STATISTICAL ANALYSIS PLAN

A Multi-Center, Phase 2b, Randomized, Double-Masked, Parallel-Group, Vehicle-Controlled, Clinical Trial to Assess the Safety and Efficacy of Reproxalap Ophthalmic Solution (0.25% and 0.1%) Compared to Vehicle in Subjects with Dry Eye Disease

Sponsor: Aldeyra Therapeutics, Inc.

Protocol Number: ADX-102-DED-009

Author: [redacted]

Date: 30-July-2018

Version: 1.0

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Statistical Analysis Plan Approval

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List of Abbreviations

AE	Adverse Event
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutic Chemical Classification
BCVA	Best Corrected Visual Acuity
CAE	Controlled Adverse Environment
CI	Confidence Interval
CRF	Case Report Form
CS	Clinically Significant
CSR	Clinical Study Report
DED	Dry Eye Disease
eCRF	Electronic Case Report Form
ESWE	Endpoint-Specific Worst Eye
ETDRS	Early Treatment of Diabetic Retinopathy Study
HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IOP	Intraocular Pressure
ITT	Intent-to-Treat
IWRS	Interactive Web Response System
LOCF	Last Observation Carried Forward
logMAR	Logarithm of the Minimum Angle of Resolution
MedDRA	Medical Dictionary for Regulatory Activities
NCS	Not clinically significant
OSDI	Ocular Surface Disease Index
PDF	Portable Document Format
PP	Per Protocol
PT	Preferred Term
RTF	Rich Text Format
SAAS	Software-as-a-Service
SAE	Serious Adverse Event
SANDE	Symptom Assessment in Dry Eye
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDC	Statistics and Data Corporation, Incorporated
SOC	System Organ Class
SOP	Standard Operating Procedure
TEAE	Treatment-Emergent Adverse Event
TE-SAE	Serious Treatment-Emergent Adverse Event
TFBUT	Tear Film Break-Up Time
VA	Visual Acuity
WHO	World Health Organization

1. Introduction

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and reporting for protocol ADX-102-DED-009, version 1.0 dated 12Dec2017.

This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports (CSR).

This SAP describes the data that will be analyzed and the subject characteristics, efficacy, and safety assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used. The statistical analysis methods presented in this document will supersede the statistical analysis methods described in the clinical protocol. In keeping with the preliminary nature of a Phase 2 study, additional analyses other than the planned analyses described herein may be conducted as ad-hoc analyses and will be identified in the CSR. The intent of any such analyses would be to better characterize treatment effects and improve the design of a future Phase 3 study.

2. Study Objectives

The study objectives are as stated below:

- [redacted]

2.1 Study Variables

In this Phase 2b study there are no primary or secondary endpoints. All endpoints are considered hypothesis-generating and not hypothesis-testing. Efficacy variables and safety variables follow.

2.2 Efficacy Variables

The efficacy variables include the following:

- [redacted]

- [redacted]
- [redacted]
- [redacted]
- Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire
- [redacted]
- [redacted]
- [redacted]

2.3 Safety Variables

The safety variables include the following:

- Visual acuity (VA) (ETDRS [Early Treatment of Diabetic Retinopathy Study])
- Slit-lamp biomicroscopy
- Adverse event (AE) query
- Dilated Fundoscopy
- Intraocular Pressure (IOP)

2.4 Statistical Hypotheses

The following hypotheses will be tested for each dose of reproxalap, each dry eye disease (DED) sign and symptom, [redacted]

3. Study Design and Procedures

3.1 General Study Design

This is a Phase 2b, multicenter, randomized, double–masked, vehicle-controlled, parallel-group design with block enrollment. Approximately 300 subjects will be randomly assigned to one of the three

