLMENT/PREOP/OP										
Accountability/Enrollment										
No. of implants by IOL model by investigational site	X	X	X	X	X	X				
Accountability table over time – (No. of eyes will be reported for: available for analysis, missing data - discontinued, In interval (no form), missed visit, lost to follow-up, active)	X	X	X	X	X	X				
Out of interval subjects listing – No. of eyes	X	X	X	X	X	X				
Demographics										
Demographic –Age in years (N, Mean, SD, Min., Max), age in groups (<60,60-69,70-79,>=80), race, sex, iris color							X	X	X	
Operative Data										
Surgical Complications: No. and percent with each response Surgical complications (none, all items listed on CRF, other) Other surgical procedures (none, all items listed on CRF, other)	X	X	X	X	X	X				
PRIMARY EFFECTIVENESS ENDPOINTS										
Monocular photopic DCIVA at 66cm (LogMAR) (N, Mean, SD, Median, Min., Max, 95% CI.)	X	X	X							
PRIMARY SAFETY ENDPOINTS										
AE rate vs. ISO SPE rate	X	X								
OTHER ENDPOINTS										
Visual Acuity – Near										

	First Eyes	First Eyes	First Eyes	Second Eyes	Second Eyes	Second Eyes	Subjects	Subjects	Subjects	Comments
	ZFR00	ZYR00	Control	ZFR00	ZYR00	Control	ZFR00	ZYR00	Control	
Monocular and binocular photopic DCNVA at 40 cm (LogMAR) (N, Mean, SD, Median, Min, Max, 90% CI) Monocular and binocular photopic DCNVA at 40cm by acuity line over time (No. and percent within each category)	X	X	X				X	X	X	
Monocular and binocular photopic UCNVA at 40cm (LogMAR) (N, Mean, SD, Median, Min, Max, 90% CI) Monocular photopic UCNVA at 40cm by acuity line over time (No. and percent within each category)	X	X	X				X	X	X	
Visual Acuity – Intermediate										
Monocular photopic DCIVA at 66cm by acuity line over time (No. and percent within each category)	X	X	X							
Monocular photopic UCIVA at 66cm (LogMAR) (N, Mean, SD, Median, Min, Max, 95% CI) Monocular photopic UCIVA at 66cm by acuity line over time (No. and percent within each category)	X	X	X							
Binocular photopic UCIVA and DCIVA at 66cm (LogMAR) (N, Mean, SD, Median, Min, Max, 95% CI) Binocular photopic UCIVA and DCIVA at 66cm by acuity line over time (No. and percent within each category)							X	X	X	
Visual Acuity – Distance										
Monocular photopic UCDVA and BCDVA at 4 m (LogMAR) (N, Mean, SD, Median, Min., Max, 90% CI) Monocular photopic UCDVA and BCDVA at 4 m by acuity line over time (No. and percent within each category)	X	X	X							
Binocular photopic UCDVA and BCDVA at 4 m (LogMAR) (N, Mean, SD, Median, Min., Max, 90% CI)							X	X	X	

	First Eyes	First Eyes	First Eyes	Second Eyes	Second Eyes	Second Eyes	Subjects	Subjects	Subjects	Comments
	ZFR00	ZYR00	Control	ZFR00	ZYR00	Control	ZFR00	ZYR00	Control	
Binocular photopic UCDVA and BCDVA at 4 m by acuity line over time (No. and percent within each category)										
Monocular low contrast acuity (10%) BCDVA at 4m (LogMAR) at 1M (N, Mean, SD, Median, Min, Max, 90% CI) Monocular low contrast acuity (10%) BCDVA at 4m by acuity line at 1M(No. and percent within each category)	X	X	X							
Binocular low contrast acuity (10%) BCDVA at 4m (LogMAR) at 6M (N, Mean, SD, Median, Min, Max, 90% CI) Binocular low contrast acuity (10%) BCDVA at 4m by acuity line at 6M(No. and percent within each category)							X	X	X	
Defocus Testing										
Best-corrected monocular defocus curve overall and by photopic pupil size (≤2.5 mm, >2.5 to <4 mm and ≥4.0 mm) at 1M	X	X	X							
Best-corrected binocular defocus curve overall and by average photopic pupil size (≤2.5 mm, >2.5 to <4 mm and ≥4.0 mm) at 6M							X	X	X	
Contrast Sensitivity										
Monocular contrast sensitivity testing overall and by pupil size at 1M (photopic: ≤2.5 mm, >2.5 to <4 mm and ≥4.0 mm mesopic: ≤4.0 mm, >4.0 to <=5.0 mm and >5.0 mm) (N, Mean, SD, Median, Min, Max, 90% CI)	X	X	X							
Binocular contrast sensitivity testing overall and by average pupil size at 6M (photopic: ≤2.5 mm, >2.5 to <4 mm and ≥4.0 mm mesopic: ≤4.0 mm, >4.0 to <=5.0 mm and >5.0 mm) (N, Mean, SD, Median, Min, Max, 90% CI)							X	X	X	
Refractive Outcomes										

