Johnson & Johnson Vision

STATISTICAL ANALYSIS PLAN

Protocol CR-6400

Clinical Evaluation of a Daily Wear Reusable Multifocal Optical Design in a Presbyopic Population

JJV Investigational senofilcon A Multifocal Contact Lens

Version: 1.0

Date: 3 November 2020

[redacted]

Compliance: The study described in this document was performed according to the principles of Good Clinical Practice (GCP).

AUTHORIZED SIGNATURES

The signature below constitutes the approval of this document and the attachments.

Author	[redacted]	DATE:03 NOV 2020
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AMENDMENT HISTORY

Version Number	Revision Date (DD/MM/YYYY)	Reasons for Revision
1.0	03 November 2020	Original

ABBREVIATIONS

AE	adverse event
CLVA	Contact Lens Visual Acuity
CrI	Credible interval
CRF	case report form
CSR	Clinical Study Report
DMC	Data Monitoring Committee
eCRF	electronic case report form
FDA	Food and Drug Administration
HLHC	High Luminance High Contrast
ICH	International Conference on Harmonization
ITT	Intent-to-Treat
IVRS	interactive voice response system
LOCF	last observation carried forward
PI	principal investigator
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
VP	Visual Performance

1. INTRODUCTION

This statistical analysis plan (SAP) describes the analyses and data presentations for protocol CR-6400 Version 4.0.

This document will serve as the final guidance for all the statistical analysis for this study and will supersede the Statistical Method section in the protocol if there are any discrepancies. Any deviation from the analysis plan will be documented as such in the clinical study report.

2. STUDY OBJECTIVES

Primary Objective:
The primary purpose of this study is to demonstrate that the Multifocal Test lens made with senofilcon A material made from the Flexible Manufacturing Platform (FMP), in its final lens design FAL100, FAL101 and FAL102 (low, mid and high ADD respectively) meets the design validation requirements for CLUE overall quality of vision scores, logMAR visual acuity, ocular physiology and lens fit acceptance.

Secondary Objective:
The secondary objective is to evaluate the number of lenses needed to optimize the subject's vision.

3. STUDY DESIGN

3.1. Overview

The clinical study is a bilateral, single-masked (partial), single-arm, clinical trial. A total of approximately 60 eligible subjects (30 myopes and 30 Hyperopes) will be targeted to complete the study.

The study begins with an initial visit, Visit 1 (Day 0), if a subject is found to meet all eligibility criteria, they will be fit with the study lens, in both eyes; otherwise the subject will be deemed ineligible and classified as a screen failure.

If a subject is dispensed lenses at the initial visit, then two additional visits will be conducted. Visit 2 will occur 3 ± 1 days after Visit 1. At Visit 2 subjects will undergo lens optimization if the subject reports unsatisfactory vision or is unable to obtain 20/30 binocular distance visual acuity with the study lenses. Subjects will return for Visit 3 (Final Evaluation) after 12±2 days. At the final visit, subjects will undergo subjective and objective assessments of vision.

Subjects will be advised to wear the study lenses every day while they are in the study for a minimum of 6 hours per day. The study lens will be replaced at the optimization visit. However, lost or damaged lenses maybe replaced when necessary. Unscheduled visit may be conducted.

3.2. Test Articles

Table 1: Test article labels

Test Article	Label
JJV Investigational Multifocal Contact Lens	Test
ACUVUE OASYS® with HYDRACLEAR® PLUS Sphere*	Test
All Test Articles	Total

***Note:** The spherical test lens (JJV Investigational Multifocal Contact Lens) is used in the troubleshooting steps only for low ADD subjects who have reported a distance vision complaint.

3.3. Targeted Study Population and Sample Size

Approximately 80 subjects will be enrolled to ensure that 60 subjects will complete the study (30 myopes and 30 hyperopes). Enrolled subjects will be habitual wearers of soft contact lenses. All subjects will be at least 40 years of age and not older than 70 years of age at the time of enrolment. Eligible presbyopes will be those that wear an a presbyopic contact lens correction (e.g., reading spectacles over contact lenses, multifocal or monovision contact lenses, etc.) or if not respond positively to at least one symptom on the "Presbyopic Symptoms Questionnaire" (CR-6400 Protocol Version 4.0, Appendix E).

Table 2: Planned Enrollment Strategy by Strata and Site

	Myopes	Hyperopes	Total
Enrolled	40	40	80
Randomized	30	30	60
Number of enrolled per site (min-max) Target	2-6	2-6	

3.4. Test Article Allocation and Masking

The study lenses will be worn in a bilateral fashion using a single-arm design. Due to the nature of the design no randomization is required.

This is a single arm study and all subjects will be assigned to the same study lens. Subjects will be unaware of the identity of the investigational product. Investigators and clinical site personnel involved in the data collection will not be masked as to the identity of the investigational product.

Subjects who have had their treatment assignment unmasked are expected to return for all remaining scheduled evaluations. Subjects who are discontinued may be replaced.

3.5. Time and Event Schedule

See Appendix 14.1 for details regarding the Time and Events Schedule.

4. STUDY ENDPOINTS

Primary Efficacy Endpoints:

CLUE Overall Quality of Vision

Overall comfort scores will be assessed using the Contact Lens User Experience (CLUE™)[1] questionnaire after approximately 2 weeks of lens wear. CLUE is a validated patient-reported outcomes questionnaire to assess patient-experience attributes of soft, disposable contact lenses (comfort, vision, handling, and packaging) in a contact-lens wearing population in the US, ages 18-65. Derived CLUE™ scores using Item Response Theory (IRT) follow a normal distribution with a population average score of 60 (SD 20), where higher scores indicate a more favorable/positive response with a range of 0-120. A 5-point increase in an average CLUE™ score translates into 10% shift in the distribution of scores for population of soft contact lens wearers.

Visual Acuity (logMAR)

Multiple assessments of binocular and monocular visual acuity will be made during the study, but the binocular measurements made after approximately 2 weeks of lens wear using high contrast letters in bright illuminance conditions will be the primary endpoint. At distance (4 meters), VA is assessed using ETDRS charts; while near (40 cm) and intermediate (64 cm) assessments will be made using reduced Guillon-Poling charts. Visual acuity will be measured using high and low contrast charts in bright illuminance conditions. [redacted]

Primary Safety Endpoints:

Slit Lamp Findings (SLF)

Slit Lamp Findings (Grade 3 or higher) will be assessed for each subject eye at all study visits (schedule and unscheduled). SLFs will be evaluated and classified using the FDA Grading scale rating from 0 to 4, where Grade 0 represents the absence of findings and 1 to 4 representing successively worse findings (i.e. Grade 1=trace, Grade 2= mile, Grade 3=moderate and Grade 4= severe). The percentage of eyes with Grade 3 or higher slit lamp findings will be analyzed and will include corneal infiltrates. [redacted]

Unacceptable Lens Fit

Unacceptable lens fit will be assessed at all study visits (scheduled and unscheduled) for each subject eye. Unacceptable fit is a binary response where Y=1 if lens fit is unacceptable and

Y=0 otherwise. Unacceptable fit was defined as unacceptable if any one of the following criteria:
- limbal exposure at primary gaze or with extreme eye movement;
- edge lift;
- excessive movement in primary up gaze;
- insufficient movement in all three of the following conditions: primary gaze, up gaze, and push up test.

