# Next Generation Cataract Surgery Study

STUDY ID

CTV678-E002

# STATISTICAL ANALYSIS PLAN

NCT06071104

Alcon

# Statistical Analysis Plan for CTV678-E002
# Title: Next Generation Cataract Surgery Study

[redacted]

This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

**Executive Summary:**

Key Objectives:

The objective of this study is to obtain device-specific safety and performance clinical data to support marketability in Europe, and to collect user preference data.

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[redacted]

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# 1 STUDY OBJECTIVES AND DESIGN

## 1.1 Study Objectives

The study objectives are to obtain device-specific safety and performance clinical data to support marketability in Europe, and to collect user preference data.

## 1.2 Study Description

This is a prospective, interventional, open-label, single-arm, nonrandomized, multicenter clinical study in the United States of America (USA) and/or Australia with approximately a 1-month follow-up. The investigational product is the UNITY Vitreoretinal Cataract System (VCS). The target patient population for this study are adults undergoing anterior segment ophthalmic surgery who meet the inclusion/exclusion criteria.

The UNITY Vitreoretinal Cataract System (VCS) consisting of the console and compatible devices, is intended to facilitate management of fluid and gases, as well as removal, grasping, cutting, illumination and coagulation of ocular materials. The UNITY VCS, consisting of the console and compatible devices, is indicated for use during anterior and posterior segment ophthalmic surgery, however, only the anterior segment functionalities will be enabled during this study. Approximately 120 subjects will be enrolled, and 100 subjects are expected to complete the study. Up to 5 study sites will participate in this clinical study and will be located in the United States and/or Australia.

Planned study visits will include screening/enrollment, cataract surgery using UNITY VCS, follow-up at 1 day, 1 week, and 1 month. Screening fail/early exit visits will be included as appropriate.

The schedule of study procedures and assessments can be found in the appendix.

## 1.3 Randomization

There will be no randomization of subjects.

If both eyes qualify for the study, the study eye will be determined per investigator’s discretion.

## 1.4 Masking

This is an open-label study.

## 1.5 Interim Analysis

No interim analyses are planned for this study.

# 2 ANALYSIS SETS

All eligible subjects will be screened to determine if they meet all inclusion and no exclusion criteria. Subjects who provide informed consent will be considered enrolled in the study.

## 2.1 All-Implanted Analysis Sets

The primary analysis set for effectiveness outcomes will be the all-implanted analysis set. The all-implanted analysis set includes all eyes with successful completion of the cataract surgery, including IOL implantation.

## 2.2 Safety Analysis Set

The safety analysis set will include all eyes with attempted use of the UNITY VCS (successful or aborted after contact with the eye) and will be used for the safety outcomes. Attempted use of the UNITY VCS is defined as any time the device makes contact with the eye.

# 3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

Subject characteristics and study conduct summaries will include subject disposition, demographics, and baseline cataract grade. Listings will be provided for medical history, screen failures by reason, protocol deviations, baseline medications, and for subjects included in the Safety analysis set but excluded from the All-Implanted analysis set. All descriptive summary statistics will be displayed with count and percent for categorical data, and with sample size (N), mean, standard deviation, median, minimum, and maximum for continuous data.

Subject characteristics and study conduct summaries will be presented for the all-implanted analysis set unless the safety analysis set is different, in which case they will be presented for both.

# 4 EFFECTIVENESS ANALYSIS STRATEGY

## 4.1 Effectiveness Endpoints:

Primary Endpoint

- From the surgeon questionnaire, which is completed after each subject surgery, the percentage of 'Yes' responses to the question: ***Did UNITY VCS using anterior segment surgical functionality perform per the intended use as defined in Protocol Section 5.1?***

Secondary Endpoint

- From the cataract surgery, time from incision entry to incision closure (seconds)

[redacted]

## 4.2 Effectiveness Hypotheses

No hypothesis testing will be performed. Analyses will be descriptive only.

