STATISTICAL ANALYSIS PLAN

A Single-Center, Phase 2a, Randomized, Double-Masked, Clinical Study to Assess the Safety, Tolerability, and Pharmacodynamic Activity of ADX-102 Ophthalmic Solution in Subjects with Dry Eye Syndrome

Sponsor: Aldeyra Therapeutics, Inc.

Protocol Number: ADX-102-DES-007

[redacted]

Date: 02-JUN-2017

Version: 1.0

SDC
STATISTICS & DATA CORPORATION

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Statistical Analysis Plan Approval

Table of Contents

List of Abbreviations

AE	Adverse Event
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutic Chemical Classification
BCVA	Best Corrected Visual Acuity
CI	Confidence Interval
CRF	Case Report Form
CS	Clinically Significant
CSR	Clinical Study Report
DMP	Data Management Plan
eCRF	Electronic Case Report Form
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
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
VA	Visual Acuity
WHO DDE	World Health Organization Drug Dictionary Enhanced

1. Introduction

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and reporting for protocol ADX-102-DES-007, version 1.0 dated 27MAR2017.

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. If additional analyses are required to supplement the planned analyses described in this SAP they may be completed and will be identified in the CSR.

2. Study Objectives

The objective of this study is to evaluate the safety, tolerability and pharmacodynamic activity of ADX-102 Ophthalmic Solutions (0.5% and 0.1%) and ADX-102 Ophthalmic Lipid Solution (0.5%) in subjects with dry eye syndrome.

2.1 Study Variables

In this Phase 2a study there are no primary or secondary endpoints. Exploratory pharmacodynamic variables and safety variables follow.

2.2 Exploratory Pharmacodynamic Variables

The exploratory pharmacodynamic variables include the following:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- Ora Calibra® Ocular Discomfort Scale;
- [redacted]
- [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;
- Undilated Fundoscopy;
- Intraocular Pressure (IOP).

2.4 Statistical Hypotheses

This is a Phase 2a study to assess the safety, tolerability and pharmacodynamic activity of ADX-102 Ophthalmic Solution in subjects with dry eye syndrome. There are no primary endpoints and no formal statistical hypotheses.

3. Study Design and Procedures

3.1 General Study Design

This is a Phase 2a, single-center, randomized, double-masked study designed to evaluate the safety, tolerability and pharmacodynamic activity of ADX-102 Ophthalmic Solution (0.5%), ADX-102 Ophthalmic Solution (0.1%), and ADX-102 Ophthalmic Lipid Solution (0.5%) in subjects with dry eye syndrome. Approximately 45 male and female subjects at least 18 years of age with a subject-reported history of dry eye in both eyes and meeting all other study eligibility criteria will be randomized to receive treatment ADX-102 Ophthalmic Solution (0.5%), ADX-102 Ophthalmic Solution (0.1%), or ADX-102 Ophthalmic Lipid Solution (0.5%) in a 1:1:1 ratio (approximately 15 subjects in each treatment group).

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 1	N/A
Visit 2	Day 8	± 1 Day
Visit 3	Day 29	± 2 Days

3.2 Schedule of Visits and Assessments

The schedule of visits and assessments is provided below.

Procedure	Visit 1 Day 1	Visit 2 Day 8 ± 1	Visit 3 Day 29 ±2
Informed Consent / HIPAA	X		
Medical / Medication History and Demographic	X		
Study Drug Collection		X	X
Medical / Medication History Update		X	X
Adverse Event Query		X	X
Urine Pregnancy Test	X[1]		X[1]
Ora Calibra® Ocular Discomfort Scale	X	X	X
[redacted]			
Visual Acuity (ETDRS)	X	X	X
Review of Qualification Criteria	X		
[redacted]			
Intraocular Pressure	X		X
Undilated Fundus Exam	X		X
Review Qualification Criteria	X		
Randomization	X		
Subject Self-instillation of Study Drug	X	X	
[redacted]			
Study Drug Dispensation	X	X	
Adverse Event Query	X	X	X
Exit Subject from Study			X
X[1] = For females of childbearing potential			

4. Study Treatments

4.1 Method of Assigning Subjects to Treatment Groups

Prior to initiation of study drug (at Visit 1), each subject who qualifies for entry will be assigned a screening number. All screening numbers will be assigned in strict numerical sequence at a site and no numbers will be skipped or omitted. If all inclusion and exclusion criteria are met at Visit 1, each qualifying subject will then be assigned a randomization number at the end of Visit 1.

A randomization schedule will be provided to the investigational site. 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 at the site. The site staff will dispense to the subject the study kit based on the subject's randomization number. The randomization number will be recorded on the subject's source document and electronic case report form (eCRF). A new kit will be dispensed at Visit 2 based on the subject's randomization. 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 arm 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. The unmasked subject will be discontinued from the study.

