

**Alcon - Business Use Only** Statistical Analysis Plan

**Effective Date:** 24-Jan-2017

**Document:** TDOC-0053343

**Version:** 1.0; CURRENT; Most-Recent; Effective

**Status:** Effective

**Short Title:**

**Statistical Analysis Plan  
LCW773-P001 / NCT03026257**

**Full Title:**

**Statistical Analysis Plan  
LCW773-P001**

**Protocol Title:** Clinical Assessment of a Regimen of AIR OPTIX<sup>®</sup> plus  
HYDRAGLYDE<sup>®</sup> Silicone Hydrogel Lenses and  
HYDRAGLYDE<sup>®</sup> Containing Lens Care Solutions

**Project Number:** LCW773-P001

**Reference Number:**

**Protocol TDOC Number:** TDOC-0052732

**Author:**



Contract Biostatistician

**Template Version:** Version 4.0, approved 16MAR2015

**Approvals:** See last page for electronic approvals.

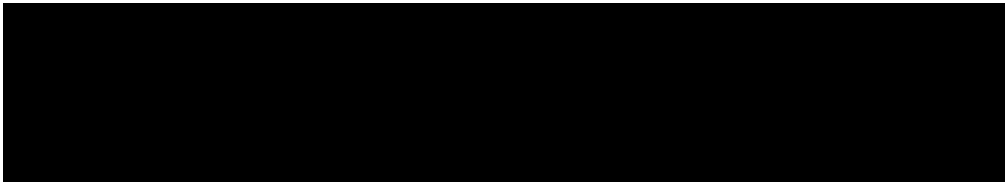
**Job Notes:**

This is the original (Version 1.0) Statistical Analysis Plan for this study. This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

**Executive Summary:**

**Key Objectives:**

To demonstrate that worn AIR OPTIX plus HYDRAGLYDE (AOHG) lenses cleaned and disinfected with HydraGlyde containing lens solutions (HGLC), 1) Opti-Free® PureMoist® (OFPM) and 2) Clear Care® Plus/AOSEPT® PLUS with HYDRAGLYDE® (CCP) for the recommended replacement period will have less cholesterol uptake compared to each of the control habitual SiHy lenses (Biofinity, Vita, Ultra, and Oasys) cleaned and disinfected with habitual multipurpose solution (HMPS)



## Table of Contents

Statistical Analysis Plan LCW773-P001 .....	1
Table of Contents .....	3
List of Tables.....	4
List of Figures .....	4
1 Study Objectives and Design.....	5
1.1 Study Objectives.....	5
1.2 Study Description .....	6
1.3 Randomization.....	7
1.4 Masking .....	7
■ [REDACTED] .....	7
2 Analysis Sets.....	8
2.1 Safety Analysis Set .....	8
2.2 Full Analysis Set.....	8
■ [REDACTED] .....	8
3 Subject Characteristics and Study Conduct Summaries.....	8
■ [REDACTED] .....	9
4.1 Efficacy Endpoints .....	9
■ [REDACTED] .....	10
■ [REDACTED] .....	10
■ [REDACTED] .....	11
■ [REDACTED] .....	12
■ [REDACTED] .....	12
■ [REDACTED] .....	12
■ [REDACTED] .....	17
■ [REDACTED] .....	18
■ [REDACTED] .....	18
5 Safety Analysis Strategy .....	18
5.1 Safety Endpoints.....	18
5.2 Safety Hypotheses .....	19
5.3 Statistical Methods for Safety Analyses .....	19

5.3.1	Adverse Events.....	19
5.3.2	Biomicroscopy Findings.....	20
5.3.3	Device Deficiencies.....	20
6	Analysis Strategy for Other Endpoints .....	20
8	References.....	21
9	Revision History .....	21
10	Appendix.....	21

List of Tables

Table 4–1	Regimen Definition.....	9
		15
		16
Table 10–1	Overview of Study Plan .....	21

List of Figures

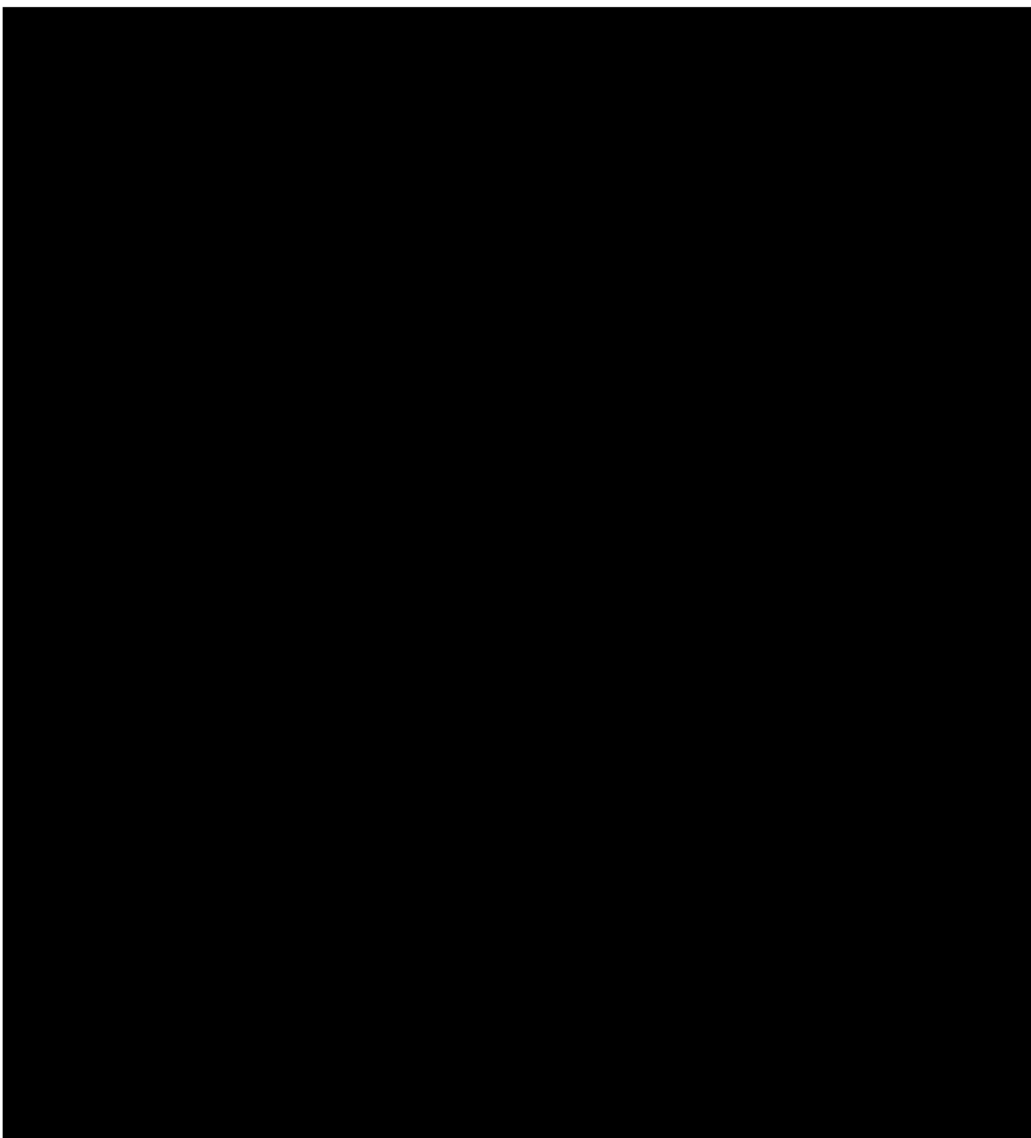
		7
--	--	---

## **1 Study Objectives and Design**

### **1.1 Study Objectives**

#### **PRIMARY OBJECTIVE**

- To demonstrate less cholesterol uptake with each of the test regimens (AOHG/OFPM, AOHG/CCP) compared to each of the control regimens (Biofinity/HMPS, Vita/HMPS, Ultra/HMPS, Oasys/HMPS)