## 4.3 Statistical Methods for Effectiveness Analyses

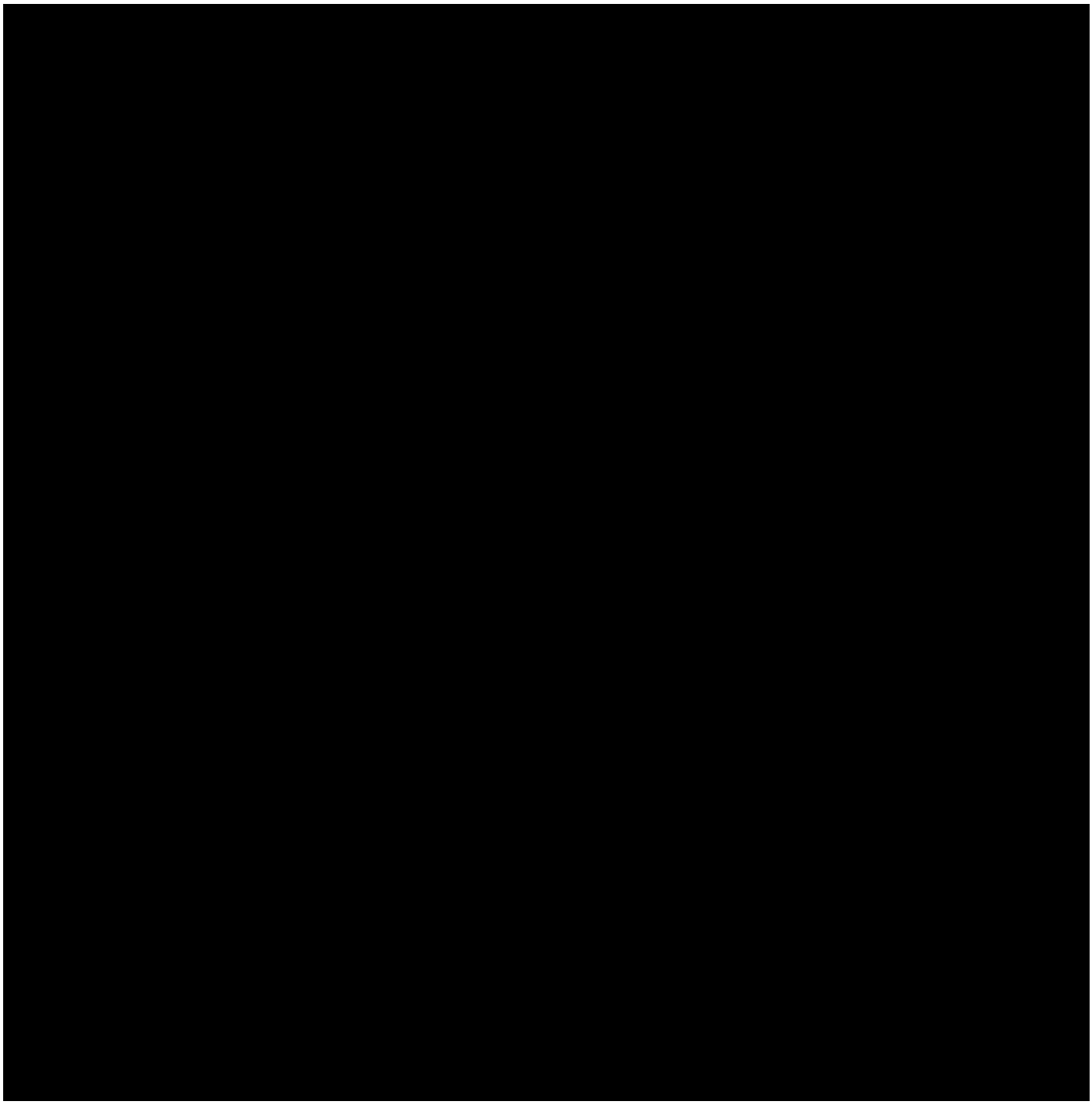
Standard descriptive statistics will be presented based on the type. Individual subject data listings will also be provided. No imputation of missing data is planned. The all-implanted analysis set will be used for all effectiveness analysis and all analyses will be based on the study eye unless otherwise stated.