Eyes with multiple unacceptable fitting events was counted only once. See CTP-2008 in Appendix H for additional details regarding lens fit assessments.

4.1. Secondary Endpoints

Summary of lenses needed to fit (optimize) the subject's vision

4.2. Other Endpoints

- Lens Deposits
- CLUE comfort/handling scores
- GSI Product Performance ratings

5. STATISTICAL HYPOTHESES FOR STUDY OBJECTIVES

5.1. Primary Hypotheses

All the following co-primary hypotheses must be satisfied in order to meet the study objectives.

Primary Hypotheses:

1. After approximately 2-weeks of wear, the mean overall quality of vision score of the Test lenses will be statistically better than 40 points for the myope population. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

2. After approximately 2-weeks of wear, the mean overall quality of vision score for the Test lenses will be statistically better than 32 points for the hyperope population. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

3. After approximately 2-weeks of wear, the mean distance, binocular, high luminance, high contrast logMAR visual acuity score of the Test lens will be statistically lower than 0.10 logMAR.

4. After approximately 2-weeks of wear, the mean intermediate, binocular, high luminance, high contrast logMAR visual acuity score of the Test lens will be statistically lower than 0.17 logMAR.

5. After approximately 2-weeks of wear the mean near, binocular, high luminance, high contrast logMAR visual acuity score of the Test lens will be statistically lower than 0.17 logMAR.

6. When wearing the Test lenses, the proportion (%) of eyes with at least one reported clinically significant slit-lamp finding (Grade 3 or 4) during the post-fit period will be significantly lower than 5%.

7. When wearing the Test lenses, the proportion (%) of eyes with an unacceptable fit during the study will be statistically less than 5%.

If all the primary hypotheses are met, the following secondary hypothesis will be tested.

5.2. Secondary Hypotheses

1. The proportion of subjects who obtain the optimum lens pair in 4 lenses or less will be at least 90% using a 95% level of confidence.

5.3. Other Hypotheses

Not applicable.

6. ANALYSIS SETS

6.1. All Enrolled

The All Enrolled population will include all participants who sign an informed consent.

6.2. Intent-to-Treat (ITT)

Intent-to-treat will include all enrolled subjects regardless of actual treatment and subsequent withdrawal from study or deviation from protocol. At least one observation should be recorded.

6.3. Safety Population

All subjects who were administered any test article with at least one observation recorded excluding subjects who dropped out prior administering any test article. Safety analyses will be based on the safety population.

6.4. Per-Protocol (PP)

Per Protocol Analysis set will be the primary analysis population. It will include all subjects who have successfully completed all visits and did not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock. Justification of excluding subjects with protocol deviations in the per-protocol population set will be documented in a memo to file.

The following is a preliminary list of criteria that may disqualify a subject from the Per-Protocol analysis. This list is simply suggestive and is subject to change at the pre-lock review:

7. DEFINITIONS AND DERIVED VARIABLES

7.1. Age

Age will be calculated using the Date of Birth (DOB) and the date of the consenting the subject and presented as age at last birthday as an integer.
Age = Integer part of [(Date of Baseline visit – Date of Birth) / 365.25]

7.2. Visit Windows

Table 3: Visit window information

Scheduled Visit Number	Time Interval (label on output)	Time Interval (Day)[a]	Target Time Point
1	Screening	0	1
1	Baseline	0	1
2	3-Day Follow-up	2 to 4	3
3	2-Week Follow-up	10 to 14	14

[a] The first treatment day is Day 0.

7.3. Average daily wear time (in Hours)

Average daily wear time will be calculated as the number of hours between subjects reported time of insertion and time of removal of the study lenses at screening 3-Day Follow-up and 2-Week Follow-up evaluation.

7.4. Definition of Subgroups

Subject will be categorized into either the Hyperope or the Myope group based on the subjects' distance spherical refraction. Subjects who have a negative distance spherical refraction will be categorized as a Myope while subjects who have a positive distance spherical refraction will be categorized as a Hyperope. However, if a subject has positive distance spherical refraction in one eye and plano refraction in the opposite eye then the subject will be categorized as a Hyperope. If the subject has negative distance spherical refraction in one eye and plano refraction in the opposite eye, then the subject will be categorized as a Myope. If the subject has positive distance spherical refraction in one eye and negative distance spherical refraction in the other eye, the eye with the highest absolute power (D) will be used to categorize the subject (i.e. if a subject spherical distance refraction is OD: +0.75, OS: -1.25; then they will be categorized as a Myope. If the subject has equal magnitude of spherical refraction but opposite sign between eyes, the subject will be categorized as a Myope.

8. GENERAL STATISTICAL CONSIDERATIONS

8.1. Statistical Software

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 or higher (SAS Institute, Cary, NC)[2].

8.2. Summary Statistics

Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis. Unscheduled visits will be summarized separately and will be excluded from the efficacy statistical analysis but will be included in the analysis of safety endpoints (slit lamp findings and lens fitting).

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, standard deviation [SD], median, minimum, and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data.

Safety and efficacy variables will be summarized on both safety and PP populations.

8.3. Reporting Numerical Values

Means, medians and confidence/credible intervals will be reported to one decimal place greater than the original data. The standard deviation will be reported to two decimal places greater than the original data. Minimum and maximum will use the same number of decimal places as the original data. P-values greater or equal than 0.0001 will be reported to 4 decimal places; p-values less than 0.0001 will be reported as "<0.0001". All percentages will be reported to one decimal place.

8.4. Sample Size Justification

This study was designed and powered to demonstrate that the Multifocal Test lens made with senofilcon A material made from the Flexible Manufacturing Platform (FMP), in its final lens design FAL100, FAL101 and FAL102 (low, mid and high ADD respectively) meets the design validation requirements for the following efficacy and safety endpoints:

- CLUE vision score at 2-week follow-up
- Binocular visual acuity (Distance, Intermediate and Near) at 2-week follow-up
- Proportion of eyes with a significant slit lamp finding (Grade 3 or higher)
- Proportion of eyes with unacceptable lens fitting

The historical data used for the sample size calculation were from 6 JJVC sponsored studies. Table 4 displays the studies, their corresponding study design and the number of subjects enrolled and

completed. The investigational product in all these studies was the multifocal Test lens in its' final design (FAL100, FAL101 and FAL102) made from different manufacturing platforms.