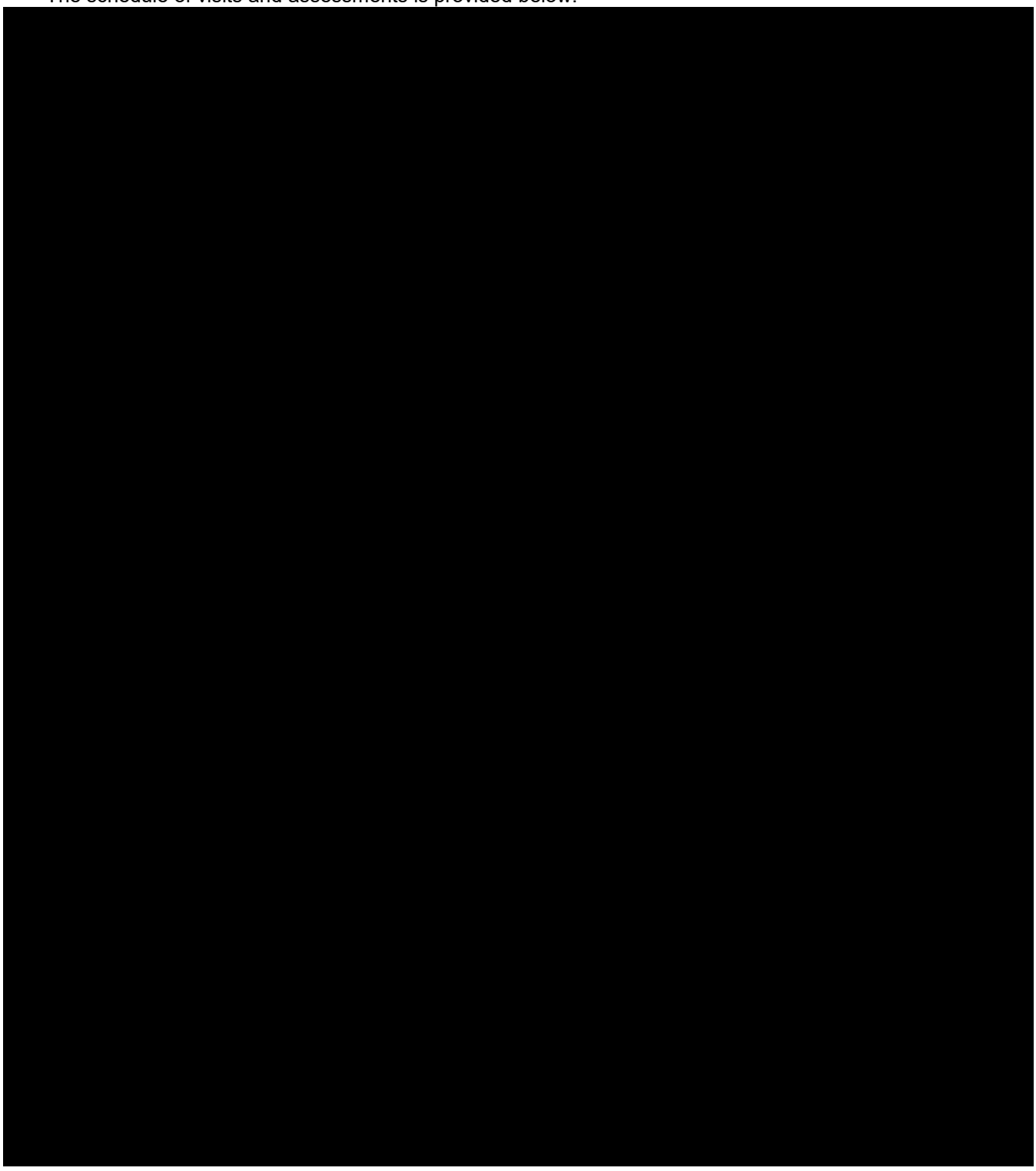
treatment groups (1:1:1) to receive either Reproxalap Ophthalmic Solution (0.1%, 0.25%) or vehicle solution as topical ophthalmic drops administered bilaterally QID.

Study visits will be referred to in all tables and listings as the expected study day corresponding to the visit to enable reviewers to understand the assessment timing without referring to the protocol visit schedule. The following table shows the scheduled study visits, their planned study day (note that there is no Day 0 and that Day 1 corresponds to the day of randomization), and the acceptable visit window for each study visit:

Scheduled Visit	Planned Study Day	Visit Window
Visit 1	Day -14	± 2 Days
Visit 2	Day 1	N/A
Visit 3	Day 15	± 2 Days
Visit 4	Day 29	± 2 Days
Visit 5	Day 57	± 3 Days
Visit 6	Day 85	± 3 Days

3.2 Schedule of Visits and Assessments

The schedule of visits and assessments is provided below.