5. Sample Size and Power Considerations

[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. 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.

[redacted]

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 and Ora in consultation with SDC.

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

- All data management requirements are met according to SDC standard operating procedures (SOP), including data entry, performance of edit and validation checks, documentation and resolution of data queries, and database lock with written authorization provided by appropriate SDC, Aldeyra and Ora personnel;
- Protocol deviations have been identified and status defined (major/minor deviations);
- Analysis populations have been determined; and
- Randomized treatment codes have been unmasked.

7. Analysis Populations

Analysis populations include the intent-to-treat (ITT) population, the per-protocol (PP) population, and the Safety population. The statistical analysis of safety data will be performed on the Safety population. The analysis of baseline and exploratory efficacy data will be performed on the ITT population, and may be performed on the PP population as sensitivity analyses if it differs substantially from the ITT population.

7.1 Intent-to-Treat

The ITT population includes all randomized subjects. Subjects in the ITT population will be analyzed as randomized.

7.2 Per Protocol

The PP population includes subjects in the ITT population who do not have significant protocol deviations and who complete the study. Protocol deviations will be assessed prior to database lock and unmasking. Subjects in the PP population will be analyzed as treated.

7.3 Safety

The Safety population includes all randomized subjects who have received at least one dose of the investigational product. Subjects in the Safety population will be analyzed as treated.

8. General Statistical Considerations

8.1 Unit of Analysis

Safety endpoints will be analyzed for both eyes. For efficacy endpoints, the unit of analysis will be the study eye, or the "worst eye," as defined by the following:

Worst Eye: Eyes are eligible for analysis if they meet all of the inclusion criteria. In the case that both eyes are eligible for analysis, the worst eye will be the eye with worst (higher) total corneal fluorescein staining, based on the sum of the inferior, superior, and central regions, at Visit 1. If the total corneal staining is the same in both eyes then the eye with the worst (higher) Ora Calibra® Ocular Discomfort Scale score at Visit 1 will be the worst eye. If the total corneal staining and ocular discomfort scores are the same for both eyes, then the right eye will be selected as the worst eye.

8.2 Missing or Inconclusive Data Handling

[redacted]

8.3 Definition of Baseline

[redacted]

8.4 Data Analysis Conventions

[redacted]

Summaries for continuous and ordinal variables will include the number of observations (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum. Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to one additional decimal place than reported in the raw values. Standard deviations will be presented to two additional decimal places than reported in the raw values. Summaries for discrete variables will include frequency counts and percentages. All percentages will be rounded to one decimal place (i.e., XX.X%).

All statistical tests will be two-sided with a significance level of 0.05 ($\alpha = 0.05$) unless otherwise specified. Confidence intervals (CI) for differences between treatment groups will be two-sided at 80% and 95% confidence levels where appropriate. All p-values will be rounded to four decimal places; p-values less than 0.0001 will be presented as "<0.0001"; p-values greater than 0.9999 will be presented as ">0.9999".

8.5 Adjustments for Multiplicity

[redacted]

9. Disposition of Subjects

Subject disposition will be presented in terms of the numbers and percentages of subjects who were randomized, completed the study, and discontinued from the study. Subjects who are not discontinued from the study will be considered study completers. Disposition will be summarized by treatment group and for all subjects.

The number of subjects in each of the analysis populations (ITT, PP and Safety) will be displayed by treatment and percentages will be calculated using randomized subjects as the denominator.

The number and percentage of subjects prematurely discontinued from the study and the reasons for study discontinuation will be summarized by treatment group for all randomized subjects. The reasons for study discontinuation that will be summarized include: (AE, protocol violation, administrative reasons (e.g., inability to continue, lost to follow up), sponsor termination of study, subject choice, and other. A subject listing will be provided that includes the date of and reason for premature study discontinuation.

The number and percentage of subjects with major protocol deviations will be summarized by treatment group for all randomized subjects. The protocol deviations that will be summarized include: Informed Consent, Inclusion / Exclusion and Randomization, Test Article / Study Drug Instillation and Assignment at Site, Improper Protocol Procedures at Site, Site's Failure to Report SAE / AE, Visit Out of Window, Subject's Non-compliance with Test Article, Subject's Use of Prohibited Concomitant Medication, Subject's Failure to Follow Instructions, and Other. A subject listing will be provided that includes the date and description of each deviation.

In addition, subject listings will be provided that include treatment, whether inclusion and exclusion criteria were met, and inclusion in the ITT, Safety, and PP populations.

10. Demographic and Pretreatment Variables

10.1 Demographic Variables

The demographic variables collected in this study include age, sex, race, ethnicity and iris color. Demographic variables will be summarized, overall and by treatment group, for the ITT and Safety populations, separately.