## 1.2 Study Description

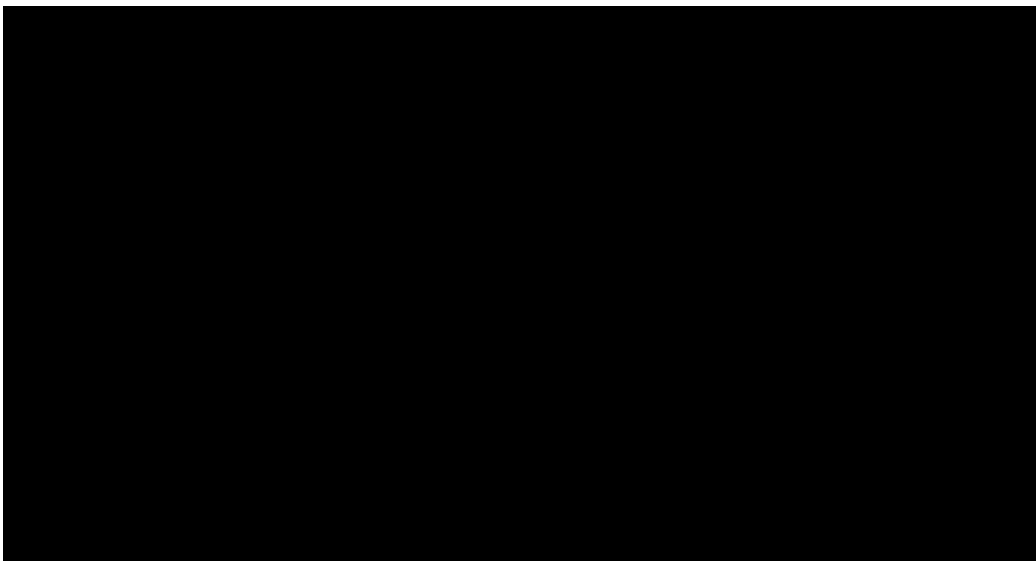
This is a multi-center, prospective, randomized, controlled, parallel-group, observer-masked and quasi-subject-masked study. The study population includes approximately 256 subjects to be randomized at approximately 8 sites, with approximately 14 to 50 subjects randomized per site.

To participate in the study, subjects must be 18 years old or older, current full-time wearer of [REDACTED] of samfilcon A, comfilcon A, senofilcon C monthly or senofilcon A 2-week replacement spherical lenses within the power range of lens powers available for the test AOHG, and currently using [REDACTED] a multipurpose solution (excluding Opti-Free PureMoist) to care for their lenses.

The qualified subject will be randomized and assigned to either AOHG or Habitual SiHy lenses in a 1:1 ratio. Subjects in the AOHG lens group will be further randomized and assigned to either OFPM or CCP in a 1:1 ratio. [REDACTED]

[REDACTED] for all subjects and by habitual lens type at baseline. [REDACTED]

The expected duration of subject participation in the study is up to 40 days and treatment will be 30 (+3) days for all subjects [REDACTED] The study design is presented in Figure 1-1.

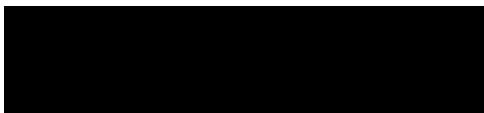


### **1.3 Randomization**

A member of the Randomization Programming group at Alcon who is not part of the study team will generate the randomized allocation schedule(s) for study treatment (regimen) assignment. Randomization will be blocked to ensure a balance of study regimen allocation within investigational sites and strata. Randomization will be implemented in an Electronic Data Capture (EDC) system.

### **1.4 Masking**

This study is observer-masked and quasi-subject-masked (masked to study lenses and test solution brand only). Alcon study personnel will be masked, with the exception of the following: Study monitor, Lead CSM, and person responsible for generating the randomization schedule. This level of masking will be maintained throughout the conduct of the study.



## **2 Analysis Sets**

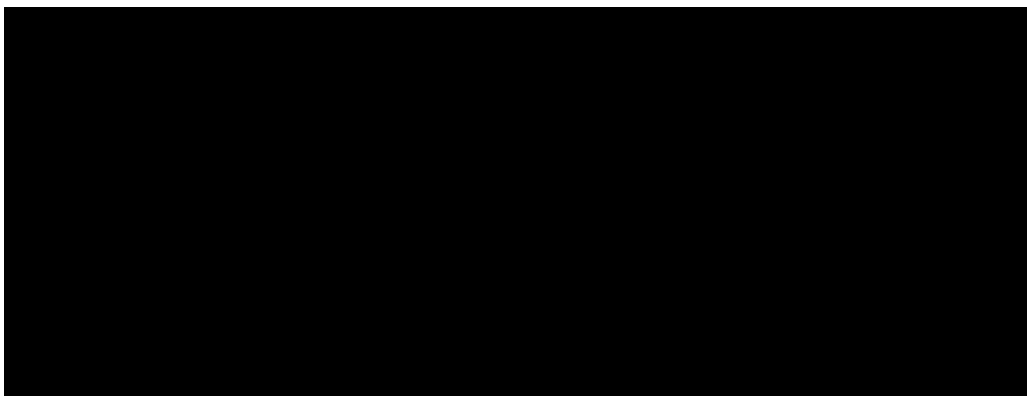
### **2.1 Safety Analysis Set**

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. The safety analysis set will include all subjects/eyes exposed to the study lens and/or the study lens care system (LCS) evaluated in this study as a regimen. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual lens or regimen exposed.



### **2.2 Full Analysis Set**

The Full Analysis Set (FAS) will be the set of all randomized subjects who are exposed to a study lens on Day 1 or a study regimen (lens and LCS) thereafter. Each subject/eye in FAS will be analyzed according to the respective lens or regimen in the randomized lens or regimen, irrespective of the exposure.

The FAS will serve as the primary analysis set for all efficacy evaluations.



## **3 Subject Characteristics and Study Conduct Summaries**

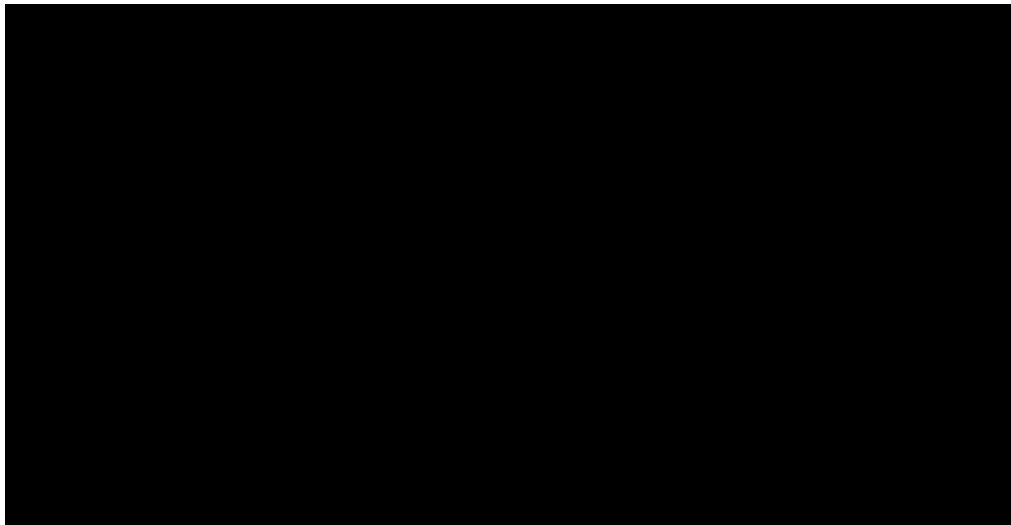
Demographic information (age, sex, ethnicity, and race) will be summarized for the safety, full  



All descriptive summary statistics will be displayed with counts and percentage for categorical data, and with n, mean, standard deviation, median, minimum, and maximum for continuous data.