4. Study Treatments

4.1 Method of Assigning Subjects to Treatment Groups

Before the initiation of study run-in at Visit 1, each subject who provides written and informed consent will be assigned to a screening number. All screening numbers will be assingned in strict numerical sequence at a site and no numbers will be skipped or omitted. Each subject who meets all the inclusion and none of the exclusion criteria at Visit 1 and Visit 2 will be assigned a randomization number at the end of Visit 2. The Interactive Web Response System (IWRS) will be used to assign all randomization numbers.

Randomization and kit numbers will be assigned automatically to each subject as they are entered into the IWRS. The site staff will dispense kit(s) required until the next visit. The randomization schedule will use block randomization, such that there will be an approximate equal number of subjects assigned to each of the three treatment arms. Both the randomization number and the dispensed study drug kit number(s) will be recorded on the subject's source document and eCRF. The Sponsor, investigators, and study staff will be masked during the randomization process and throughout the study.

4.2 Masking and Unmasking

All subjects, investigators, and study personnel involved with the conduct of the study will be masked with regard to treatment assignments. When medically necessary, the investigator may need to determine what treatment group has been assigned to a subject. When possible (i.e., in non-emergent situations), Ora and/or the study Sponsor should be notified before unmasking study drug. Ora and/or the study Sponsor must be informed immediately about any unmasking event. Unmasked subjects will be discontinued from the study.

5. Sample Size and Power Considerations

The study sample size of 100 per group was selected [redacted]

[redacted]

6. Data Preparation

Electronic Case Report Forms (eCRF) will be developed by Statistics and Data Corporation, Incorporated (SDC) following SDTM standards unless otherwise specified by Aldeyra Therapeutics, Inc. Data from source documents will be entered into the eCRF by site personnel. All users will complete role-based system and study-specific eCRF training prior to receiving access to the study database. User access will be granted based on a user's role in the study and will be controlled through individual login credentials including a unique User ID and password.

The clinical study database will be developed and tested in [redacted] delivered as a single-instance multi-tenant Software-as-a-Service (SaaS) EDC system and is developed, maintained, and hosted by [redacted]. Therefore, over the duration of the study, [redacted] may apply system updates to the EDC system as part of their continuous improvement efforts.

After data are entered into the clinical study database, electronic edit checks and data review will be performed. All data validation specifications and procedures are detailed in the Data Validation Manual as a separate document. When the database has been declared to be complete and accurate, the database will be locked. Any changes to the database after data have been locked can only be made with the approval of Aldeyra Therapeutics, Inc. and Ora, Inc. in consultation with SDC.

All analyses outlined in this document will be carried out after the following have occurred:

- [redacted]
- [redacted]
- [redacted]
- [redacted].

7. Analysis Populations

Analysis populations include [redacted].

7.1 Intent-to-Treat

The ITT population includes [redacted]

7.2 Per Protocol

The PP population includes [redacted].

7.3 Safety

The safety population includes [redacted].

8. General Statistical Considerations

8.1 Unit of Analysis

Safety endpoints will be analyzed [redacted]

8.2 Missing or Inconclusive Data Handling

Analyses will be performed [redacted]

8.3 Definition of Baseline

Baseline measures are defined [redacted]

8.4 Data Analysis Conventions

All data analysis will be performed [redacted]

[redacted]

8.5 Adjustments for Multiplicity

As this is a Phase 2b study, there will be no multiplicity adjustments for the two active treatments or for the multiple endpoints.

9. Disposition of Subjects

Subject disposition will be presented [redacted]

[redacted]

10. Demographic and Pretreatment Variables

10.1 Demographic Variables

The demographic variables collected in this study [redacted]

[redacted]

A subject listing that includes all demographic variables for the ITT population will be provided.