### 4.3.1 Analysis of the Primary Endpoint

After each surgery, the surgeon completes a user preference questionnaire. For subjects in the all-implanted analysis set, the rate of 'Yes' responses to the question ***Did UNITY VCS using anterior segment surgical functionality perform per the intended use as defined in Protocol Section 5.1?*** will be presented with a count and percentage and will be accompanied by a two-sided exact binomial 95% confidence interval.

### 4.3.2 Analysis of the Secondary Endpoint

The time from incision entry to incision closure for the cataract surgery will be summarized for subjects in the all-implanted analysis set. The number of subjects, mean, median, standard deviation, minimum, and maximum will be reported. A two-sided 95% confidence interval based on the t-distribution will be produced for the mean. Additionally, a two-sided 95% confidence interval for the median will be reported, using nonparametric methods. Individual subject data listings will also be provided for this endpoint.



# 5 SAFETY ANALYSIS STRATEGY

## 5.1 Safety Endpoints

The safety endpoints are:

- Adverse events
- Device deficiencies

- Secondary surgical interventions
- Unplanned intraoperative surgical procedures

## 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 safety analysis set will be used for all safety analysis and will be based on the study eye unless otherwise stated.

### 5.3.1 Adverse Events

All adverse events reported to Alcon will be accounted for in the reporting. Descriptive summaries (counts and percentages) and listings will be presented. The applicable definition of an adverse event is in the study protocol. A listing of all adverse events will be constructed to provide further details.

### 5.3.2 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, a listing of all device deficiencies will be provided.

### 5.3.3 Secondary Surgical Interventions

Descriptive statistics (numbers and percentages) of eyes with secondary surgical interventions (SSI) will be presented. In addition, a listing of subjects with SSIs will be produced.

### 5.3.4 Unplanned intraoperative surgical procedures

Unplanned intraoperative surgical procedures that occur during the cataract surgery will be reported. Descriptive statistics will be presented for these procedures and a listing will be constructed.

## 5.4 Additional Safety Assessments

### 5.4.1 Visual Acuity

Best corrected distance visual acuity (BCDVA) is assessed at the screening, 1 week, and 1 month visits, and uncorrected distance visual acuity (UCDVA) is assessed at the 1 day visit, using a Snellen chart.

BCDVA will be converted to decimal VA by dividing the numerator by the denominator for the Snellen value. For example, 20/25 vision would be converted to a value of 0.8. Observed decimal BCDVA values at each study visit and change from 1 month post-operative visit to screening values for the study eye will be presented descriptively (count, mean, median, standard deviation, minimum, and maximum). A categorical summary of Snellen values (not converted to decimal VA) will be produced and will include counts and percentages for each category at screening, 1 week and 1 month. A listing will be provided which presents BCDVA and UCDVA for all subjects at each visit.

### 5.4.2 Biomicroscopy Findings/Slit Lamp Examination

A slit-lamp examination will be performed at the screening, 1 day, 1 week, and 1 month visits to evaluate the anterior segment of the eye, including eyelids/conjunctiva, cornea, lens, and iris/anterior chamber.

A summary of grading at each visit for corneal edema, aqueous cells, and aqueous flare will be presented. Cataract grading and cataract type will be presented for the screening visit. A listing with this information, plus details on any abnormal slit lamp findings, will be provided. Additionally, a listing of postoperative IOL observations will be created.

### 5.4.3 Intraocular Pressure

Intraocular pressure (IOP) measurements will be recorded in mmHg and rounded to the nearest whole mmHg. IOP measurements will be conducted at the screening, 1 day, 1 week, and 1 month visits.

Descriptive summaries (count, mean, median, standard deviation, minimum and maximum) of observed values will be presented at each study visit and for the change at 1 month from baseline. A listing will supplement the summary table.

### 5.4.4 Dilated Fundus Examination

The dilated fundus examination will be conducted at the screening and 1 month visits. The examination will be performed to evaluate the health of the vitreous, retina, macula, choroid, and optic nerve. A listing of fundus findings will delineate the results.