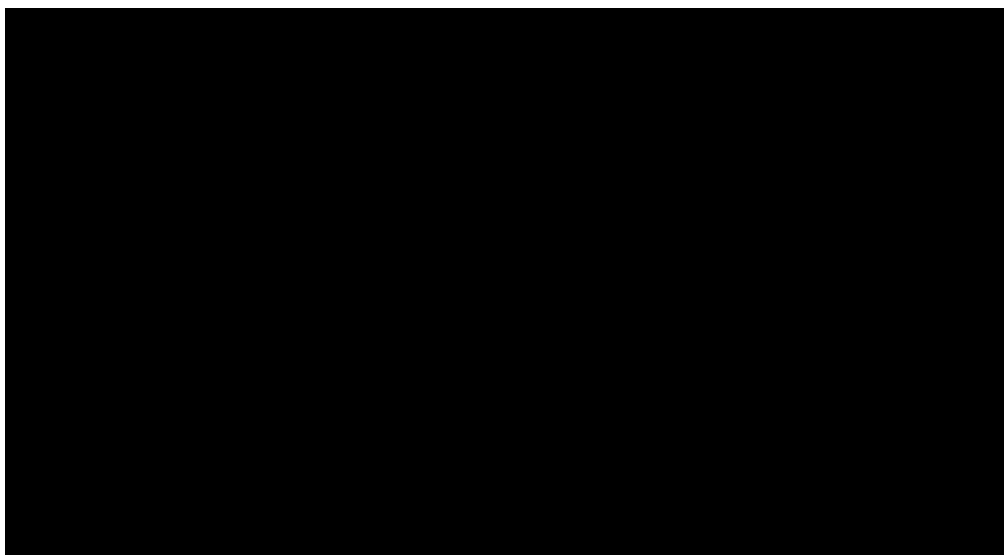
## 4 Efficacy Analysis Strategy

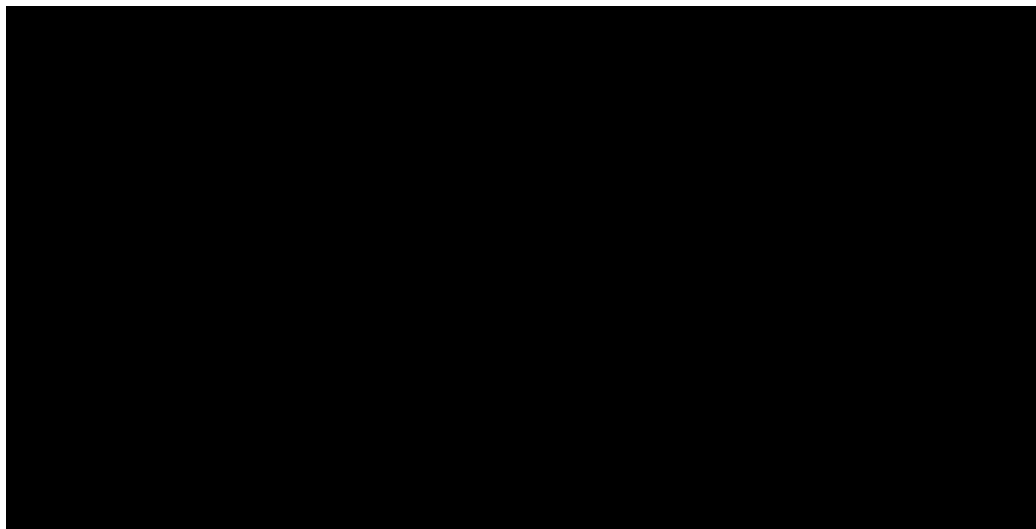
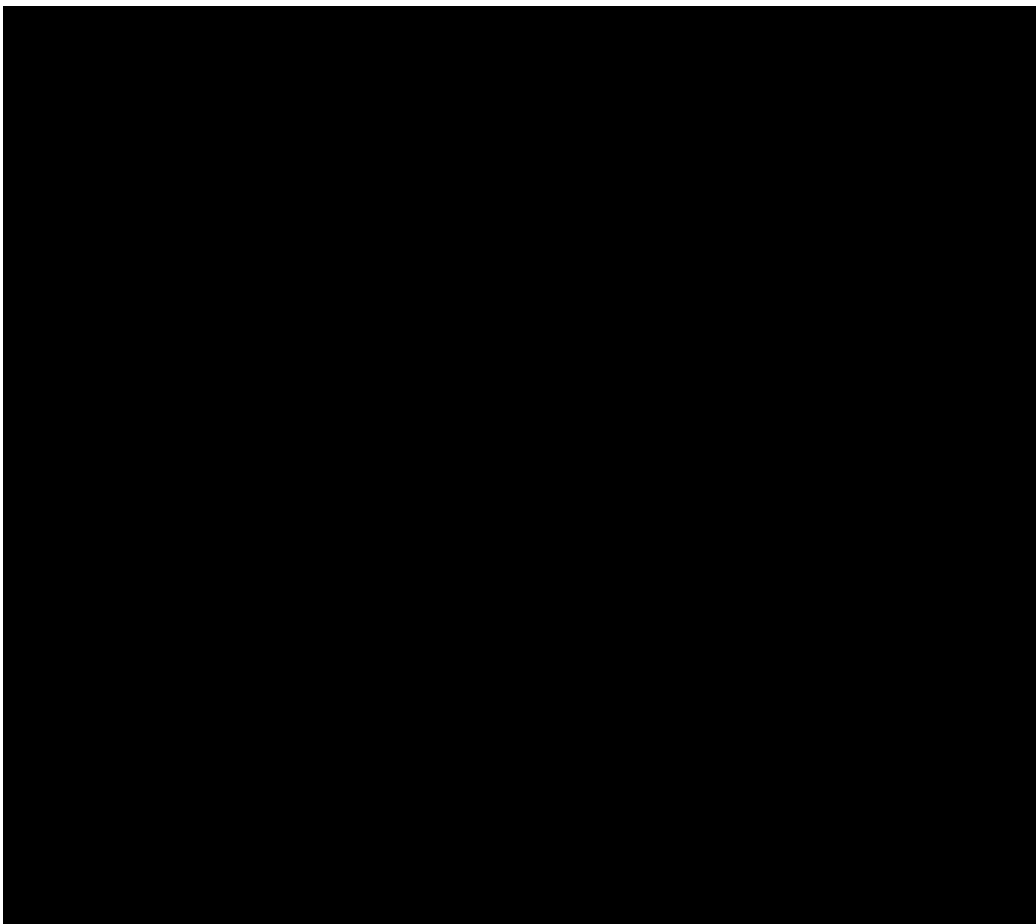