Age (years) will be summarized using continuous descriptive statistics. Age will also be categorized as follows: <65 years and ≥65 years. Age will be reported in years and calculated using the following formula:

Age = (informed consent date – date of birth) / 365.25 truncated as an integer

The number and percentage of subjects will be presented for age category, sex, race, ethnicity and iris color.

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 by treatment group using continuous descriptive statistics for Ora Calibra® Ocular Discomfort Scale, corneal sum and total fluorescein staining, conjunctival sum and total lissamine green staining, TFBUT, SANDE questionnaire, VA, tear osmolarity, unanesthetized Schirmer's test, OSDI©, and IOP.

11. Medical History and Concomitant Medications

11.1 Medical History

Medical history will be coded using MedDRA Version 20.0.

Non-ocular medical history will be summarized using discrete summary statistics and presented by treatment group at the subject and event level by System Organ Class (SOC) and Preferred Term (PT) using the ITT population. Ocular medical history 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.

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

11.2 Concomitant Medications

Concomitant medications will be coded using WHO Drug Dictionary March 2017 and summarized to the therapeutic drug class (Anatomical Therapeutic Chemical (ATC) 4 classification) and preferred name. ATC classifications are applied based on the route and indication by which the drug was taken. If no route or indication is reported/available, the first ATC in alphabetic order will be applied. In cases where the trade name of the drug is reported, SDC will code to the trade name. If this is not available in the dictionary, then the generic name of the drug will be selected. If neither the trade nor generic names are available, SDC will code the medication to the appropriate general category based on the indication and route. If a multi-ingredient/combination drug trade name is not available in the current dictionary, SDC will code to the generic combination if available. If this is not available, SDC will code to the General category based on the reported Indication. Additional coding guidelines are specified in the Data Management Plan (DMP). Terms that remain uncoded after the coding guidelines have been followed will be forwarded to the Medical Monitor along with a list of potential coding links available in the dictionary. The Medical Monitor will either select one of the terms from the potential coding links or specify an alternate term that is available in the dictionary.

Concomitant medications are defined as those medications listed as having been taken 1) within 30 days prior to initiation of study drug administration and continuing for any period of time following the first administration of study drug or 2) at any time following the first administration of study drug.

Concomitant medications will be summarized using the ITT population. Ocular and non-ocular medications will be summarized separately. Medications will be tabulated for each treatment group using frequencies and percentages. Subjects may have more than 1 medication per ATC text. At each level of subject summarization, a subject will be counted once if he/she reports 1 or more medications. Percentages will be based on the number of subjects in each treatment group. Listings of concomitant medications will be generated separately for ocular and non-ocular data.

12. Dosing Compliance and Treatment Exposure

12.1 Dosing Compliance

[redacted]

[redacted]

12.2 Treatment Exposure

Extent of treatment exposure for completed or discontinued subjects will be calculated in days using the following:

Extent of Exposure (days) = Date of completion/discontinuation – date of Visit 1 (Day 1)

Extent of treatment exposure for subjects who were lost to follow-up will be calculated in days using the following:

Extent of Exposure (days) = Date of last recorded visit – date of Visit 1 (Day 1) + 1

Extent of treatment exposure (days) for each subject exposed to study drug will be summarized with continuous descriptive statistics for each treatment group, using the Safety population. A subject listing of treatment exposure will also be produced.

13. Efficacy Analyses

13.1 Primary Analysis

There are no primary endpoints in this Phase 2a study.

13.2 Secondary Analyses

There are no secondary endpoints in this Phase 2a study.

14. Exploratory Analyses

[redacted]

The following exploratory endpoints will be tested:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- Ora Calibra® Ocular Discomfort Scale;
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