10.2 Pretreatment Variables

Baseline disease characteristics will be summarized [redacted]

11. Medical History and Concomitant Medications

11.1 Medical History

Medical history will be coded [redacted]

Non-ocular medical history will be summarized [redacted]

[redacted]

Listings of medical history will be generated separately for ocular and non-ocular data.

11.2 Concomitant Medications

Concomitant medications will be coded [redacted]

[redacted] Listings of concomitant medications will be generated separately for ocular and non-ocular data.

12. Dosing Compliance and Treatment Exposure

12.1 Dosing Compliance

Subjects will be instructed on proper use of the subject daily diary and proper instillation and storage of study drug [redacted]

[redacted]

A subject listing of dosing compliance will also be produced.

12.2 Treatment Exposure

Extent of treatment exposure [redacted] A subject listing of treatment exposure will also be produced.

13. Efficacy Analyses

Quantitative efficacy measures collected [redacted]

[redacted]

All efficacy measures will also be presented in subject listings.

The following efficacy endpoints will be tested:

[redacted]

- Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire

[redacted]

13.1 Lissamine Green Staining

Corneal and conjunctival lissamine green staining will be performed [redacted]

[redacted]

13.2 Fluorescein Staining

Corneal and conjunctival fluorescein staining will be performed [redacted]

[redacted]

13.3 Tear Film Break-Up Time (TFBUT)

TFBUT will be measured [redacted]

13.4 Unanesthetized Schirmer's Test

Unanesthetized Schirmer's Test will be assessed [redacted]

[redacted]

13.5 Ora Calibra® Ocular Discomfort Scale

Ocular discomfort scores will be subjectively graded [redacted]

13.5.1 ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]

[redacted] assessments of ocular discomfort will be made [redacted]

13.5.2 ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]

Ocular discomfort scores will be assessed [redacted]

[redacted]

13.6 Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire

Ocular discomfort and dry eye symptoms will be assessed [redacted]

13.6.1 Assessments During Visits

Pre-CAE®, post-CAE®, change from pre-CAE® to post-CAE® and changes from baseline in ocular discomfort and dry eye symptoms will be analyzed [redacted]

13.6.2 Diary Assessments

Each day [redacted] subjects will grade the severity of their dry eye symptoms in their diary [redacted]

[redacted]

[redacted]

13.7 Ocular Surface Disease Index©

The OSDI© will be assessed [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

13.8 SANDE Questionnaire

The SANDE Questionnaire will be used [redacted]

[redacted]

[redacted]

13.9 Tear Osmolarity

Tear osmolarity will be measured [redacted]

14. Safety Analyses

All safety analyses will be conducted using the safety population.

14.1 Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of an IP in humans, whether or not considered IP-related. An AE can be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of an IP, without any judgment about causality. Exacerbation of conditions related to the signs and symptoms of Dry Eye will not be reported as an AE. The AE reporting period ends upon study exit. Study drug includes the investigational drug under evaluation. All AEs will be coded using MedDRA Version 20.0.

Treatment-emergent adverse events (TEAEs) are defined as any adverse event that occurs or worsens after the first dose of study treatment. AEs recorded in the eCRF which began prior to treatment will not be included in the summary tables but will be included in the AE data listings.

An overall summary will be presented that includes the number of AEs, TEAEs, serious AEs (SAE), and serious TEAEs (TE-SAE). The summary will also include the number and percentage of subjects withdrawn due to an AE, the number and percentage of subjects with an AE resulting in death, and the number and percentage of subjects who experienced at least one AE, TEAE, SAE and TE-SAE, by treatment group and for all subjects. This summary will include breakdowns of AEs further categorized as ocular or non-ocular.

Additional summaries of TEAEs will be provided showing the number and percentage of subjects who experienced at least one TEAE. These summaries will be presented by SOC and PT. Non-ocular TEAEs will be summarized using discrete summary statistics and presented by treatment group at the subject and event level by SOC and PT. Ocular TEAEs will be similarly summarized at the subject and event level. If a subject reports the same PT multiple times within the same SOC, that PT will only be reported once within that SOC. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once. In the summary, SOC will be listed in order of descending frequency for all subjects; PTs will be listed in order of descending frequency for all subjects within each SOC. The occurrence of non-ocular and ocular TEAEs will also be tabulated by SOC, PT, and maximal severity, and by SOC, PT, and study day of onset.