Table 4: Historical Studies Utilized for Sample Size Calculation

Study	Study Design	Manufacturing Platform	#Enrolled	#Completed	Population	SKU
[redacted]	Crossover	FMP[1]	46	43	Hyperopes	+1.00 to +4.00
[redacted]	Crossover	TAM21[2]	71	61	Hyperopes	+1.00 to +4.00
[redacted]	Crossover	TAM21	63	60	Myopes	-1.00 to-4.00
[redacted]	Crossover	SCLM[3]	45	45	Hyperopes	+1.00 to +4.00
[redacted]	Parallel	MCLM[4]	189	168	Myopes	-1.00 to-4.00
[redacted]	Crossover	SCLM	40	34	Hyperopes	+1.00 to +4.00
Total			454	411		

[1]FMP: Flexible Manufacturing Platform
[2]TAM21: Tokyo Automatic Machinery -3GT (3rd Generation Technology) manufacturing line
[3]SCLM: Single Cavity Lens Machine
[4]MCLM: Multi Cavity Lens Machine

Summaries of efficacy data pooled across all the 6 studies are presented in Table 5. Results showed that near, intermediate and distance VA have similar variation across studies, therefore a 0.11 was utilized for the variation in the power calculation for all positions. Historical data have shown that the average CLUE vision score of hyperopes is lower that of myopes.

Table 5: Descriptive summary of Efficacy Endpoints Period 1 Only - 2-Week Follow-up

Endpoint	Mean	Median	Standard Deviation	Minimum	Maximum
Distance VA (3m)	-0.077	-0.100	0.1026	-0.320	0.560
Intermediate VA (64cm)	-0.054	-0.060	0.1014	-0.300	0.360
Near VAR (40cm)	0.077	0.060	0.1100	-0.260	0.460
Hyperopes' CLUE Vision score	47.71	48.07	17.514	10.22	93.50
Myopes' CLUE Vision score	56.46	53.37	19.227	21.51	108.04

The proportion of eyes with Grade 3 or higher SLFs and the proportion of eyes with unacceptable lens fittings pooled across all historical studies is presented in the table below. As shown, there was only 1 unacceptable lens fitting in any of the 6 historical study while there have been 5 eyes with reported Grade 3 or higher SLFs.

Table 6: Descriptive Summary of Safety Endpoints all available Data

Endpoint	Test n(%)
Unacceptable lens fitting	1 (0.2)
SLF Grade 3+	5 (1.4)
Total Eyes (N)	350
Total Subjects	175

%= nx100/N

Safety Analysis

Our plan for safety analysis is to incorporate historical individual subject data from the 6 studies using power prior distributions in a Bayesian framework (see section 14.5). The level of influence of historical data on current is determined by a discounting factor a constrained between 0 and 1 ($0 \leq a_0 \leq 1$). $a_0 = 0$ corresponds to no borrowing of the historical data; while $a_0 = 1$ corresponds to full borrowing (See section 14.5 for more details). For this study we considered a low level of borrowing ranging by 0.1 and 0.30 based on the manufacturing platform where the historical study lens was made from. Table 7 displays the number of subjects and the degrees of borrowing that will be used in the safety analysis. The approved investigational product will be manufactured from the FMP platform; therefore, the borrowing strength is larger to lenses from the FMP platform. Furthermore, the TAM21 platform is considered equivalent with respect to lens performance and lenses from these platforms are given the same borrowing strength as those from the FMP platform. While all historical studies used the lens in its final design, lenses made from the pilot line are only given a borrowing strength of 10%.

Table 7: Degrees of Borrowing Historical Data by Manufacturing Platform

Manufacturing Platform	Number of Subjects	Level of borrowing (a_0)
FMP	23	0.3
TAM21	66	0.3
Pilot Line (SCLM, MCLM)	86	0.1

We calculated the required sample size with and without borrowing historical data. To achieve a minimum of 80% power with a 2-sided type I error rate of 5%, the required sample size with no borrowing ($a_0 = 0$) was 120 subjects (240 eyes); while the sample size with borrowing was 60 subjects (120 eyes). The sample calculation in each scenario of borrowing was conducted using a Monte Carlo simulation of 1000 trials of samples of size 120 subjects (240 eyes) were drawn from a multivariate binary distribution assuming a compound symmetric (CS) covariance structure between left and right eye from the same subject. Assuming a true proportion of eyes with grade 3 or higher SLFs of p=0.014 and a correlation of ρ=0.70 between left and right eyes. The same approach was considered for the proportion of eyes with unacceptable fitting assuming a true proportion of eyes with unacceptable fit of p=0.01 and a correlation of ρ=0.80 between left and right eyes.

The sample size was mainly driven by safety analysis, the power calculation of the efficacy analysis showed that a sample size of 60 subjects is sufficiently large to test the efficacy hypotheses. No borrowing was considered for the primary efficacy analysis. Table 8 summarize the statistical power of a sample size of 60 subjects (120 eyes) for all endpoints.

Table 8: Power calculation by endpoint/hypothesis assuming a sample size of 60 subjects

Endpoint	Borrowing	Hypothesis (H_A)	Power (%)
Grade 3 or Higher SLFs	Yes	$p_t < 0.05$	80
Unacceptable lens tit	Yes	$p_t < 0.05$	90
VA Distance	No	$\mu_t < +0.10$	> 99
VA Intermediate	No	$\mu_t < +0.17$	> 99
VA Near	No	$\mu_t < +0.17$	> 99
CLUE Vision (Hyperopes)	No	$\mu_t \geq 32$	99
CLUE Vision (Myopes)	No	$\mu_t \geq 40$	99

The power calculation of the efficacy analyses (CLUE and VA) was conducted using historical data presented in Table 5 above using PROC POWER for one sample means test for equivalence to test each hypothesis.

The plan is to enroll 80 eligible subjects with a target completion of 60 subjects. During the enrollment period, the subject drop-out rate with be closely monitored, if an unexpectedly high dropout rate is observed, then the targeted total enrollment number maybe be increased accordingly to ensure that a minimum of 60 subjects complete the study.

8.5. Statistical Significance Level

All planned analysis for this study will be conducted with an overall type I error rate of 5%.

8.6. Handling of Missing Data and Drop-outs

Missing or spurious values will not be imputed. The count of missing values will be included in the summary tables and listings.

Subject dropout is expected to be one of the main reasons of missing data in this clinical trial. Past clinical trials don't provide the evidence that subject dropout is systematic or not-at-random. To evaluate the impact of missing data, sensitivity analysis will be conducted using fully Bayesian imputation by imputing missing values.