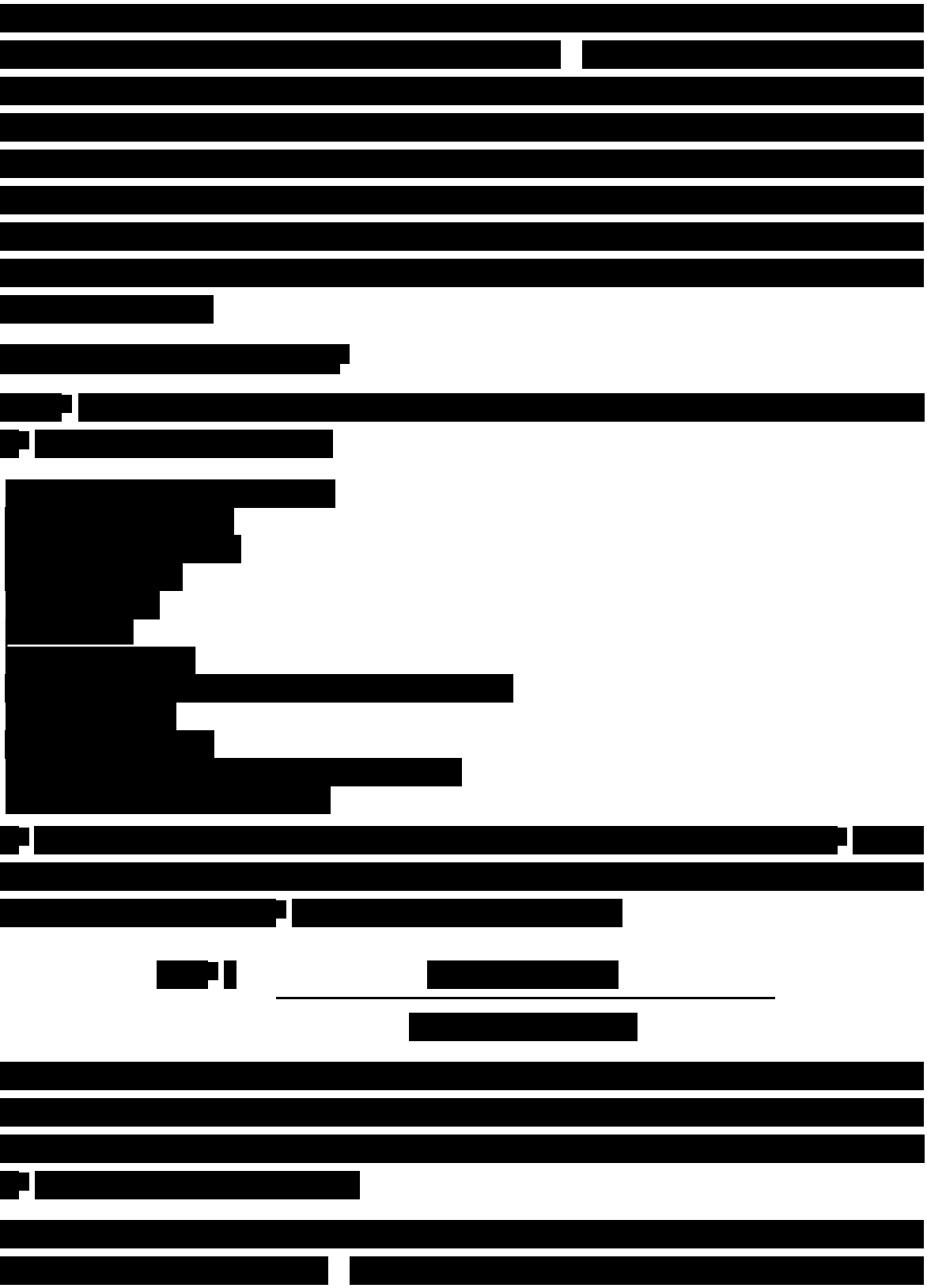
14.6 Ora Calibra® Ocular Discomfort Scale

Ocular discomfort scores will be subjectively graded by the subjects using the Ora Calibra® Ocular Discomfort Scale at all scheduled visits. The ocular discomfort scale ranges from 0 to 4 where [redacted]

Continuous descriptive statistics, including 80% and 95% CIs, as well as changes from baseline will be summarized by treatment group and visit. Pairwise two-sample t-tests will be employed to compare the observed treatment means as well as the changes from baseline at each visit. The mean treatment differences, two-sided 80% and 95% confidence intervals (CIs) for the mean differences and p-values will be reported. Wilcoxon rank sum tests will be conducted as sensitivity analyses to assess robustness of the results. Changes from baseline will also be compared between treatment groups using an ANCOVA model that includes the baseline score as a covariate as an additional sensitivity analysis. All analyses will be performed on the ITT population with LOCF.

Ocular discomfort changes from baseline in the study eye will be displayed graphically in a bar chart with standard error bars by visit and treatment group.

[redacted]



[redacted]

15. Safety Analyses

All safety analyses will be conducted using the Safety population.

15.1 Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not the event is considered drug-related. An AE can therefore be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease occurring after the subject started dosing with the study drug, without any judgment about causality. Any pre-existing medical condition that worsens after administration of the study drug will also be considered a new adverse event. 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 as well as for study and fellow eyes separately. 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.

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

- Ocular TEAEs in the study eye
- Ocular TEAEs in the fellow eye
- Non-ocular TEAEs

- Treatment-related ocular TEAEs
- Treatment-related non-ocular TEAEs
- SAEs

Severity of an adverse event 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:

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 explanations:

- *Definite:* When there are good reason and sufficient documentation to demonstrate a direct causal relationship between investigational product and adverse event.
- *Probable:* When there are good reasons and sufficient documentation to assume a causal relationship in the sense of plausible, conceivable, likely but not necessarily highly probable.
- *Possible:* When there is sufficient information to accept the possibility of a causal relationship in the sense of not impossible and not unlikely, although the connection is uncertain or doubtful, for example; due to missing data or insufficient evidence.
- *None:* When there is sufficient information to accept a lack of a causal relationship, in the sense of impossible and improbable.
- *Unclassified:* When the causal relationship is not assessable for whatever reason due to insufficient evidence, conflicting data or poor documentation.