	First Eyes	First Eyes	First Eyes	Second Eyes	Second Eyes	Second Eyes	Subjects	Subjects	Subjects	Comments
	ZFR00	ZYR00	Control	ZFR00	ZYR00	Control	ZFR00	ZYR00	Control	
Sphere, absolute cylinder and spherical equivalent (N, Mean, SD, Median, Min, Max)	X	X	X	X	X	X				
Absolute spherical equivalent by diopter level (<=0.50, 0.51-1.00, 1.01-1.50, 1.51-2.00,>2.00) (No. and percent within each category)	X	X	X	X	X	X				
Absolute refractive cylinder by diopter level (<=0.50, 0.51-1.00, 1.01-1.50, 1.51-2.00,>2.00) (No. and percent within each category)	X	X	X	X	X	X				
Ocular/Visual Symptoms										
Non-directed optical/visual symptoms at each visit and Cumulative (No. and percent with each item)	X	X	X	X	X	X				
Visual symptoms from questionnaire							X	X	X	
Questionnaire Data										
Subject questionnaire for spectacle independence, satisfaction and other questionnaire (No. and percent within each category)							X	X	X	
Medical/Lens Findings and Other Adverse Event Tables										
Serious and/or device-related Adverse events listing	X	X	X	X	X	X	X	X	X	
Medical (including adverse event) and Lens Findings at each visit and Cumulative (No. and percent with each item)	X	X	X	X	X	X				
Dilated Fundus (No. and percent Normal/Not Normal) at 6M visit	X	X	X	X	X	X				
Non-adverse events (No. and Percent – all items listed in the database)	X	X	X	X	X	X				

KEY:VA=Visual acuity, UCDVA= uncorrected distance visual acuity at 4m, BCDVA= best corrected distance visual acuity at 4m, UCIVA=uncorrected intermediate visual acuity at 66cm, DCIVA=distance corrected intermediate visual acuity at 66cm, UCNVA=uncorrected near visual acuity at 40cm, DCNVA=distance corrected near visual acuity at 40cm, SD=Standard Deviation, D=Diopter, X=tables will be provided – blank indicates table will not be generated, Bilateral=Subjects implanted with the same study IOL in both eyes

TIME FRAME: Key study timeframe for endpoints will be 1 month.

STATISTICS: See text portion of the statistical analysis plan for information on inferential statistics for comparisons between IOL groups.

APPENDIX II: FORMULAS USED FOR VISUAL ACUITY REFRACTIVE DATA AND CONTRAST SENSITIVITY

Postoperative distance and intermediate visual acuity testing will be performed using the M&S Technologies CTS-1000 Smart System© computerized vision testing system (M&S system). Postoperative near visual acuity testing will be performed using the Good-Lite self-calibrating, retro-illuminated box with 100% contrast ETDRS near charts at a test distance of 40 cm.

Key : " * " = multiplication, " - " = subtraction, " / " = division, " ** " = exponent, log10 = log in base 10

Formulas for Converting Distance and Intermediate VA to LogMAR Values (M&S System):

LogMAR value = (85-letter score)/50

Example: A subject has distance letter score of 78
Converting to LogMAR: (85-78)/50 = 0.14 LogMAR

If the standard test distance is not used for the M&S system, no calculation adjustment will be needed since the M&S system already takes that into account.

Formulas for Converting Near VA to LogMAR Values (ETDRS chart):

LogMAR value = (70-letter score)/50

If the standard test distance for the chart was not used, then the following formulas will be used:

For near VA not tested at 40cm:
LogMAR=LogMAR(from formulas above) + (log10(40)-log10(test distance in cm))

Example: A subject has a near letter score of 65 and a test distance of 33 cm
Converting to LogMAR: (70 - 65)/50 = 0.10 LogMAR
Adjusting for test distance=0.1 + (log10(40)-log10(33))=0.10 + 0.083 = 0.183

Formulas for Converting from LogMAR to Snellen and Decimal Equivalent:

Snellen denominator=20*(10**(LogMAR value))
Decimal VA= 20/(Snellen Denominator)

Example: A subject has a LogMAR score of 0.20
The Snellen denominator is: 20*(10**(0.20) = 20*(1.585) = 31.7=20/32
Decimal VA = 20/32=0.625

Formulas for Refractive Data

Converting to Plus Cylinder Notation:

If the original cylinder value is negative, then the following formulas are used:

1. New sphere value=original sphere value + original cylinder value
2. Final cylinder value=absolute value of the original cylinder value
3. Final axis value: if original axis is >0 and ≤90, then final axis=original axis +90; if the original axis >90 and ≤180, then final axis=original axis – 90

Adjusting for Infinity: Final sphere=sphere (in plus cylinder notation) – 0.25

Spherical Equivalent (SEQ)

1. Spherical equivalent=final sphere + (0.5*final cylinder)
2. Adjusted spherical equivalent=spherical equivalent – target spherical equivalent

Examples:

Refraction: sphere: -0.25 cylinder: -0.50 axis: 80 with target SEQ=-0.13

In plus cylinder notation: sphere=-0.75, cylinder=0.50 axis=170
Adjusting for infinity: sphere=-1.00, cylinder=0.50 axis=170
Spherical equivalent=-1.00 + 0.5*(0.50) = -0.75
Adjusted spherical equivalent=-0.75 – (-0.13) = -0.62

Formulas for Converting Contrast Sensitivity to Log Units (M&S System):

Log units = log10(1/% value from the CRF)
For example: 50% contrast will be log10(1/0.5) = log10(2) = 0.3010