9. INTERIM ANALYSIS AND DATA MONITORING COMMITTEE REVIEW

There will be no interim read performed on this study.

10. SUBJECT INFORMATION

10.1. Disposition Information

Enrolled subjects will be allocated to one of the three mutually exclusive:

1. Completed: Subjects are considered to have completed the study if they (a) provided informed consent and/or assent; (b) they are eligible; (c) completed all three phases of testing; and (d) have not withdrawn/discontinued from the study.

2. Discontinued: Subjects are considered to have discontinued from the study if (i) test article was administered and (ii) discontinued from the study. Reasons for discontinuation include: (a) Adverse Event (b) unsatisfactory visual response due to test article (c) satisfaction lens fitting due to test article (d) lens discomfort (e) lens handling difficulties (e) withdrew consent during study (f) lost to follow-up (g) subject no longer meets eligibility criteria (h) subject withdrawn by PI to non-compliance to protocol (i) test article no longer available

3. Assigned and Test Article Administered: Total number subjects for which test articles were administered (Completed + Discontinued).

4. Enrolled but Not Dispensed: Subjects are considered to be Enrolled Not Dispensed Subjects if they were (i) enrolled to the study (provided informed consent and/or assent) but failed to satisfy the eligibility criteria (inclusion/exclusion criteria) or (ii) if they are randomized but did not receive a test article.

5. Total enrolled: Completed + Discontinued + Enrolled but Not Dispensed.

10.2. Protocol Deviations

Any protocol deviation that could impact the primary endpoints will result in the subject being excluded from the Per-Protocol analysis population. No analysis on protocol deviations will be performed. All reported protocol deviations will be listed.

10.3. Demographics and Baseline Characteristics

Demographic characteristics will be summarized by Per-Protocol, safety, and all enrolled population by strata (myopes and hyperopes) using descriptive statistics for continuous variables, and numbers and percentages of subjects for categorical variables. Demographic information will include age, gender, race, ethnicity and ADD power.

10.4. Treatment Compliance and Extent of Exposure

Average daily wear time and average daily comfort wear time will be provided in the summary table. Non-compliance will be reported in protocol deviation.

10.5. Prior and Concomitant Medications

Prior and concomitant medications will be documented during screening and updated during the study when applicable. A listing for both prior and concomitant medications will be created for all enrolled subjects.

Disallowed medications for this study include: Anticholinergics, Oral Phenothiazines, Oral Retinoids, Corticosteroids and Oral Tetracycline.

Concomitant therapies that are disallowed include: Not applicable.

10.6. Medical History

A listing of medical and surgical history will be created for all enrolled subjects.

11. STATISTICAL ANALYSIS

11.1. Primary Analysis

Primary Safety Analyses

Strategy of Incorporating Historical Data:

Safety analysis will be performed by incorporating of historical data from studies: [redacted] All these studies evaluated the same Test lens that was built in different manufacturing platforms to the same in vitro product requirements and are also considered to be representative of final commercial production. The historical individual data will be incorporated using is the power prior distribution (Ibrahim and Chen; 2000)[3].

Let **(y, z)** and ($\mathbf{y_0}$, $\mathbf{z_0}$) denote the data from current study, and from historical data respectively, p the proportion of eyes with response 1 and ρ the correlation between left and right eyes. To construct a power prior distribution for parameter of interests (p, ρ), we use the formula

$$P(p, \rho \mid \mathbf{y_0, z_0}, a_0) \propto L(p, \rho \mid \mathbf{y_0, z_0})^{a0} \pi_0(p, \rho),$$

where $L(p, \rho \mid \mathbf{y_0, z_0}) \propto P(\mathbf{y_0, z_0} \mid p, \rho)$ is the likelihood of (p, ρ) based on the historical data and a_0 is a discounting parameter constrained between 0 and 1. This parameter a_0 controls the amount of the historical data we are borrowing: $a_0 = 0$ corresponds to no incorporation of the historical data, while $a_0 = 1$ corresponds to full borrowing of historical data. We set $a_0 = 0.30$ for historical data of the Test lens was made in FMP and TAM21 platforms and $a_0 = 0.10$ for Test lens made in the pilot line.

The posterior distribution of (p, ρ) given the current and historical data is

$$P(p, \rho \mid \mathbf{y, z, y_0, z_0}, a_0) \propto L(p, \rho \mid \mathbf{y, z}) L(p, \rho \mid \mathbf{y_0, z_0})^{a0} \pi_0(p, \rho),$$

where $L(p, \rho \mid \mathbf{y, z}) \propto P(\mathbf{y, z} \mid p, \rho)$ is the likelihood of (p, ρ) based on the current data.

Primary Safety Analyses:

Slit lamp finding grade 3 or higher and unacceptable lens fitting responses (yes/no) will be analyzed separately on the safety population using the Bayesian model described below. A sensitivity analysis will be conducted with no borrowing of historical data.

The Model:

Let Y1 and Y2 denote the binary outcomes for the left and right eyes, respectively, when wearing the test lens. Considering the correlation, ρ, between Y1 and Y2, the distribution of the

sum Y = Y1 + Y2 is obtained by the mixture of two variables. One of them follow a binomial distribution Bin(2, p) with mixing probability (1-ρ) and the other one follows a modified Bernoulli distribution MBern(p), taking value 0 and 2 rather than conventional 0 and 1, with mixing probability p:

$$P(Y = y| p, \rho) = (1- \rho)Bin(2, p)I_{A1} + \rho MBern(p)I_{A2};$$

where $I_{A1} = \{0, 1, 2\}$ and $I_{A2} = \{0, 2\}$

To overcome the complexity of the mixture likelihood a latent variable Z_i, i = 1, 2 is introduced in the model to indicate in which component of the model the observation y_i, i=1, 2, belongs to, that is,

$$z_i = \begin{cases} 1, \text{if the observation belong to the MBern(p)}, \\ 0, \text{if the observation belong to the Bin}(2, p) \end{cases}$$

The joint distribution of the augmented data (Y_i, Z_i), i=1, 2, is given by

$$P(Y = y_i, Z = z_i| p, \rho) = \rho^{z_i} p^{y_i z_i/2}(1-p)^{(2-y_i)z_i/2}(1-\rho)^{1-z_i}\binom{2}{y_i} p^{y_i(1-z_i)}(1-p)^{(2-y_i)(1-z_i)}$$

The posterior distribution of (p, ρ) given (y, z), (y_0, z_0) and a_0 is

$$P(p, \rho | | \mathbf{y, z, y_0, z_0,} a_0) = P(\mathbf{y, z} | p, \rho)\, P(\mathbf{y_0, z_0}| p, \rho)^{a_0}\, \pi_0(p, \rho)$$

where, π_0 is joint prior distribution of (p, ρ). Here we assume p and ρ to be independent with a prior beta (α, β) for p and uniform (0,1) for ρ. Hence the joint distribution of (p, ρ) is given by π_0 (p, ρ| α, β) $\propto p^{\alpha-1}(1-p)^{\beta-1}$. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC Procedure will be used to estimate the posterior distributions of the parameters (p, ρ). Inferences will be made based on a posterior credible interval for the relevant parameters.