Only probable and definite TEAEs are considered as treatment-related TEAEs.

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.

15.2 Visual Acuity (ETDRS)

The visual acuity procedure will be performed according to Ora, Inc. standard operating procedures and/or guidance documents. The logarithm of the minimum angle of resolution (logMAR) VA must be assessed using an ETDRS chart. The procedure used will be consistent with the recommendations provided for using the ETDRS eye chart. Visual Acuity should be evaluated at the beginning of each visit in the study (i.e., prior to slit-lamp examination). Subjects should use their most recent correction to attain their best-corrected visual acuity (BCVA).

The observed and change from baseline visual acuity will be summarized for each eye (study eye and fellow eye) using continuous descriptive statistics by visit for each treatment group. A subject listing of visual acuity will also be produced.

15.3 Slit-Lamp Biomicroscopy Examination

A slit-lamp biomicroscopy examination of the cornea, conjunctiva, anterior chamber, iris, lens, and lid will be performed at each visit, and potentially at an Early Termination Visit. The results will be graded as normal, Abnormal Not Clinically Significant (NCS) or Abnormal Clinically Significant (CS). Abnormal findings will be described.

The results will be summarized using counts and percentages for each treatment group at each visit for each eye (study eye and fellow eye). Percentages will be based on the number of subjects in each treatment group with responses. Shift tables for the slit-lamp biomicroscopy parameters will also be provided comparing each follow-up visit to baseline (Visit 1). A subject listing of the slit-lamp biomicroscopy parameters will also be produced.

15.4 Undilated Fundoscopy Examination

An undilated fundoscopy exam will be performed during the study at Visits 1 and 3, and potentially at an Early Termination Visit. Observations will be graded as Normal or Abnormal NCS or Abnormal CS. Abnormal findings will be described. The following will be examined:

- Vitreous
- Retina
- Macula
- Choroid
- Optic Nerve

The results will be summarized using counts and percentages for each treatment group at each visit for each eye (study eye and fellow eye). Percentages will be based on the number of subjects in each treatment group with responses. Shift tables for the undilated fundoscopy parameters will also be provided comparing Visit 3 to baseline (Visit 1). A subject listing of the undilated fundoscopy parameters will also be produced.

15.5 Intraocular Pressure (IOP)

IOP will be measured in each eye by contact tonometry by the examiner and the results will be recorded in mmHg at Visits 1 and 3, and potentially at an Early Termination Visit. A single measurement is made to obtain a determination of IOP. The same tonometer employing the investigator's standard technique will be used throughout the study. In addition, all reasonable efforts will be made to have the same examiner obtain all IOP measurements for a given subject.

The IOP values and changes from baseline for each eye (study eye and fellow eye) will be summarized using continuous descriptive statistics by visit and eye for each treatment group and for all actively treated subjects. A subject listing of IOP will also be produced.