## 6 SAMPLE SIZE AND POWER CALCULATIONS

Based on a sample of 100 surgeries, the expected half-width of the 95% confidence interval for the percentage of surgeons reporting 'Yes' to the question "***Did UNITY VCS using anterior segment surgical functionality perform per the intended use as defined in Protocol Section 5.1?***" will be $1.96 \cdot \sqrt{(p(1-p)/100)}$. This half-width is widest at p = 50%. Under this conservative assumption, the expected half-width is <10% given the sample size of 100.

Allow enrollment for an additional 10% for screen failure and 10% for lost to follow-up to ensure 100 completed subjects. (See also Section 8 of the protocol for more details.)

## 7 REFERENCES

Base SAS(R) 9.4 Procedures Guide: Statistical Procedures, Second Edition, December 2013

[redacted]

## 8 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.

# 9 APPENDIX

**Table 9–1 Schedule of Study Procedures and Assessments**

| Visit | Visit 0 Screening | Visit 00 Surgery | Visit 1 1 Day | Visit 2 1 Week | Visit 3 1 Month / Exit | Early Exit | Unscheduled Visit [7] |
|---|---|---|---|---|---|---|---|
| Day Number | **Day -60 to 0** | **Day 0** | **Day 1 to 3** | **Day 4 to 10** | **Day 28 to 42** | **N/A** | **N/A** |
| Eye | Both Eyes | Study eye | Study eye | Study eye | Study eye | Study eye | Study eye |
| Informed Consent | X | | | | | | |
| Demographics | X | | | | | | |
| Medical and Ocular History | X | | | | | | |
| Concomitant Medications | X | X | X | X | X | X | X |
| Inclusion/Exclusion | X | | | | | | |
| Urine Pregnancy Test [1]* | X | | | | | | |
| Dilated Pupil Size | X | | | | | | |
| Keratometry | X | | | | | | |
| Biometry (ACD, AL) | X | | | | | | |
| Slit Lamp Examination | X | | X | X | X | X | (✓) |

| Visit | Visit 0<br>Screening | Visit 00<br>Surgery | Visit 1<br>1 Day | Visit 2<br>1 Week | Visit 3<br>1 Month / Exit | Early Exit | Unscheduled Visit [7] |
|---|---|---|---|---|---|---|---|
| Day Number | **Day -60 to 0** | **Day 0** | **Day 1 to 3** | **Day 4 to 10** | **Day 28 to 42** | **N/A** | **N/A** |
| Eye | Both Eyes | Study eye | Study eye | Study eye | Study eye | Study eye | Study eye |
| UCDVA[2] | | | X | | | | |
| BCDVA[3] | X | | | X | X | X | (✓) |
| Intraocular Pressure | X | | X | X | X | X | (✓) |
| Dilated Fundus Exam[4] | X | | | | X | X | (✓) |
| Treatment (cataract surgery) | | X | | | | | |
| [redacted] | | | | | | | |
| Time from incision entry to incision closure | | X | | | | | |
| [redacted] | | | | | | | |

| Visit | Visit 0<br>Screening | Visit 00<br>Surgery | Visit 1<br>1 Day | Visit 2<br>1 Week | Visit 3<br>1 Month / Exit | Early Exit | Unscheduled Visit [7] |
|---|---|---|---|---|---|---|---|
| Day Number | **Day -60 to 0** | **Day 0** | **Day 1 to 3** | **Day 4 to 10** | **Day 28 to 42** | **N/A** | **N/A** |
| Eye | Both Eyes | Study eye | Study eye | Study eye | Study eye | Study eye | Study eye |
| [redacted] | | | | | | | |
| User Preference Questionnaire | | X | | | | | |
| Adverse Events | X | X | X | X | X | X | X |
| Device Deficiencies | X | X | X | X | X | X | X |
| Exit Form | (✓) | (✓) | (✓) | (✓) | X | X | (✓) |

(✓) Assessment performed as necessary

[1] Women of child-bearing potential only

[2] VA to be conducted per site's SOC using Snellen chart

[3] VA to be conducted per site's SOC using manifest refraction and Snellen chart

[4] Assessment must be performed dilated

[redacted]

[7] Unscheduled Visit – additional study assessments may be performed per investigator's discretion

* Source only entries

[redacted]