Hypothesis Testing

With respect to unacceptable lens fit the null and alternative hypothesis for superiority is as follows:

$$H_o : p_T \geq 0.05$$
$$H_A : p_T < 0.05$$

Where, p_T represents the proportion of subject eyes that are considered to have unacceptable fit for the study lens after 2-weeks of lens wear. Success for unacceptable fit will be declared if the upper bound of the 2-sided 95% credible interval of the proportion is lower than 0.05; i.e. $P(p_T < 0.05) \geq .975$.

With respect to Grade 3 or Higher SLFs the null and alternative hypothesis for superiority is as follows:

$$H_o : p_T \geq 0.05$$

$$H_A : p_T < 0.05$$

Where, p_T represents the proportion of subject that experienced any Grade 3 or Higher SLF or experienced a corneal infiltrate. Success for Grade 3 or higher SLFs will be declared if the upper bound of the 2-sided 95% credible interval of the proportion is lower than 0.05; i.e. $P(p_T < 0.05) \geq .975$.

If no SLF findings of Grade 3 or higher or unacceptable lens fit is observed, alternative analysis methods may be considered.

Primary Efficacy Analyses

Efficacy analysis will be conducted the Per-Protocol Population without borrowing from historical data. A sensitivity analysis will be performed by incorporating historical data. The level of borrowing used in the safety analysis will be considered. Further sensitivity analyses on the Safety population may also be considered if the observed subject dropout rate exceeds 15%.

CLUE Vision

CLUE vision scores will be analyzed using a multivariate Bayesian normal random effects model. The model will include baseline clue score, age, add power, gender and strata (Hyperopes and Myopes) as fixed effects. Site will be included as a random effect. An unstructured (UN) covariance structure will be used to model the residual errors from measurements within the same subject across timepoints. Heterogeneous residuals covariance structures (R-side) across strata will be considered when appropriate.

The Model:

Let y_{ijk}= $(y1_{ijk}$, $y2_{ijk}$ $)^{\mathrm{T}}$ denote the CLUE vision scores for the K^{th} subject at the J^{th} site, in i^{th} stratum (Hyperope or Myope) at the 3-Day and 2-Week Follow-up evaluations. The likelihood for y_{ijk} is constructed as follows:

$$y_{ijk} \sim \mathrm{N}(\mu_{ijk}, \Sigma)$$

μ_{ijk} = $(\mu 1_{ijk}$, $\mu 2_{ijk}$ $)^T$ and Σ is a 2X2 variance-covariance matrix. Here,

$$\mu 1_{ijk} = \pi_1 + \mu_0 + \beta_1 Baseline_k + \beta_2 age_k + \beta_3 stratum_k + \beta_4 Gender_k + \beta_5 ADD_k + \gamma_j$$
$$\mu 2_{ijk} = \pi_2 + \mu_0 + \beta_1 Baseline_k + \beta_2 age_k + \beta_3 stratum_k + \beta_4 Gender_k + \beta_5 ADD_k + \gamma_j$$

In this model π_1, π_2, represent the effect of time point with the constraint $\pi_1 + \pi_2 = 0$. In this model, we define $stratum_k$=0 for the Myope Strata and $stratum_k = 1$ for the Hyperope Strata. So β_3 stands for the difference between the Hyperope and Myope Strata with respect to CLUE vision; A positive β_3 indicates the Hyperopes performed better than the Myopes.

We assume random site effects are independent and identically distributed (i.i.d) as $\gamma_j \sim \mathrm{N}(0, \sigma^2_{site})$ for site for j=1, 2, 3, 4, 5…, 11 (site) . For the β coefficients, independent non-informative

priors N(0, 1000) will be used. For the variance of random effect of σ^2_{site} an independent non-informative conjugate prior, inverse-gamma(0.001, 0.001) will be used. For Σ, non-informative conjugate priors inverse-Wishart(2,S) will be used where S is a 2X2 variance-covariance matrix of y_{ijk}. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC 15.1[5] procedure will be used to estimate the posterior distribution of the unknown parameters. Inferences will be made based on the 95% posterior credible intervals for relevant parameters.

Hypothesis Testing

Hypothesis testing for CLUE Vision Scores endpoints will be conducted separately for each stratum (Hyperope and Myope):

The null and alternative hypotheses for CLUE vision for statistical superiority of the Hyperope stratum are as follows:

$$H_o: \mu_{Hyperope} \leq 32$$

$$H_A: \mu_{Hyperope} > 32$$

The null hypothesis will be rejected if the lower bound of the 2-sided 95% credible interval of the clue vision posterior mean estimate for the Hyperope stratum is above 32. i.e., $P(\mu_{Hyperopes} > 32) \geq 0.975$.

The null and alternative hypotheses for CLUE vision for statistical superiority of the Myopes stratum are as follows:

$$H_o: \mu_{Myope} \leq 40$$

$$H_A: \mu_{Myope} > 40$$

The null hypothesis will be rejected if the lower bound of the 2-sided 95% credible interval of the clue vision posterior mean estimate for the Myope stratum is above 40. i.e., $P(\mu_{Myopes} > 40) \geq 0.975$.

Binocular Visual Performance

Binocular high luminance, high contrast (HLHC) visual performance (logMAR) at the 2-week follow-up evaluation will be analyzed using a Bayesian normal random-effects model for repeated measures. The model will include strata (Hyperope and Myope), add power, age, gender as fixed effects. Site and will be included as a random effect. An unstructured (UN) covariance structure will be used to model the residual errors from measurements within the same subject across different positions. Heterogeneous residuals covariance structures (R-side) across position will be considered when appropriate.

Let y_{ijkl}denote the visual performance for the study lens for the j^{th} subject in the k^{th} strata (Hyperope or Myope), at the l^{th}site for the i^{th}position.