16. Interim Analyses

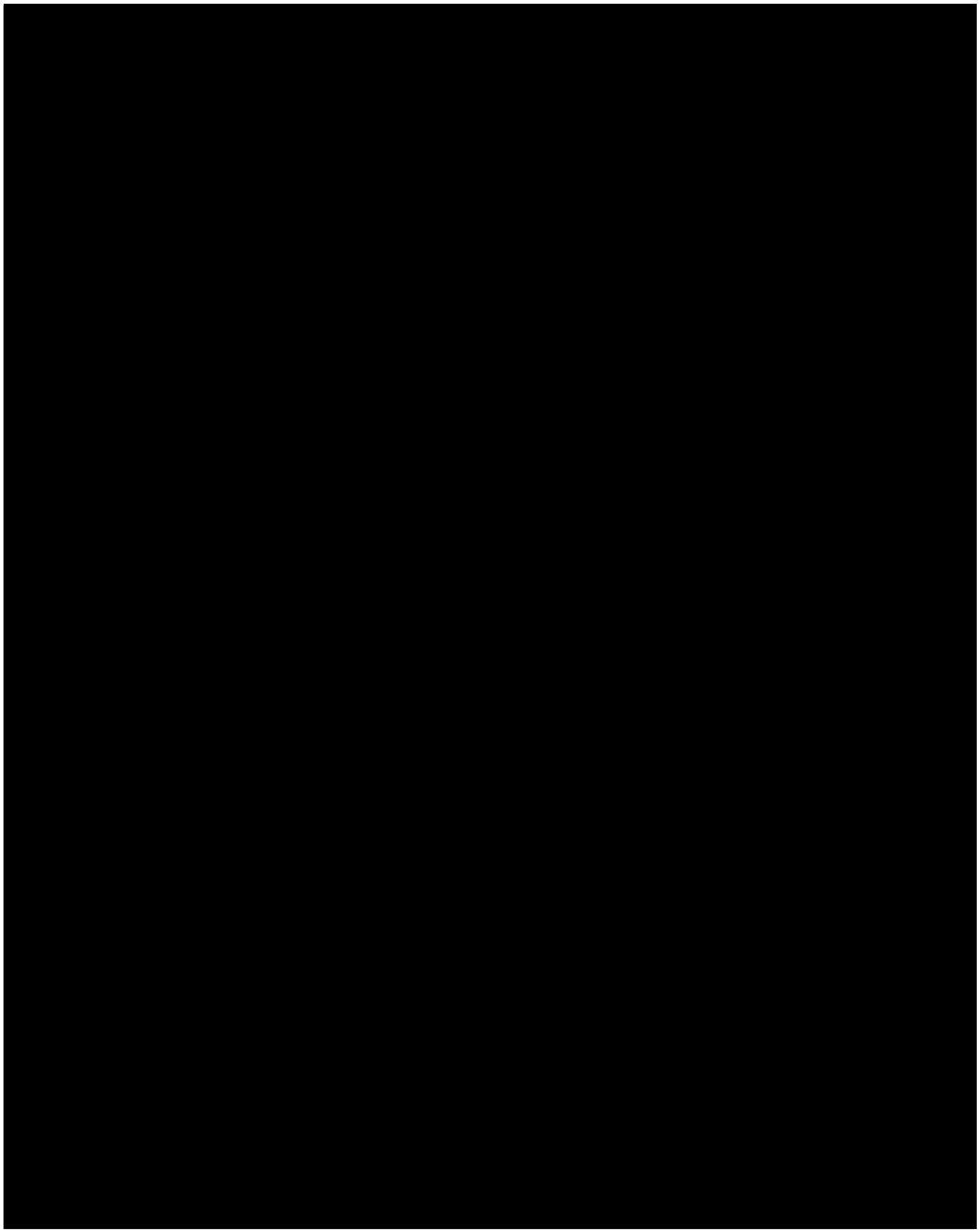
There will be no interim analyses in this study.

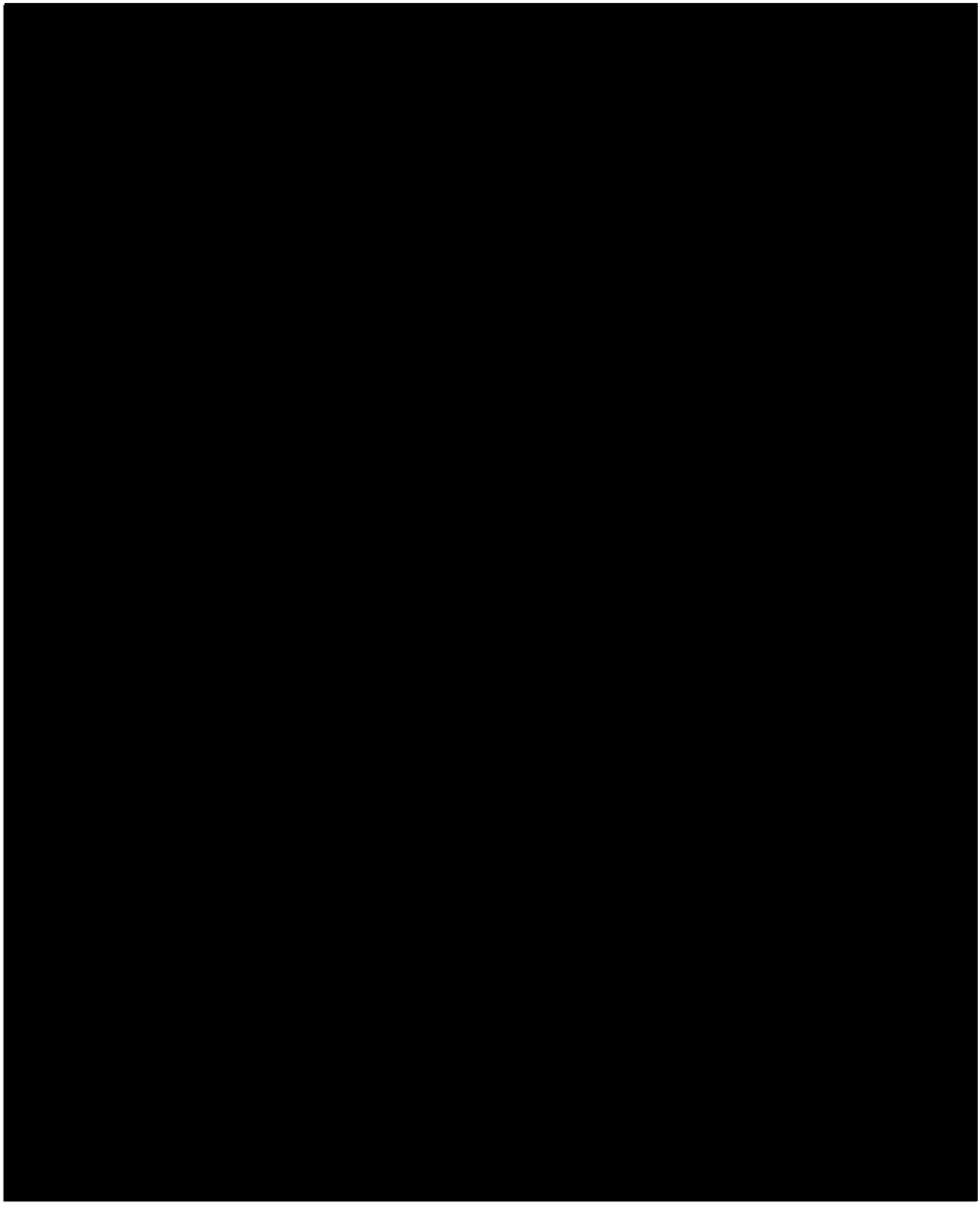
17. Changes from Protocol-Stated Analyses