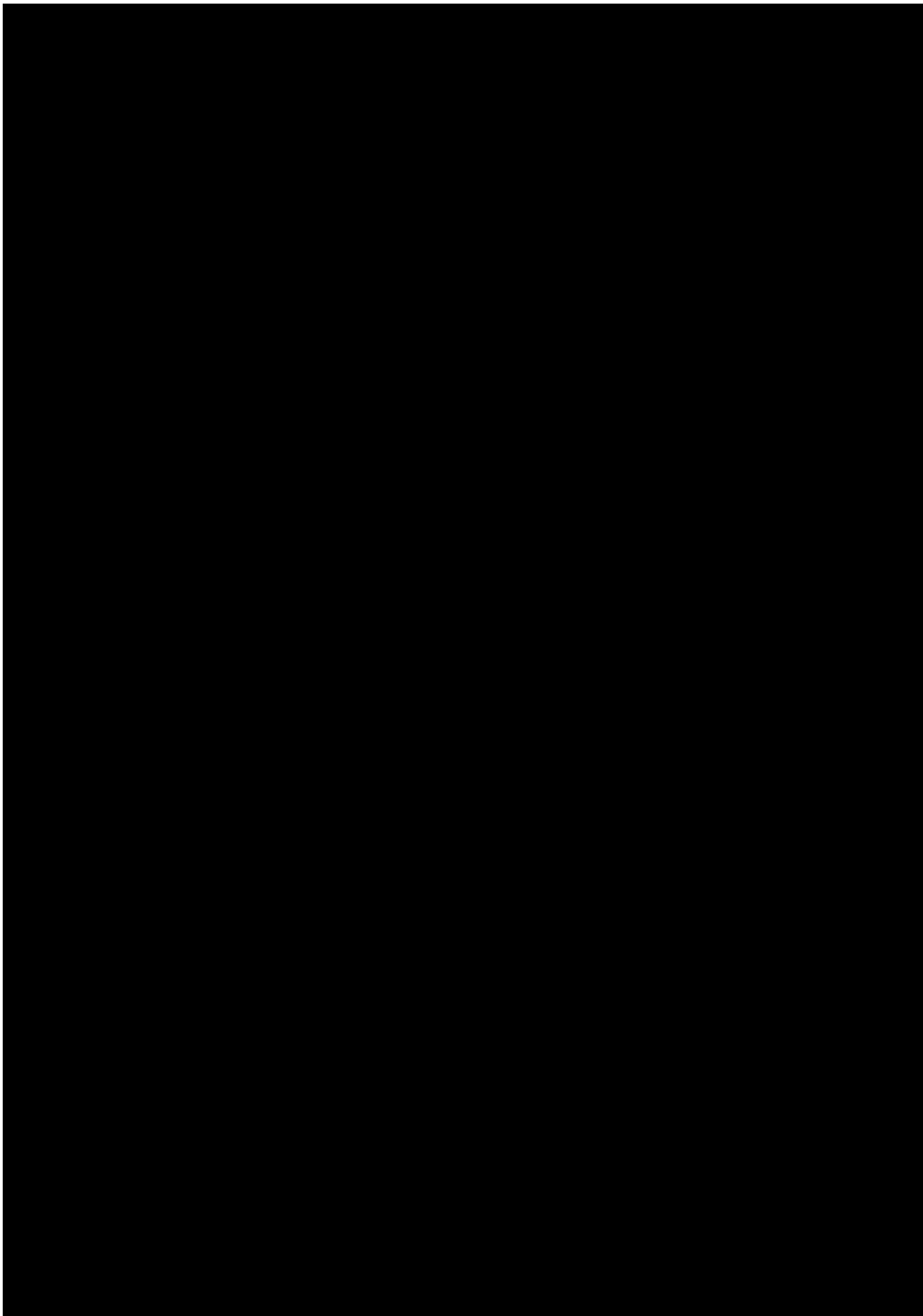
### 4.1 Efficacy Endpoints

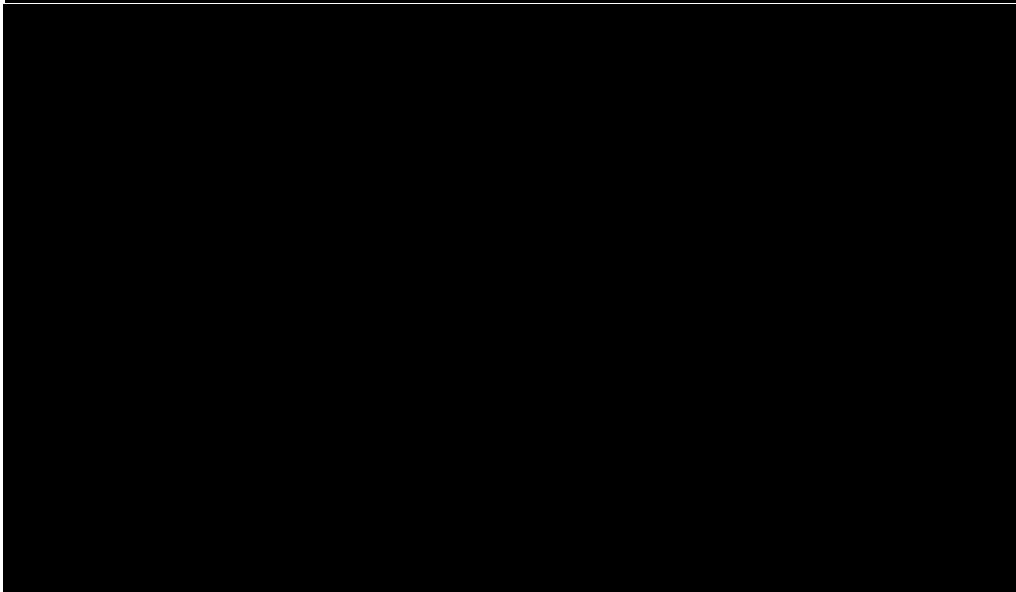
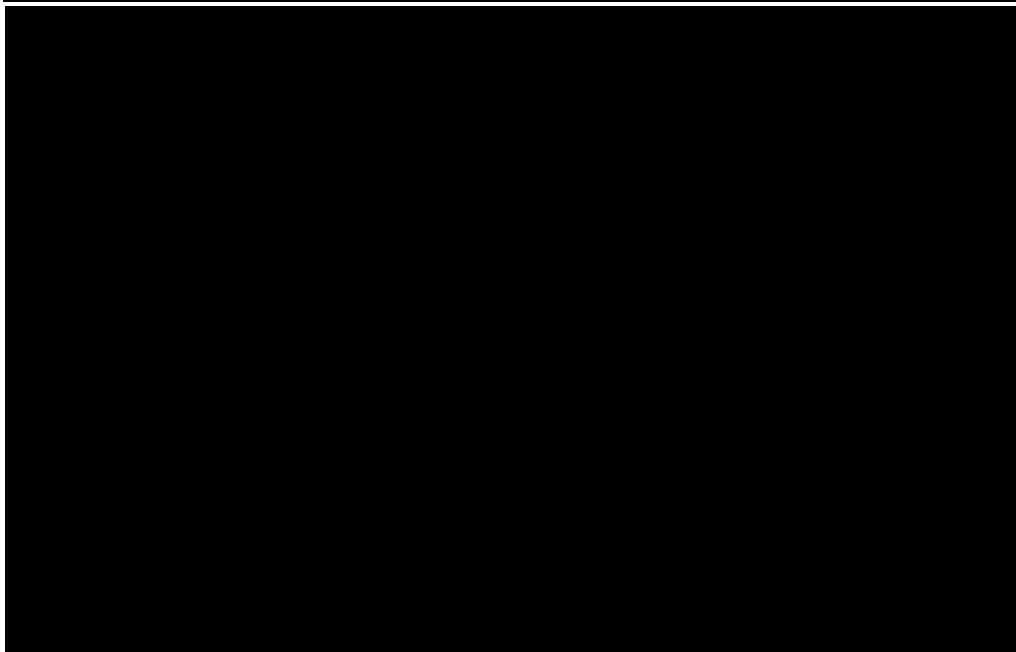
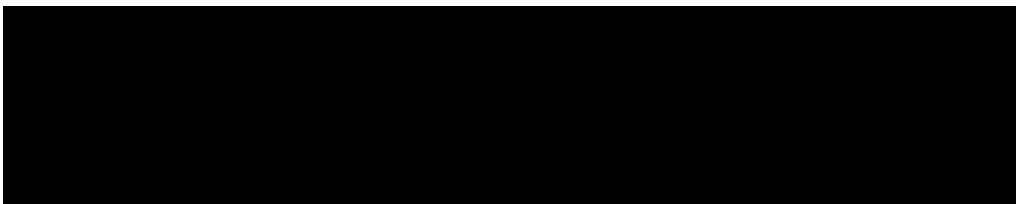
#### Primary Endpoint