Separate summaries will be provided for the following categories of AEs:

- Ocular TEAEs
- Non-ocular TEAEs
- Treatment-related TEAEs
- SAEs

Severity of an AE is defined as a qualitative assessment of the degree of intensity of an adverse event as determined by the investigator or reported to him/her by the patient/subject. The assessment of severity is made irrespective of relationship to study drug or seriousness of the event and should be evaluated according to the following scale:

- *Mild*: Event is noticeable to the subject, but is easily tolerated and does not interfere with the subject's daily activities.
- *Moderate*: Event is bothersome, possibly requiring additional therapy, and may interfere with the subject's daily activities.
- *Severe*: Event is intolerable, necessitates additional therapy or alteration of therapy, and interferes with the subject's daily activities.

Summaries of TEAEs by maximal severity will be presented for ocular AEs and non-ocular AEs separately. The number of subjects with any TEAEs (along with percentages) will be tabulated by SOC

and PT within each SOC by treatment group. To count the number of subjects with any TEAEs, if a subject has multiple TEAEs coded to the same PT within the same SOC, the subject will be counted once under the maximal severity.

The relationship of each adverse event to the investigational product should be determined by the investigator (in a blinded manner) using these descriptions:

- *Definitely Related*
- *Probably Related*
- *Possibly Related*
- *Unlikely to be Related*
- *Not Related*

Definitely related, probably related, and possibly related TEAEs will be considered as treatment-related TEAEs. Any TEAEs with missing relationships will also be considered as treatment-related.

All AEs will be presented in a subject listing that classifies each AE as ocular or non-ocular and indicates whether it is a TEAE. Separate listings will be produced for AEs leading to study discontinuation, AEs leading to death and SAEs.

14.2 Visual Acuity (ETDRS)

The VA procedure will be performed [redacted] A subject listing of VA will also be produced.

14.3 Slit-Lamp Biomicroscopy Examination

A slit-lamp biomicroscopy examination o[redacted] will be performed [redacted]

[redacted] A subject listing of the slit-lamp biomicroscopy parameters will also be produced.

14.4 Dilated Fundoscopy Examination

A dilated fundoscopy exam will be performed [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted] A subject listing of the dilated fundoscopy parameters will also be produced.

14.5 Intraocular Pressure (IOP)

IOP will be measured [redacted] A subject listing of IOP will also be produced.

15. Interim Analyses

There will be no interim analyses in this study.

16. Optimization Analyses

Upon completion of this study [redacted]

17. Changes from Protocol-Stated Analyses

[redacted]

The statistical significance level for all tests [redacted].

18. Additional Analyses

In keeping with the preliminary nature of a Phase 2 study, additional analyses other than the planned analyses described herein may be conducted as ad-hoc analyses. The intent of any such analyses would be to better characterize treatment effects and improve the design of a future Phase 3 study.

19. Revision History

Documentation of revision to the SAP will commence after approval of the Final version 1.0.

20. Tables

Table Number	Title	Population
TABLE 14.1.1	SUBJECT DISPOSITION	ALL ENROLLED SUBJECTS
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Table Number	Title	Population
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TABLE 14.2.1A	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.1B	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.1C	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH LOCF
TABLE 14.2.1D	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH LOCF
TABLE 14.2.1E	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.1F	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.1G	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.1H	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.2A	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.2B	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.2C	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.2D	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.2E	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.2F	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.2G	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.2H	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3A	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3B	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3C	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.3D	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3E	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3F	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3G	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.3H	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4A	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4B	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4C	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4D	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE) : [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
	[redacted]	
TABLE 14.2.4E	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4F	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4G	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.4H	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.5A	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.5B	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.5C	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.5D	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.5E	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF

Table Number	Title	Population
TABLE 14.2.5F	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.5G	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.5H	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH LOCF
TABLE 14.2.6A	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6B	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6C	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6D	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6E	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6F	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6G	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.6H	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.7A	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7B	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7C	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7D	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7E	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7F	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7G	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.7H	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8A	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.8B	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8C	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8D	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8E	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8F	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8G	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.8H	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE): [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.9	STAINING RESPONDER ANALYSIS	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.10	TEAR FILM BREAK-UP TIME	ITT WITH LOCF
TABLE 14.2.11	TEAR FILM BREAK-UP TIME	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.12	TEAR FILM BREAK-UP TIME [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.13	TEAR FILM BREAK-UP TIME [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.14	UNANESTHETIZED SCHIRMER'S TEST	ITT WITH LOCF
TABLE 14.2.15	UNANESTHETIZED SCHIRMER'S TEST	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.16	UNANESTHETIZED SCHIRMER'S TEST [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.17	UNANESTHETIZED SCHIRMER'S TEST [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.18	ORA CALIBRA® OCULAR DISCOMFORT SCALE	ITT WITH LOCF
TABLE 14.2.19	ORA CALIBRA® OCULAR DISCOMFORT SCALE	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.20	ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.21	ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.22	ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]	ITT WITH LOCF

Table Number	Title	Population
TABLE 14.2.23	ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.24	ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.25	ORA CALIBRA® OCULAR DISCOMFORT SCALE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.26A	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH LOCF
TABLE 14.2.26B	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH LOCF
TABLE 14.2.26C	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH LOCF
TABLE 14.2.26D	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH LOCF
TABLE 14.2.26E	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH LOCF
TABLE 14.2.27A	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.27B	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.27C	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.27D	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.27E	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.28A	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
TABLE 14.2.28B	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
TABLE 14.2.28C	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
TABLE 14.2.28D	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
TABLE 14.2.28E	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
TABLE 14.2.28F	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
TABLE 14.2.29A	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.29B	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.29C	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.29D	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.29E	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.29F	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.30A	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30B	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30C	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30D	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30E	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30F	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30G	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30H	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30I	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30J	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF

Table Number	Title	Population
TABLE 14.2.30K	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30L	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.30M	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH LOCF
TABLE 14.2.31A	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31B	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31C	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31D	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31E	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31F	OCULAR SURFACE DISEASE INDEX (OSDI)© [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31G	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31H	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.31I	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31J	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31K	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31L	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.31M	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	[redacted] WITH OBSERVED DATA ONLY
TABLE 14.2.32	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.33	OCULAR SURFACE DISEASE INDEX (OSDI)©: [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.34	SANDE QUESTIONNAIRE	ITT WITH LOCF
TABLE 14.2.35	SANDE QUESTIONNAIRE	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.36	SANDE QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY

Table Number	Title	Population
TABLE 14.2.37	SANDE QUESTIONNAIRE [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.38	TEAR OSMOLARITY	ITT WITH LOCF
TABLE 14.2.39	TEAR OSMOLARITY	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.40	TEAR OSMOLARITY [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.2.41	TEAR OSMOLARITY [redacted]	ITT WITH OBSERVED DATA ONLY
TABLE 14.3.1.1	ADVERSE EVENT SUMMARY	SAFETY
TABLE 14.3.1.2	ALL OCULAR ADVERSE EVENTS	SAFETY
TABLE 14.3.1.3	ALL NON-OCULAR ADVERSE EVENTS	SAFETY
TABLE 14.3.1.4	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS	SAFETY
TABLE 14.3.1.5	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS	SAFETY
TABLE 14.3.1.6	ALL TREATMENT-RELATED TREATMENT-EMERGENT ADVERSE EVENTS	SAFETY
TABLE 14.3.1.7	ALL SERIOUS ADVERSE EVENTS	SAFETY
TABLE 14.3.1.8	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY	SAFETY
TABLE 14.3.1.9	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY MAXIMAL SEVERITY	SAFETY
TABLE 14.3.1.10	ALL OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET	SAFETY