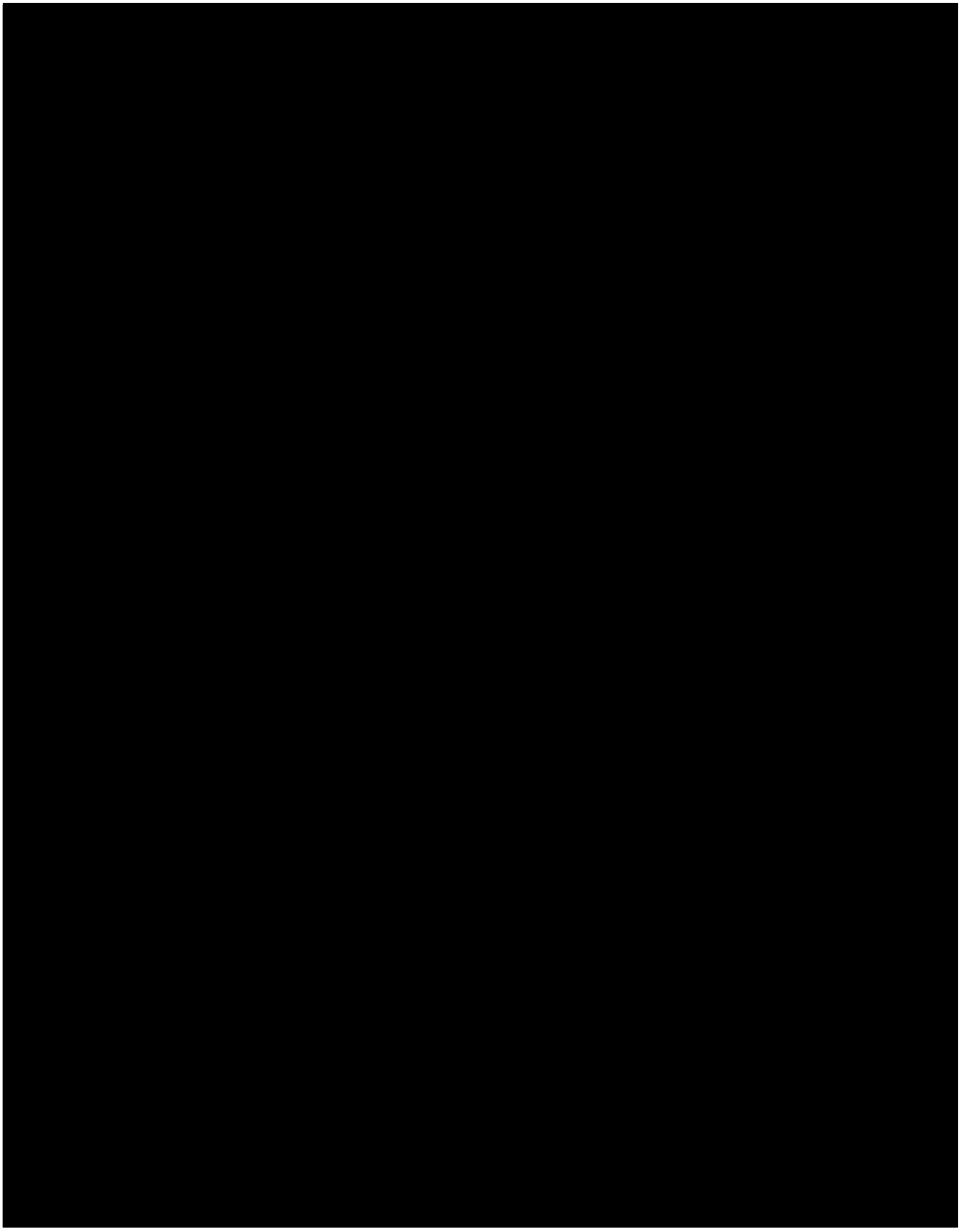
There are no changes from the protocol-stated analyses.