The Model:
y_{ijkl}= μ_0+ β_1 age_i + β_2 $addpwr_j$+ $\beta_3$dist_yn $_i$ + $\beta_4$inter_yn $_i$+ $\beta_5 Female_j$ + $\beta_6 Strata_k$ + δ_l + ε_{ijkl}

- μ_0: overall intercept
- $addpwr_i$: ADD Power
- dist_yn $_k$: Distance vs. Intermediate and Near
- inter_yn $_k$: Intermediate vs. Distance and Near
- $Female_i$: Female indicator; Female=1 if sex='Female' and 0 otherwise
- $Strata_j$: Strata indicator; Strata=1 if strata='Hyperope' and 0 otherwise
- δ_l : effect of the l^{th} clinical site, a random effect
- ε_{jkl}: random error associated with the i^{th}position for the j^{th} subject in the k^{th} strata at the l^{th} investigational site

Here we assume δ_j and ε_{jkl} are independent where

- $\delta_j \sim N(0, \sigma^2_{site})$;
- $\begin{bmatrix}\varepsilon_{1jkl}\\ \varepsilon_{2jkl}\\ \varepsilon_{3jkl}\end{bmatrix} \sim N\left(\begin{bmatrix}0\\0\\0\end{bmatrix}, \begin{bmatrix}\sigma^2_{11} & \sigma_{12} & \sigma_{13}\\ \sigma_{21} & \sigma^2_{22} & \sigma_{23}\\ \sigma_{31} & \sigma_{32} & \sigma^2_{33}\end{bmatrix}\right)$

We assume random site effects are independent and identically distributed (i.i.d) as γ_j ~ N(0, σ^2_{site}) for site for j=1, 2, 3, 4, 5…, 11 (site) . For the β coefficients, independent non-informative priors N(0, 1000) will be used. For the variance of random effect of σ^2_{site} an independent non-informative conjugate prior, inverse-gamma(0.001, 0.001) will be used. For the variance of y_{ijkl} an independent non-informative conjugate prior, inverse-gamma(0.001, 0.001) will be also used. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC 15.1[5] procedure will be used to estimate the posterior distribution of the unknown parameters. Inferences will be made based on the 95% posterior credible intervals for relevant parameters.

Hypothesis Testing

The null and alternative hypothesis for binocular distance HLHC visual performance to test for superiority of the Test lens relative to the pre-defined threshold of 0 logMAR is as follows:

$$H_o: \mu_{Test} \geq 0.10 \text{ logMAR}$$
$$H_A: \mu_{Test} < 0.10 \text{ logMAR}$$

Superiority will be declared if the upper limit of the 95% CrI is below 0.10 logMAR. i.e. P(μ_{Test}< 0.10) ≥ 0.975.

The null and alternative hypothesis for binocular near HLHC visual performance to test for superiority of the Test lens relative to the pre-defined threshold of 0.17 logMAR is as follows:

$$H_o: \mu_{Test} \geq 0.17 \text{ logMAR}$$
$$H_A: \mu_{Test} < 0.17 \text{ logMAR}$$

Superiority will be declared if the upper limit of the 95% CrI is below 0.17 logMAR. i.e. $P(\mu_{Test} < 0.17) \geq 0.975$.

The null and alternative hypothesis for binocular distance HLHC visual performance to test for superiority of the Test lens relative to the pre-defined threshold of 0.17 logMAR is as follows:

$$H_o: \mu_{Test} \geq 0.17 \text{ logMAR}$$
$$H_A: \mu_{Test} < 0.17 \text{ logMAR}$$

Superiority will be declared if the upper limit of the 95% CrI is below 0.17 logMAR. i.e. $P(\mu_{Test} < 0.17) \geq 0.975$.

11.2. Secondary Analysis

Proportion of Subjects with Optimal Lens Pair

The number of lenses used for each subject will be calculated as the original pair (2) plus all the required modifications to reach the optimal pair. In this study the minimum number of lenses per subject used would be 2 where the max would be 6. The data will be dichotomized as 1 if the subject was able to achieve optimal lens pair in 4 lenses or less and 0 otherwise. The binary response will be analyzed using Bayesian logistic regression random-effects model to estimate the proportion of eyes that reached optimal lens pair in 4 lenses or less. The regression model will include strata (Hyperope and Myope), add power, age, gender, event (fitting, optimization, 2-week follow-up) and the interaction between strata by event. Site will be included in the model as a random effect. Non-informative priors will be used for the unknown parameter. For the β coefficients, independent non-informative priors $N(0, 1000)$ will be used. For the variance of random effects of σ^2_{site} non-informative conjugate prior, inverse-gamma (0.001, 0.001) will be used. Inferences will be made based on the posterior credible interval for the relevant parameters.

Hypothesis Testing

With respect to the proportion of subjects that have achieved optimal fitting in 4 lenses or less, the null and alternative hypothesis for superiority is as follows:

$$H_o : p_T \leq 0.90$$
$$H_A : p_T > 0.90$$

Where, p_T represents the proportion of subjects that have achieved optimal fitting in 4 lenses or less. Success for will be declared if the lower bound of the 2-sided 95% credible interval of the proportion is greater than 0.90; i.e. $\mathrm{P}(p_T > 0.90) \geq .975$.

If not enough events occur during the duration of this study the model presented for the safety population.

11.3. Other Analysis

There are no other pre-planned analyses for this study.

12. SAFETY EVALUATION

12.1. Adverse Events

Listings of all reported ocular and non-ocular AEs and SAEs will be reported and will include lens type, eye diagnosis, severity of the AE, the number of days the subject spent in the study, the slit lamp findings at discovery of the AE, whether or not it is lens related, the possible cause, and treatments provided to the patient, the outcome, the subjects final Snellen visual acuity, whether or not the subject eye had a scar at the resolution of the AE and the action taken. In addition, the total number of subjects and the total number of eyes with each type of AE (SAEs, ocular AEs and non-ocular AEs) will be tabulated and presented as a footnote in each summary.

12.2. Keratometry and Over Refraction

Keratometry will be assessed for each eye at Entrance (Visit 1) for the following metrics: (1) Steep Dioptric Power, (2) Steep Degrees, (3) Flat Dioptric Power and (4) Flat Degree. Each keratometry metric will be summarized using n, mean, min, and max across eye type and summarized by stratum (Hyperopes and Myopes) and across all subjects.

12.3. Contact lens Corrected Visual Acuity

Contact lens visual acuity will be assessed using Snellen visual acuity Charts at both 4m (Distance) and 40cm (Near) at the fitting evaluation, lens dispensing, 3-day follow-up and the 2-week Follow-up evaluations. CLVA will be assessed both monocularly and binocularly. Summaries for Monocular CLVA and binocular CLVA will be presented using counts and percentages of eyes and subjects, for monocular CLVA and binocular CLVA, respectively.