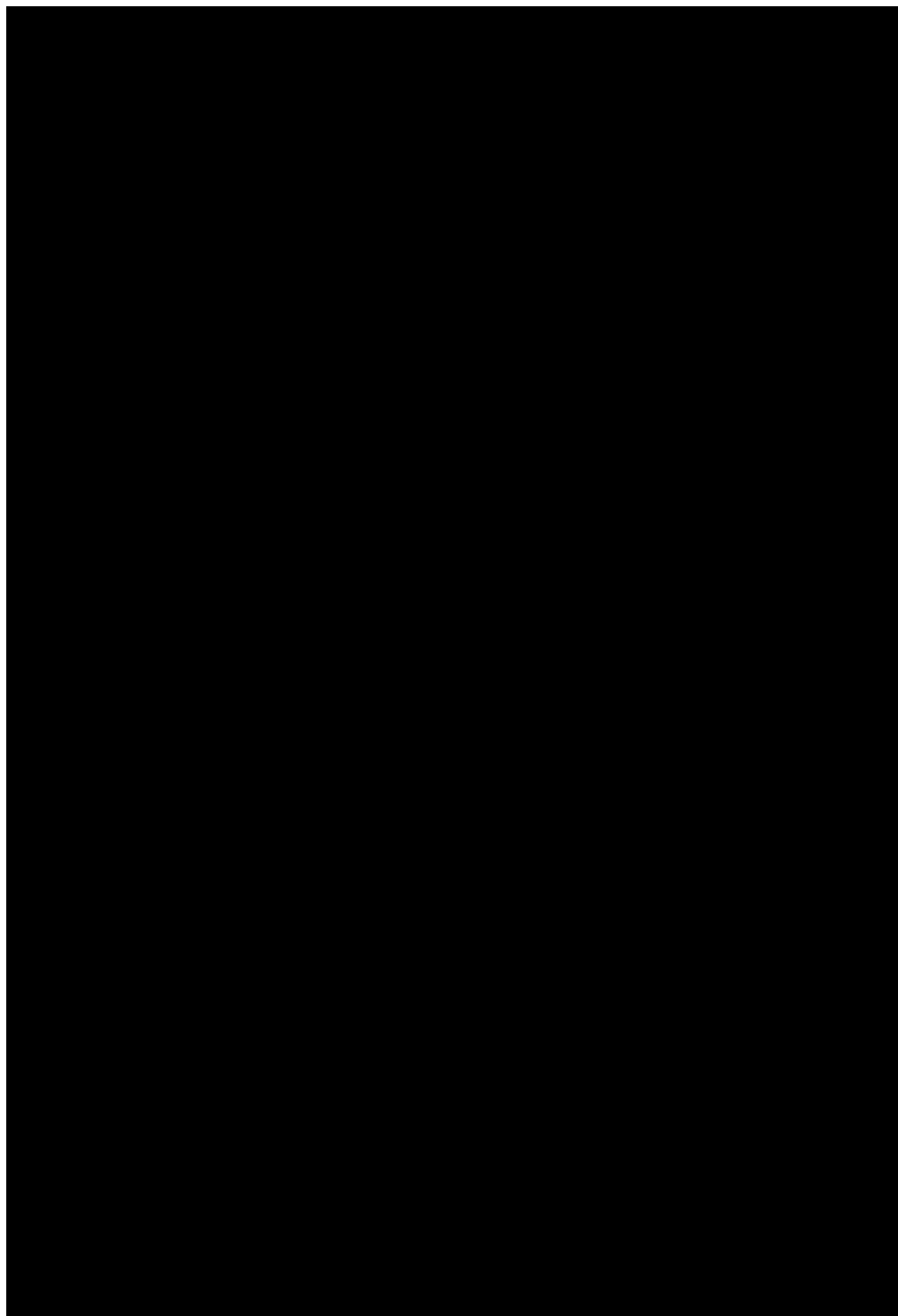
The primary endpoint is the cholesterol uptake (deposits) measured from worn lenses at Day 30 (2-week wear of Oasys and 30-day wear for other), for each of the test and control *combined* regimens. OD lenses from approximately 25 subjects per regimen will be analyzed for the *ex vivo* analysis.