Table Number	Title	Population
TABLE 14.3.1.11	ALL NON-OCULAR TREATMENT-EMERGENT ADVERSE EVENTS BY STUDY DAY OF ONSET	SAFETY
TABLE 14.3.2	BEST CORRECTED VISUAL ACUITY [redacted]	SAFETY
TABLE 14.3.3.1	SLIT LAMP BIOMICROSCOPY	SAFETY
TABLE 14.3.3.2	SHIFT IN SLIT LAMP BIOMICROSCOPY	SAFETY
TABLE 14.3.4.1	DILATED FUNDOSCOPY	SAFETY
TABLE 14.3.4.2	SHIFT IN DILATED FUNDOSCOPY	SAFETY
TABLE 14.3.5	INTRAOCULAR PRESSURE	SAFETY
TABLE 14.3.6	COMPLIANCE WITH STUDY DRUG	SAFETY
TABLE 14.3.7	EXPOSURE TO STUDY DRUG	SAFETY

21. Listings

Listing Number	Title
LISTING 16.1.7	RANDOMIZATION SCHEDULE
LISTING 16.2.1	SUBJECT DISPOSITION
LISTING 16.2.2	PROTOCOL DEVIATIONS
LISTING 16.2.3	STUDY POPULATION INCLUSION
LISTING 16.2.4.1	DEMOGRAPHICS
LISTING 16.2.4.2	OCULAR MEDICAL HISTORY
LISTING 16.2.4.3	NON-OCULAR MEDICAL HISTORY
LISTING 16.2.4.4	PRIOR AND CONCOMITANT OCULAR MEDICATIONS
LISTING 16.2.4.5	PRIOR AND CONCOMITANT NON-OCULAR MEDICATIONS
LISTING 16.2.5.1	IN-OFFICE INSTILLATION
LISTING 16.2.5.2	STUDY DRUG EXPOSURE AND DOSING COMPLIANCE
LISTING 16.2.5.3	STUDY DRUG ACCOUNTABILITY

Listing Number	Title
LISTING 16.2.5.4	URINE PREGNANCY TEST
LISTING 16.2.6.1	LISSAMINE GREEN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE)
LISTING 16.2.6.2	FLUORESCEIN CORNEAL AND CONJUNCTIVAL STAINING (ORA CALIBRA® SCALE)
LISTING 16.2.6.3	TEAR FILM BREAK-UP TIME (TFBUT)
LISTING 16.2.6.4	UNANESTHETIZED SCHIRMER'S TEST
LISTING 16.2.6.5	ORA CALIBRA® OCULAR DISCOMFORT SCALE
LISTING 16.2.6.6	ORA CALIBRA® OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE
LISTING 16.2.6.7	STUDY MEDICATION INSTILLATION AND DRY EYE SYMPTOMS REPORTED IN THE SUBJECT DIARY
LISTING 16.2.6.8	OCULAR SURFACE DISEASE INDEX (OSDI)©
LISTING 16.2.6.9	SANDE QUESTIONNAIRE
LISTING 16.2.6.10	TEAR OSMOLARITY
LISTING 16.2.7.1	ALL ADVERSE EVENTS
LISTING 16.2.7.2	SERIOUS ADVERSE EVENTS
LISTING 16.2.7.3	ADVERSE EVENTS LEADING TO TREATMENT DISCONTINUATION
LISTING 16.2.7.4	ADVERSE EVENTS LEADING TO DEATH
LISTING 16.2.8.1	BEST CORRECTED VISUAL ACUITY - LOGMAR
LISTING 16.2.8.2	SLIT LAMP BIOMICROSCOPY
LISTING 16.2.8.3	DILATED FUNDOSCOPY
LISTING 16.2.8.4	INTRAOCULAR PRESSURE (IOP)

22. Figures

Figure Number	Title	Population
FIGURE 14.2.1	INFERIOR AND TOTAL SUM LISSAMINE GREEN STAINING (ORA CALIBRA® SCALE) [redacted]	ITT WITH LOCF
FIGURE 14.2.2	INFERIOR AND TOTAL SUM FLUORESCEIN STAINING (ORA CALIBRA® SCALE) [redacted]	ITT WITH LOCF
FIGURE 14.2.3	OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF
FIGURE 14.2.4	OCULAR DISCOMFORT & 4-SYMPTOM QUESTIONNAIRE [redacted]	ITT WITH LOCF