12.4. Reasons for Discontinuation

The number of discontinued subjects by the analysis time point will be displayed by visit.
Reasons for discontinuation include the following:

1. Adverse Event
2. Unsatisfactory lens fitting due to test article
3. Unsatisfactory visual response due to test articles

4. Lens discomfort
5. Withdrew consent during study
6. Lost to follow-up
7. Subject no longer meet eligibility criteria
8. Subject withdrawn by PI due to non-compliance to protocol
9. Test article no longer available
10. Other

12.5. Unscheduled Lens Replacement

The number of unscheduled lens replacements and corresponding reasons will be tabulated by visit and overall, across eyes for both completed and discontinued eyes.

12.6. Physical Examination Findings

Slit lamp findings will be assessed for each subject eye at baseline, 3-day Follow-up, the 2-week follow-up and at any unscheduled visit using the FDA Grading scale (Grade 0=None, Grade 1=Trace, Grade2=Mild, Grade 3=Moderate, Grade 4=Severe). Slit lamp finding assessments include the following metrics:

- Corneal Infiltrates (Yes/No)
- Corneal Edema
- Corneal Neovascularization
- Corneal Neovascularization Location
- Corneal Staining
- Corneal Staining Location
- Conjunctival Injection
- Tarsal Abnormalities
- Other

12.7. Clinical Laboratory Tests

Not applicable.

12.8. Other Safety Parameters

Subject's Reported Ocular Symptoms

Frequency and severity by eye of subject's reported ocular symptoms and problems with the study lens at fitting and post-fitting evaluation visits including the 2-Week Follow-up and unscheduled visits. Severity of the symptoms can be:

- 0 = Not Applicable or Not Recorded;
- 1 = Mild and results in little or no interference with lens wear;
- 2 = Moderate AND/OR occasionally interferes with lens wear;
- 3 = Severe AND/OR frequently interferes with lens wear.

[redacted]

Lens fitting characteristics

Frequency by eye of mechanical lens fitting characteristics at fitting and 2-Week Follow-up evaluations. Lens fitting characteristics to be reported are:

- Lens Centration Grade
- Decentered Direction
- Limbal Exposure Grade
- Edge Lift (Present or Absent)
- Primary Gaze Movement Grade
- Upgaze Movement Grade
- Lens Tightness Grade (Push-up Test)
- Acceptable Fitting (yes/no)

Contact Lens Deposits

Contact lens deposits will be assessed for each eye at the 2-week Follow-up on the front and back surface of the study lens; the amount of deposits will be Graded using the scale:

- None = Grade 0 (No deposition).
- Slight = Grade 1 (Deposition which occupies 1-5% of the lens surface area.)
- Mild = Grade 2 (Deposition which occupies 6-15% of the lens surface area.)
- Moderate = Grade 3 (Deposition which occupies 16-25% of the lens surface area.)
- Severe = Grade 4 (Deposition which occupies =26% of the lens surface area.)

Contact Lens Wettability

Contact lens Wettability will be assessed for each eye at the 2-week Follow-up. Wettability will be Graded using the scale:

- Grade 0 = All regions of lens surface are wettable between blinks (a minimum of 6 seconds between blinks).
- Grade 1 = Discrete non-wetting area(s) after a minimum of 3 seconds post blink.
- Grade 2 = Single non-wetting area within 2-3 seconds of blink.
- Grade 3 = Several non-wetting areas within 2-3 seconds of blink.
- Grade 4 = Immediate area(s) of non-wetting after blink.

13. REFERENCES

1. Wirth RJ, et al. Development of the Contact Lens User Experience: CLUE Scales. Optom Vis Sci. 2016; 93(8): 801-808.

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3. Ibrahim JG, Chen M-H, Gwon Y, Chen F. The power prior: theory and applications. Stat Med. 2015;34(28):3724-3749.

4. Jovanovic, B.D. and Levy, P.S. (1997). A Look at the Rule of Three. *The American Statistician* **51**, 137-139.

5. SAS Institute Inc. 2018. SAS/STAT® 15.1 User's Guide. Cary, NC: SAS Institute Inc.

14. APPENDICES

14.1. Time and Event Schedule

Visit Information	Visit 1 Screening, Baseline, Treatment 1 Fitting	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2
Time Point	Day 0	Day 3±1 from V1	Day 12±2 from V2
Estimated Visit Duration	2.5 hours	1.0 hours	1.5 hours
Statement of Informed Consent	x		
Demographics	x		
Medical History/Concomitant Medications	x		
Adverse Events and Concomitant Medications Review		x	x
Compliance		x	x
Habitual Contact Lens Information	x		
Contact Lens History	x		
Wear Time and Comfortable Wear Time with Habitual Lenses	x		
Wear Time and Comfortable Wear Time with Study Lenses		x	x
Screening Inclusion/Exclusion Criteria	x		
Subject Reported Ocular Symptoms	x	x	x
Baseline Questionnaire	x		
CLDEQ-8 Questionnaire	x	x	x

Visit Information	Visit 1 Screening, Baseline, Treatment 1 Fitting	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2
Time Point	Day 0	Day 3±1 from V1	Day 12±2 from V2
Estimated Visit Duration	2.5 hours	1.0 hours	1.5 hours
Distance and Near Entrance Visual Acuity	x	x	x
Lens Removal	x	x	x
Keratometry	x		
Subjective Refraction and Distance Visual Acuity	x		
Near ADD Determination	x		
Ocular Dominance	x		
ADD Refinement	x		
Near Visual Acuity	x		
Biomicroscopy	x	x	x
Baseline Inclusion/Exclusion Criteria	x		
Eligibility	x		
Lens Selection	x	x (if modified)	
Lens Insertion	x	x	x
10 Minute Settling	x	x (if modified)	
Visual Satisfaction / Subjective Acceptance	x	x	x
Study Lens Distance and Near Visual Acuity	x	x	x
Distance Over Refraction and Visual Acuity	x	x	
Lens Fit Assessment	x	x	x
Binocular Over Refraction		x	x
Lens Deposits			x
Lens Wettability			x

Visit Information	Visit 1 Screening, Baseline, Treatment 1 Fitting	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2
Time Point	Day 0	Day 3±1 from V1	Day 12±2 from V2
Estimated Visit Duration	2.5 hours	1.0 hours	1.5 hours
Visual Performance			x
Modifications	x	x	
Post-Fit GSI Questionnaire	x	x	
Worn Lens Collection		x	x
Study Lens Questionnaire		x	x
Distance and Near Exit Visual Acuity	x	x	
Dispensing Criteria	x	x	
Instructions	x	x	
Schedule Follow-up	x	x	
Final Evaluation			x (or when subject discontinued)