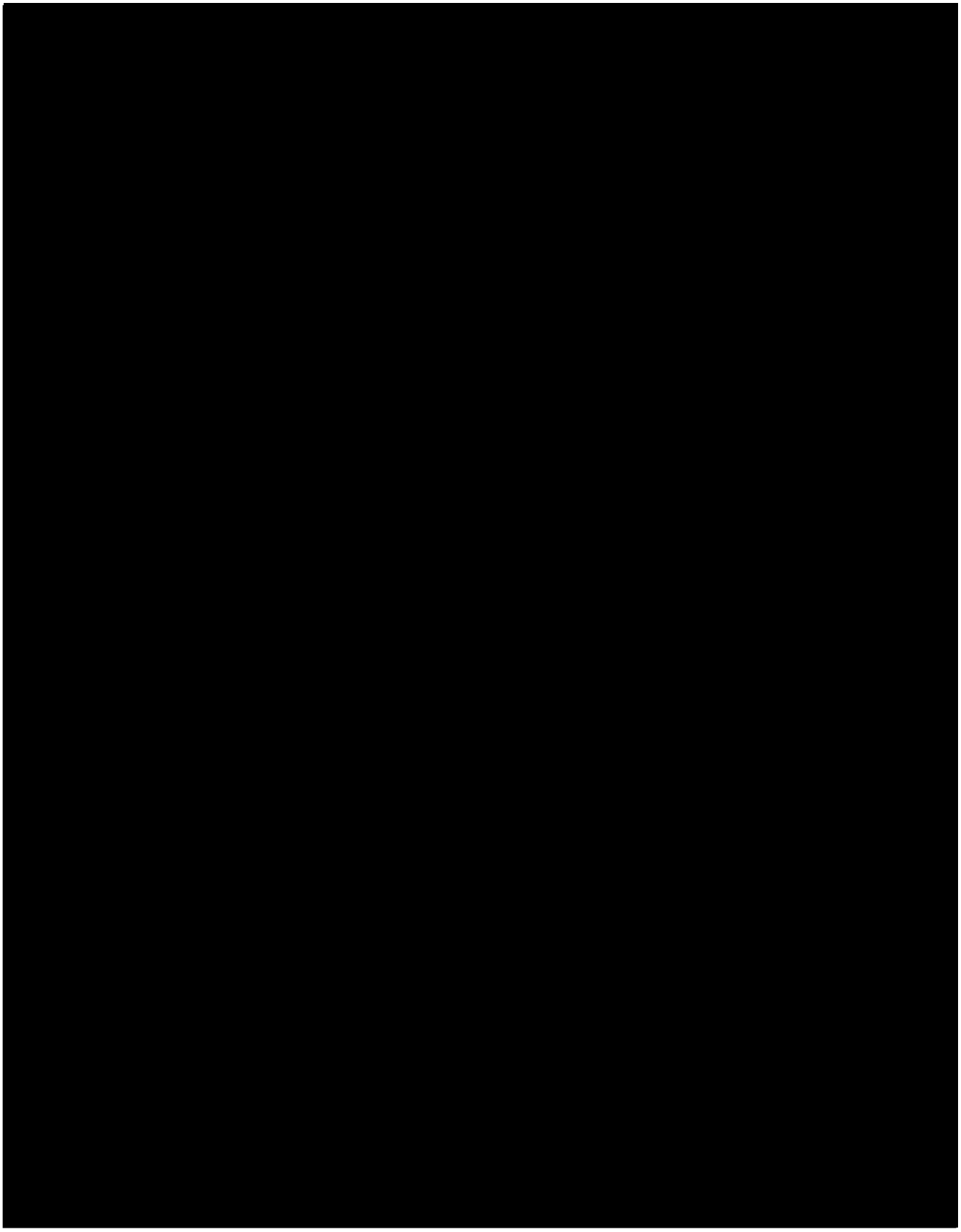
18. Revision History

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









[redacted]

20. Listings

[redacted]

[redacted]

21. Figures

[redacted]