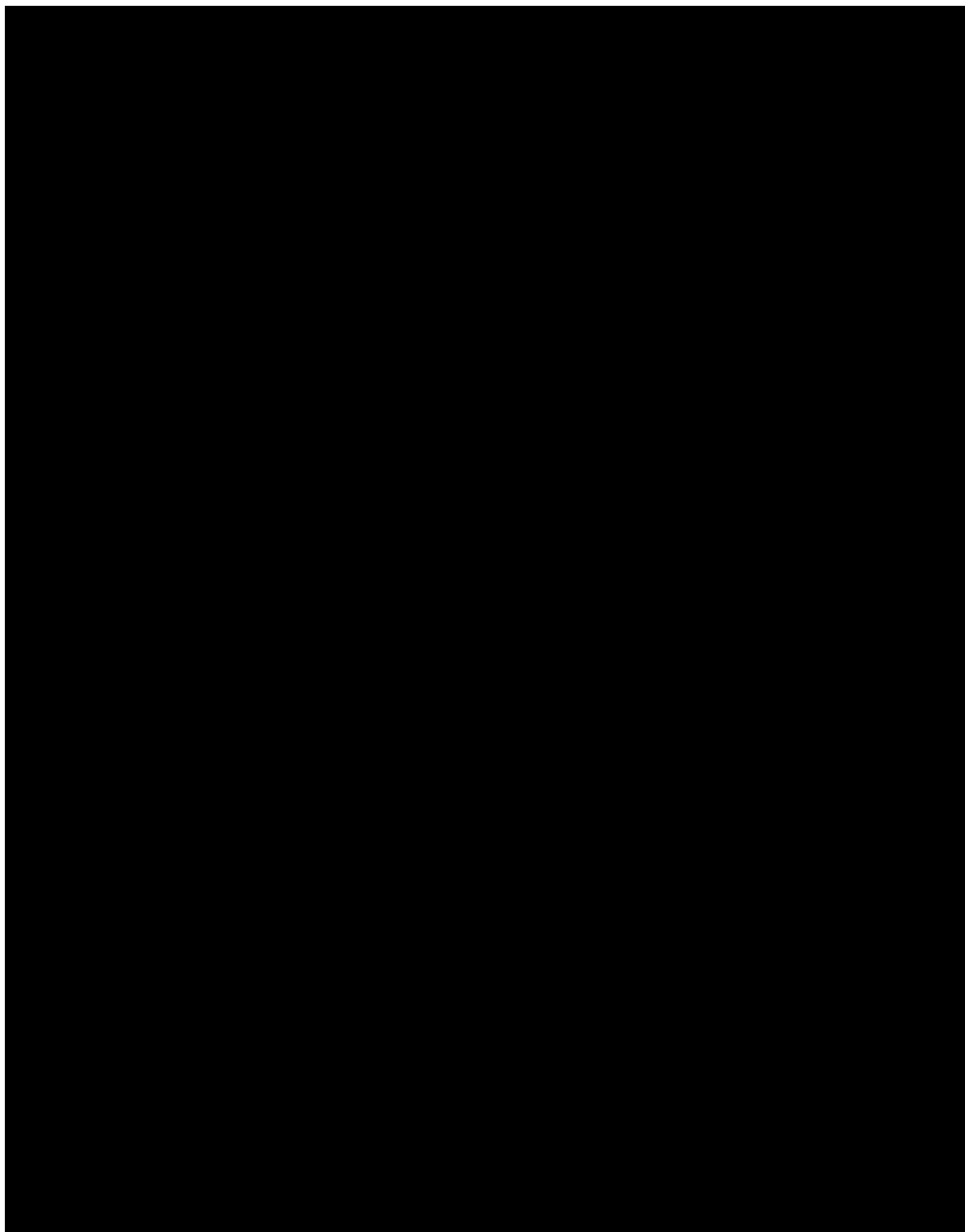


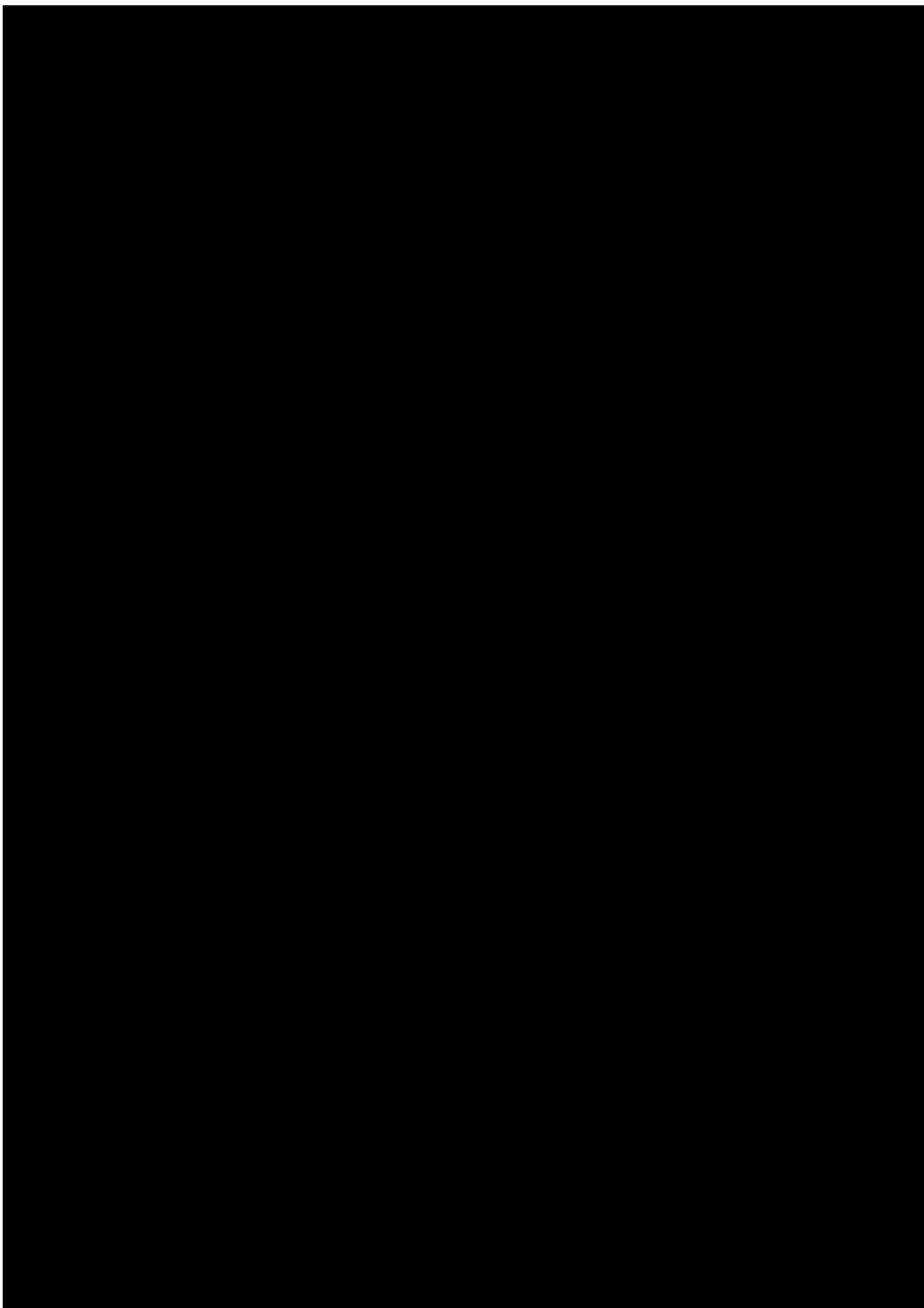


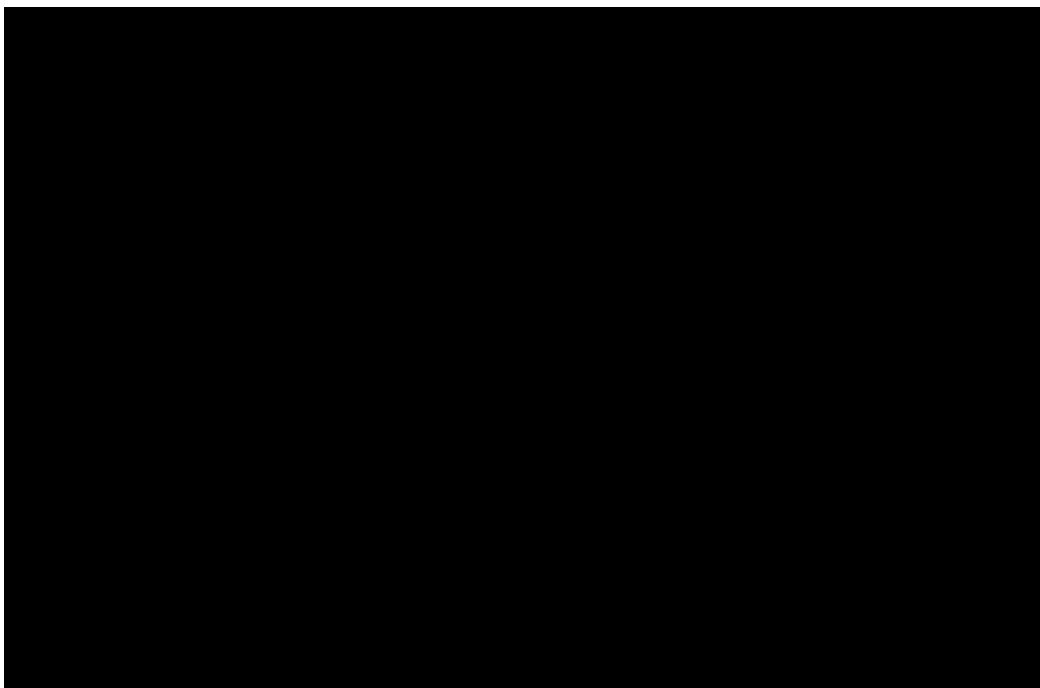
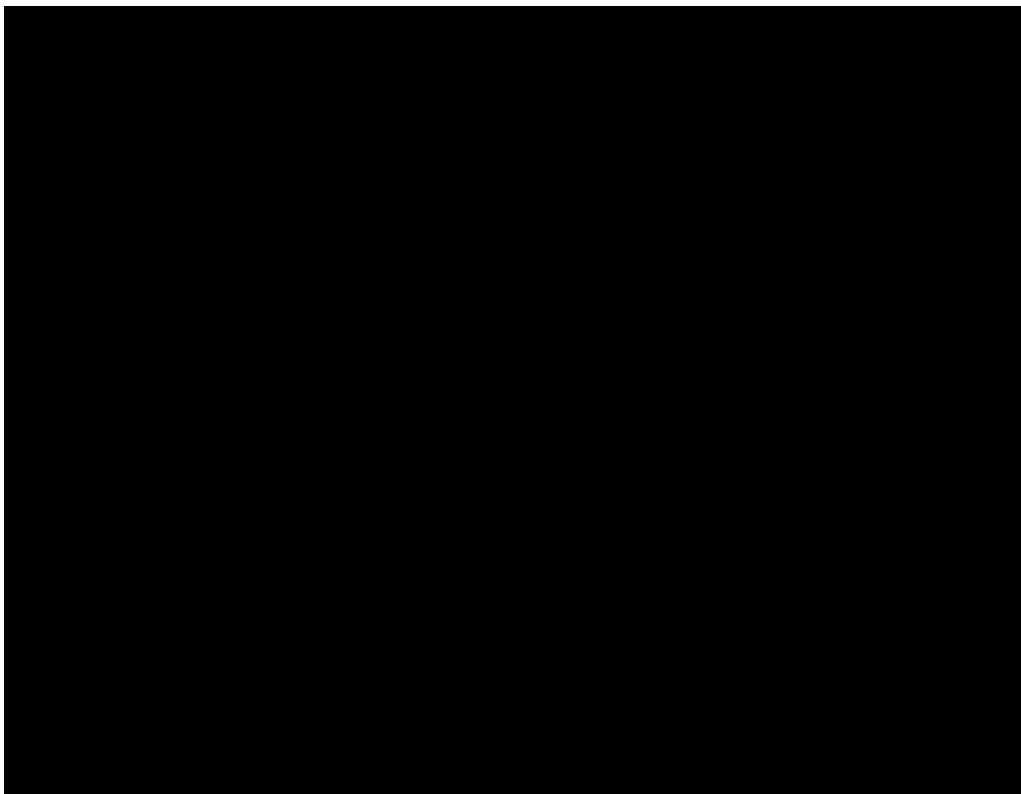