14.2. Statistical Analysis Code

14.2.1. Primary Analysis

CLUE Vision

```
PROC MCMC DATA =ads  NTHREADS =12  SEED  =18965237  NBI =15000 NMC
=100000 THIN=20 DIAG = ALL OUTPOST = simout DIC PLOTS(SMOOTH FRINGE) =
ALL MCHISTORY = BRIEF PROPCOV = QUANEW STATS = ALL STATS(ALPHA =
(0.05) PERCENTAGE = (2.5 50 97.5)) plots(smooth)=ALL MONITOR=(_parms_
Hyperopes_3day Myopes_3day Hyperopes_2wk Myopes_2wk);

ARRAY aval[2]  FU1 FU2;
ARRAY mu[2]    mu1 mu2;
ARRAY sigma[2,2];
ARRAY S[2,2]    ( 1 0
                  0 1 );
PARMS  p1 0.5 p2 0.1 beta0-beta5 ;
PARMS sigma  { 1 0
                 0 1};
PARMS sigma_site;

PRIOR beta:      ~ NORMAL(0, var = 1000);
prior p: ~ NORMAL(0, var=1000);
PRIOR sigma      ~ IWISH(2, S);
PRIOR sigma_site ~ IGAMMA(shape = 0.01, scale = 0.01);

RANDOM gamma_site ~ NORMAL(0, VAR = sigma_site) SUBJECT = siteid;

mu1 = p1      + beta0 + beta1*stratan + beta2*Base + beta3*age + beta4*sexn + beta5*addpwr +
Gamma_site;

mu2 = p1 - p2 + beta0 + beta1*stratan + beta2*Base + beta3*age + beta4*sexn + beta5*addpwr
+ Gamma  site;
MODEL aval ~ MVN(mu, sigma);

  BEGINNODATA;
        Hyperopes  2wk    = p1       + beta0 + beta1 + 0.5*beta4;
        Myopes  2wk       = p1       + beta0         + 0.5*beta4;
        Hyperopes_3Day  = p1 - p2 + beta0 + beta1 + 0.5*beta4;
        Myopes  3Day      = p1 - p2 + beta0         + 0.5*beta4;
  ENDNODATA;
RUN;
```

Where,

Ads = Analysis dataset for CLUE Vision Scores
Stratan=numerical representation of strata, where Hyperopes=1 and Myopes=0
Base= Baseline CLUE Vision Score
Age= Age of subject at time of consent
Sexn=numerical representation of sex, where Female=1 and Male=0;
Addpwr=Add power of subject at baseline
Siteid=Site Identifier

Visual Performance

```
PROC MCMC DATA =ads  vp NTHREADS=12 SEED=20180906 NBI=80000  NMC=150000
THIN=30  DIAG=ALL OUTPOST=simout DIC PLOTS(SMOOTH FRINGE)=ALL
MCHISTORY=BRIEF PROPCOV=QUANEW  STATS=ALL STATS(ALPHA = (0.05)
PERCENTAGE=(2.5 50 97.5))  plots(smooth)=ALL MONITOR=(_parms_  mu_D mu_I
mu_N);

PARMS beta0 0 beta1  0 beta2 0 beta3 0 beta4 0 beta5 0 beta6 0;
PARMS s2 1;
PARMS s2g_site s2g_site1;

PRIOR beta: ~ NORMAL(0, var = 1000);
PRIOR s2 ~ IGAMMA(.001, s =.001);
PRIOR s2g_site  s2g_subj~ IGAMMA(.001, s =.001);

RANDOM Gamma  site ~ NORMAL(0, VAR = s2g  site) SUBJECT=SITEID;
RANDOM Gamma_subj ~ NORMAL(0, VAR = s2g_subj) SUBJECT=USBJID;

mu = beta0 + beta1*dist  yn + beta2*inter  yn + beta3*age + beta4*sexn + beta5*stratan +
beta6*addpwr + Gamma  subj + Gamma  site;
MODEL AVAL ~ NORMAL (mu, VAR = s2);

BEGINNODATA;
    mu  D   =  beta0 + beta1 + 0.5*beta4 + 0.5*beta5;
    mu  I   =  beta0  + beta2 + 0.5*beta4 + 0.5*beta5;
   mu  N   =  beta0          + 0.5*beta4 + 0.5*beta5;
ENDNODATA;

 RUN;
```

Where,
ads vp = Analysis dataset for Binocular HLHC Visual Performance
dist_yn= numerical representation of position, where distance=1 and Intermediate and Near=0
inter_yn= numerical representation of position, where Intermediate=1 and Distance and Near=0
Stratan=numerical representation of strata, where Hyperopes=1 and Myopes=0

Age= Age of subject at time of consent
Sexn=numerical representation of sex, where Female=1 and Male=0;
Addpwr=Add power of subject at baseline
Siteid=Site Identifier

SLF (Grade 3 or Higher) and Unacceptable Lens Fitting

- With Borrowing

```
PROC MCMC DATA= ADS DIC =brief
NBI=50000 NMC=80000 THIN=15 STATS=ALL MONITOR=( parms_ )STATS(ALPHA=(0.05)
PERCENTAGE=(2.5 25 50 75 97.5) ) SEED=14789652  ;
PARM p  ro .5 ;
PRIOR ro ~ UNIFORM(0,1);
PRIOR p ~ BETA(0.5, 0.5);
BEGINCNST;
IF studyid in [redacted] ) THEN a0 = 0.3;
ELSE IF studyid in ([redacted] THEN a0 = 0.3;
ELSE IF studyid in [redacted]) THEN a0=0.1;
ENDCNST;
llike = log( (1-ro)*PDF('BINOMIAL', y, p, 2) + z*ro*(p**y*(1-p)**(2-
y))**(1/2) );
IF studyid in ([redacted]) THEN llike = llike; ELSE llike = a0*llike;
MODEL y ~ GENERAL(llike);
RUN;
```

- Without Borrowing

```
PROC MCMC DATA= ADS DIC =brief
NBI=50000 NMC=80000 THIN=15 STATS=ALL MONITOR=(_parms_ )STATS(ALPHA=(0.05)
PERCENTAGE=(2.5 25 50 75 97.5) ) SEED=14256983  ;
PARM p  ro .5 ;
PRIOR ro ~ UNIFORM(0,1);
PRIOR p ~ BETA(0.5, 0.5);
BEGINCNST;
IF studyid in [redacted] ) THEN a0 = 0;
ELSE IF studyid in ([redacted]) THEN a0 = 0;
ELSE IF studyid in [redacted] THEN a0=0;
ENDCNST;
llike = log( (1-ro)*PDF('BINOMIAL', y, p, 2) + z*ro*(p**y*(1-p)**(2-
y))**(1/2) );
IF studyid in ([redacted]) THEN llike = llike; ELSE llike = a0*llike;
MODEL y ~ GENERAL(llike);
RUN;
```

Where,
ads = Analysis dataset for Grade 3 or higher SLFs or Unacceptable Lens Fitting
a0 = degree of borrowing
stuyid=Study Identifier