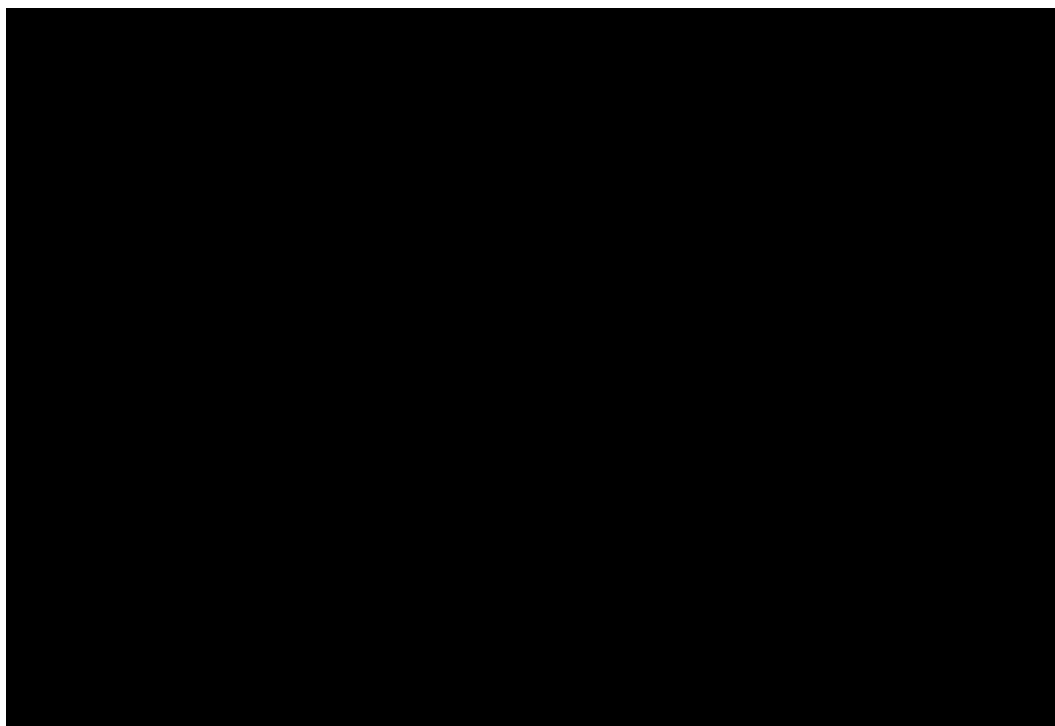
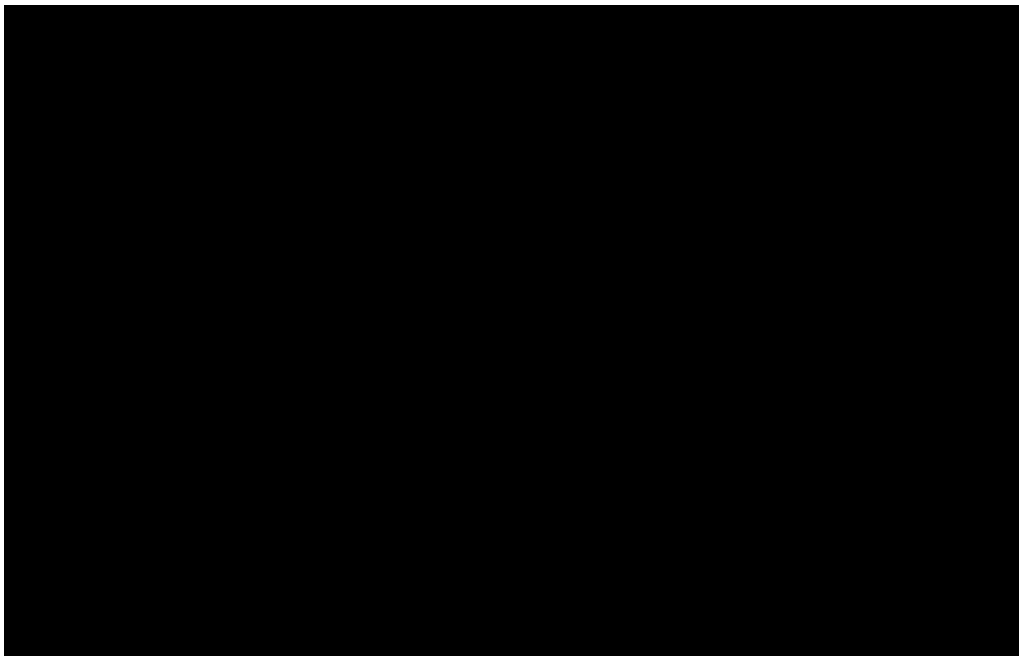














## **5 Safety Analysis Strategy**

### **5.1 Safety Endpoints**

The safety endpoints are

- Adverse events
- Biomicroscopy findings
  - Limbal hyperemia
  - Bulbar hyperemia
  - Bulbar conjunctival compression/indentation
  - Chemosis
  - Palpebral conjunctival observations
  - Corneal infiltrates
  - Anterior segment inflammation
    - Endothelial dusting
    - Anterior chamber flare
    - Keratitic precipitates
    - Hypopyon

- Conjunctival staining
  - Circumlimbal conjunctival staining
  - Bulbar conjunctival staining
- Corneal staining
- Other findings
- Device deficiencies

## **5.2 Safety Hypotheses**

There are no formal safety hypotheses in this study. The focus of the safety analysis will be a comprehensive descriptive assessment of safety endpoints listed in Section 5.1.

## **5.3 Statistical Methods for Safety Analyses**

The analysis set for all safety analyses is the safety analysis set as defined in Section 2.1. Safety variables will be summarized descriptively.

### **5.3.1 Adverse Events**

The applicable definition of an Adverse Event (AE) is in the study protocol. All AEs occurring from when a subject signs informed consent to when a subject exits the study will be accounted for in the reporting.

Analysis and presentation of pre-treatment AEs will be separated from treatment-emergent AEs occurring during the study period. A pre-treatment AE is an event that occurs after signing informed consent but prior to exposure to study lens and/or the study lens care system. The period for treatment-emergent AE analysis starts from exposure to study lens and/or the study lens care system until the subject completes or is discontinued from the study.

Descriptive summaries (counts and percentages) for ocular and non-ocular AEs will be presented by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC) and Preferred Terms (PT). Serious AEs will be summarized separately. Additionally, relationship to regimen (lens and/or solution) will be identified in all AE tables. Unit of presentation for ocular AEs will be eyes and non-ocular AEs will be subjects.

Individual subject's listings will be provided for both pre-treatment and treatment emergent AEs, where any AE leading to study discontinuation will be indicated.

### 5.3.2 Biomicroscopy Findings

Biomicroscopy assessment will be performed at all study visits, including Visit 1 to 4 and unscheduled visits, except no fluorescein or lissamine green staining to be conducted at Day 1 Insertion (Visit 2) and Day 1 8 hrs (Visit 3) . The reporting unit for each biomicroscopy finding will be eyes. A summary of grade category counts and percentages will be presented for each parameter by visit. A shift table showing grade at baseline relative to follow-up visits will be presented by visit for each parameter. Baseline will be defined as Visit 2, except for circumlimbal/bulbar conjunctival staining and corneal staining, for which baseline will be defined as Visit 1.

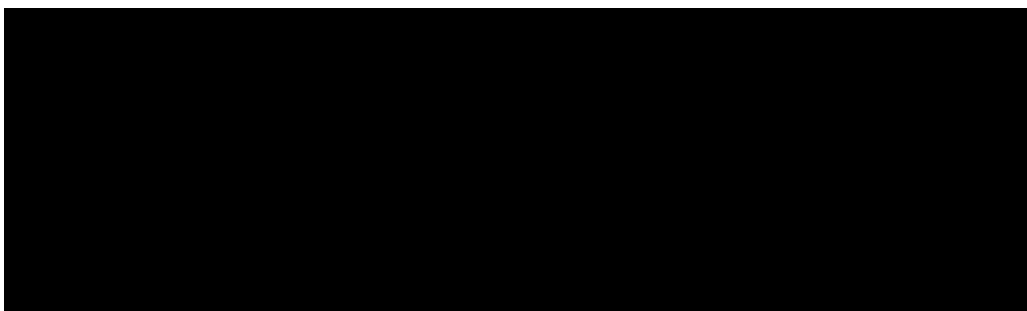
For each biomicroscopy parameter, counts and percentages of eyes which experience an increase of  $\geq 2$  grades from baseline to any subsequent visit (including unscheduled visits) will be presented. Bulbar compression/indentation, chemosis and anterior segment inflammation will not be included in this table, as a binary scale (absent/present) is used for these parameters. A listing will be provided which presents all eyes with an increase of  $\geq 2$  grades in any biomicroscopy parameter at any visit compared to the grade for the same eye at baseline. The listing will include all biomicroscopy data from all visits for these eyes and will be presented by regimen, investigator, subject, age, sex, visit, eye, parameter, baseline value, and value at the visit.

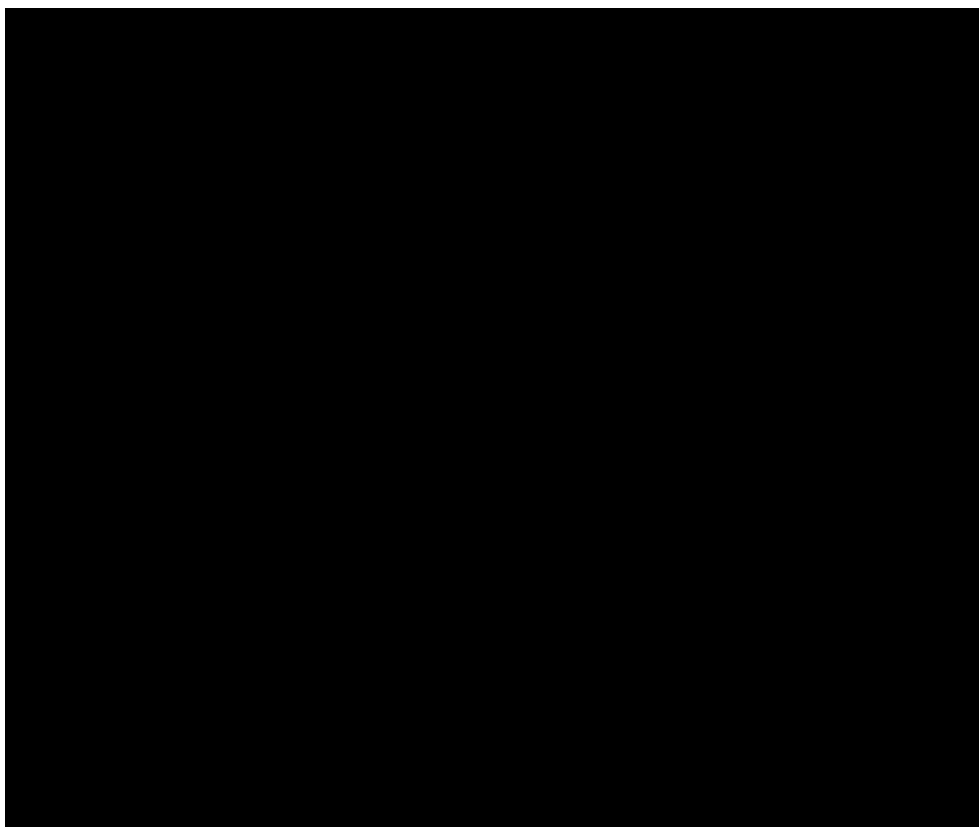
### 5.3.3 Device Deficiencies

The applicable definition of a device deficiency is in the study protocol. A frequency table showing counts for each Device Deficiency category will be presented. In addition, listings for treatment-emergent and pre-treatment device deficiencies will be provided.

## 6 Analysis Strategy for Other Endpoints

Not applicable.





## **8       References**

## **9       Revision History**

This is the original (Version 1.0) Statistical Analysis Plan for this study. This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

## **10      Appendix**

### **Table 10–1        Overview of Study Plan**

	Visit 1	Visit 2	Visit 3	Visit 4 / Exit	USV
Procedure/ Assessment	Screening	Day 1- Insertion 1-7 days from Visit 1. <i>No lenses worn on day of the visit</i>	Day 1: 8hrs (± 30 min)	Day 30 (+3 days): 8hrs (± 30 min) / Exit	Unscheduled Visit
Informed Consent	✓				
Demographics	✓				
Medical History	✓				
Concomitant Medications	✓	✓	✓	✓	✓
Inclusion/Exclusion	✓				
Biomicroscopy (Note: conjunctival staining conducted at designated sites only)					
Randomize Eligible Subjects	✓				
Dispense assigned study lenses in a masked manner		✓ <sup>g</sup>			(✓)
Collect lenses for shipping and analyses				✓	(✓)
Exit Form	(✓)	(✓)	(✓)	✓	(✓)
Assess Adverse Events (Both observed and reported)	✓ <sup>d</sup>	✓	✓	✓	✓
Assess Device Deficiencies		✓	✓	✓	✓

[REDACTED]

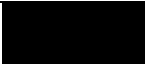



[REDACTED] [REDACTED]. <sup>c</sup> Without lenses at baseline to determine eligibility. [REDACTED]

[REDACTED] <sup>d</sup> AEs are collected from the time of informed consent. [REDACTED]

[REDACTED] <sup>g</sup> Lenses

also dispensed at Day 15±1 in office for subjects assigned to continue wearing Oasys. [REDACTED]

**Alcon - Business Use Only** Statistical Analysis Plan**Effective Date:** 24-Jan-2017**Document:** TDOC-0053343**Version:** 1.0; CURRENT; Most-Recent; Effective**Status:** Effective

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
01/24/2017 01:42:20		
01/24/2017 14:27:35		

Printed By:

Print Date: