# Evaluation of the Symfony with Optiblue Intraocular Lens Compared to The Vivity IOL Under Mesopic Conditions

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**Study Product:** Symfony ™OptiBlue®IOL models DXR00V and DXWxxx
Clareon® Vivity® IOL models CCWET0 and CCWETx

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**Investigator Agreement:** I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practices (GCP), the Declaration of Helsinki, this protocol, and all applicable regulatory requirements. Additionally, I will comply with all procedures for obtaining informed consent, data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the sponsor.

Name of the Investigator: _____

Name of the Institution: _____

Address: _____

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**Investigator:** _____
Signature Date

## INTRODUCTION

Cataract surgery is one of the most frequently performed surgical procedures and offers significant improvement to the patients' quality of life. For refraction correction at the time of cataract surgery, the range of intraocular lenses available goes from monofocal intraocular lenses to the multifocal ones, including among the options, trifocal and extended depth of focus lenses (EDOF).

Conventional monofocal intraocular lens (IOL) are the most common device implanted[1] due to their low cost, highly predictable distance visual outcome and low incidence of photic symptoms. However, monofocal IOLs have no power to meet the visual expectations for those patients that wish to be less dependent on glasses while performing simple activities brought to us by modern life, like computer work and cell phone usage, since these activities demand an increased need for intermediate or near vision. Trifocal lenses provide the most extended range of vision, and could meet the intermediate and near vision expectations, but also with limitations. Due to their design, these diffractive lenses split the light to distinct foci; as a result, at one focus the indistinct image from the other foci introduces the potential for glare and halos. For some patients, even if they notice this phenomenon, it is not bothersome to the point to complain about it; to others, on the other hand, glare and halos can be so disturbing that they have a very hard time adapting to this new visual reality. Another common complaint is the lower contrast sensitivity, reported by patients with trifocal lenses implanted.

Extended depth of focus, or EDOF, lenses were developed as a bridge to cover the gap between the monofocal and trifocal or multifocal intraocular lenses. EDOF lenses provide spectacle independence for far and intermediate vision and need only a minimal negative defocus for optimized near vision; they are considered the best option for patients aiming to be less spectacle dependent and, at the same time, to avoid some of the side effects and the compromising from trifocal and multifocal IOLs.

Although the performance of EDOF lenses under photopic conditions has been widely investigated,[2-7] the question about their performance under mesopic conditions remains unanswered.

1. OBJECTIVE:

The purpose of this study is to evaluate the visual outcomes of the Symfony lens with OptiBlue and the Vivity lens under mesopic lighting conditions in patients undergoing routine cataract surgery.

2. STUDY DESIGN AND METHODS:

A. Test article:

- Symfony ™OptiBlue®IOL models DXR00V and DXWxxx
- Clareon® Vivity® IOL models CCWET0 and CCWETx

A. **Study Design:** Prospective, multicenter (up to 2 sites), double masked (subject and evaluator) study.

B. **Subjects:** A total of 64 subjects who meet the Inclusion/Exclusion criteria will be enrolled.

1. Inclusion Criteria:

Subjects MUST fulfill the following conditions to qualify for enrollment into the trial

1. Subject is undergoing bilateral lens extraction with implantation of an EDOF IOL with a target refraction of plano OU.
2. Gender: Males and Females.
3. Age: 50 years and older.
4. Willing and able to provide written informed consent for participation in the study
5. Willing and able to comply with scheduled visits and other study procedures.
6. Scheduled to undergo standard cataract surgery in both eyes, with 1 to 30 days between surgeries.
7. Potential postoperative visual acuity of 0.2 logMAR (20/32 Snellen) or better in both eyes.

2. Exclusion Criteria:

Subjects with ANY of the following conditions on the eligibility exam may NOT be enrolled into the trial.

1. Severe preoperative ocular pathology: amblyopia, rubella cataract, proliferative diabetic retinopathy, shallow anterior chamber, macular edema, retinal detachment, aniridia or iris atrophy, uveitis, history of iritis, iris neovascularization, medically uncontrolled glaucoma, microphthalmos or macrophthalmos, optic nerve atrophy, macular degeneration (with anticipated best postoperative visual acuity less than 20/30), advanced glaucomatous damage, etc.
2. Uncontrolled diabetes.
3. Use of any systemic or topical drug known to interfere with visual performance.
4. Contact lens use during the active treatment portion of the trial.
5. Any concurrent infectious/non-infectious conjunctivitis, keratitis, or uveitis.
6. Clinically significant corneal dystrophy.
7. Corneal irregularities potentially affecting visual acuity (i.e., keratoconus, corneal opacities.
8. History of chronic intraocular inflammation.
9. History of retinal detachment.
10. Pseudoexfoliation syndrome or any other condition that has the potential to weaken the zonules.
11. Previous intraocular surgery.
12. Previous corneal refractive surgery (i.e., LASIK, PRK, RK).
13. Subject who declined any type of presbyopia correcting IOL due to concerns with visual disturbances (i.e., halos)
14. Previous keratoplasty
15. Severe dry eye
16. Pupil abnormalities
17. Subject who may reasonably be expected to require a secondary surgical intervention at any time during the study (other than YAG capsulotomy, i.e., LASIK)
18. Any clinically significant, serious, or severe medical or psychiatric condition that may increase the risk associated with study participation or may interfere with the interpretation of study results.
19. Participation in (or current participation) any ophthalmic investigational drug or ophthalmic device trial within the previous 30 days prior to the start date of this trial.

The principal investigator reserves the right to declare a patient ineligible or non-evaluable based on medical evidence that indicates the patient is unsuitable for the trial.

3. Exclusion Criteria during surgery

If any of the following exclusion criteria are applicable to the study eye, the subject should not continue in the study.

1. Other planned ocular surgery procedures, i.e., iStent.
2. Significant vitreous loss.
3. Significant anterior chamber hyphema.
4. Uncontrollable intraocular pressure.
5. Zonular or capsular rupture.
6. Bag-sulcus, sulcus-sulcus, or unknown placement of the haptics.
7. Suturing of incision required at time of surgery.
8. Intraocular lens tilt or decentration
9. Significant sedation or retrobulbar block during surgery.
10. Other procedures such as pupil stretch, expanders, or iris hooks during surgery.

Note: Any subject in which surgery has been aborted for either eye should immediately be discontinued from the study and an exit form completed for that subject. These subjects will be followed up as per the clinic standard of care, monitored for safety, and their data will be excluded from the study efficacy analysis (obtained from FDA Database Research Results Feb 05, 2009). All adverse events will be appropriately documented and reported.

Additionally, participants who are considered to be a vulnerable subject population are not to be enrolled into the study without prior written authorization from both the Sponsor and the IRB to ensure that a description of additional safeguards are in place during the consenting and enrollment processes. Vulnerable populations include, but are not limited to, the following:

1. Prisoners
2. Nursing home residents /institutionalized individuals
3. Mentally disabled /cognitively impaired individuals

4. Sponsor employees and their family members
5. Site employees and their family members that are directly and indirectly involved with the study
6. Students of the principal investigator participating in the study
7. Economically and/or educationally disadvantaged individuals
8. Comatose individuals / traumatized individuals
9. Adults who do not read and/or write
10. Hearing impaired individuals
11. Terminally ill individuals / individuals with life-threatening conditions

## 3. STUDY PROCEDURES

### A. Informed Consent / Subject enrollment

Potential subjects will be identified from the patients presenting at the clinic. Additionally, a flyer will be placed in the check-in area and an ad will be placed in social media and on the practice website, if deemed necessary. Once identified as a study candidate, the patient will be asked if he/she would like to participate. The sub-investigator, study coordinator or an appropriately trained staff member will answer any and all questions and will obtain informed consent. A copy of the signed informed consent document will be given to the subject. The principal investigator will be available if the subject wants to discuss further details with him. Any testing that is part of the investigative site's standard preoperative cataract evaluation may be performed prior to the informed consent being signed, provided these tests are conducted within 90 days of surgery. The patient will understand that participation in the study, or declining to participate, will not affect his/her quality of care.

No subject will be enrolled into the study that does not meet the inclusion/exclusion criteria and does not sign the current approved informed consent document. Informed consent will be obtained prior to collecting any data for the study. The original signed documents will be maintained by the investigator as a permanent part of the subject's research records.

### B. Surgery Procedures:

Patients will be randomly assigned to one of two groups:

- Group A, bilateral Symfony.
- Group B, bilateral Vivity.

C. Study Visit Schedule and Assessments (Table 1).

1. **Visit Schedule:** Subjects will be examined at the following intervals:

    1. Visit 0: Screening and enrollment: Preoperative evaluation completed not more than eight weeks before surgery
    2. Visit 1/1A: Day of Surgery for each eye
    3. Visit 2: Month 3: 90 ±15 days postoperative after second eye surgery

2. Measurements and evaluations

1. Visit 0 (screening): Informed consent process will be conducted during this visit. Assessments include best-corrected distance visual acuity (BCDVA, Snellen chart), manifest refraction, halo and glare simulator, slit lamp examination including dilated fundus exam, cataract density and type, patient satisfaction, visual symptoms and spectacle independence questionnaires, Additionally, patients enrolled at one site (CEP) will have an iTrace done. Any testing that is part of the site's standard of care related to preoperative cataract surgery evaluation may be performed prior to the informed consent being signed, provided these tests are conducted within 90 days of the surgery and notation of the date performed is entered onto the CRF. The surgeon's standard pre cataract surgery treatment will be used in all his patients

2. Visit 1/1A (day of surgery for each eye): The surgeon may use his preferred small incision cataract extraction technique (manual phacoemulsification or laser assisted). The lens will be implanted in the capsular bag. The following information will be captured from the day of surgery: phaco technique (manual or laser), lens implanted and power, target refraction for IOL power implanted, additional surgical procedures, intraoperative complications, and any device deficiencies. The surgeon's standard post cataract surgery treatment will be used in all his/her patients.

3. Visit 2 (Month 3): Monocular and binocular UCDVA and BCDVA at 4 m, binocular UCIVA and DCIVA (at 66 cm), binocular UCNVA and DCNVA (at 40 cm), binocular BCDVA low contrast (10% and 25%), DC binocular defocus curve, pupil size at 66 and 40 cm will be performed under mesopic conditions (3-5 cd/$m^2$). Additionally, bilateral BCDVA as well as DCIVA and DCNVA will be performed under photopic conditions. Other assessments will include the manifest refraction, I-Trace (at one site only), halo and glare simulator, IOL

orientation (if a toric lens) and dilated fundus exam as deemed necessary by the investigator, patient satisfaction, visual symptoms and spectacle independence questionnaires, and any device deficiencies. A routine slit lamp examination will also be conducted.

All adverse events and complaints will be monitored and recorded at all study visits.

Table 1. Visits and Study Assessments

| | Visit 0 Screening | Visit 1/1A DOS | Visit 2 3-Month 90 ±15 days |
|---|---|---|---|
| Informed Consent | X | | |
| Inclusion/Exclusion | X | X | |
| Demographics/Ocular history | X | | |
| BCVA Snellen | X | | |
| UCVA ETDRS (4m) under mesopic conditions | | | X* |
| UCIVA ETDRS (66 cm) under mesopic conditions | | | X** |
| UCNVA ETDRS (40 cm) under mesopic conditions | | | X** |
| Manifest refraction – Max Plus | | | X |
| BCVA ETDRS (4m) under photopic conditions | | | X** |
| DCIVA ETDRS (66 cm) under photopic conditions | | | X** |
| DCNVA ETDRS (40 cm) under photopic conditions | | | X** |
| BCVA ETDRS (4m) under mesopic conditions | | | X* |
| BCVA Mesopic low contrast (10%) at 4 m under mesopic conditions | | | X** |
| BCVA Mesopic low contrast (25%) at 4 m under mesopic conditions | | | X** |
| DCIVA ETDRS (66 cm) under mesopic conditions | | | X** |
| DCNVA ETDRS (40 cm) under mesopic conditions | | | X** |
| Defocus curve under mesopic conditions | | | X** |

| | | | |
|---|---|---|---|
| Pupil size at 66 cm under mesopic conditions | | | X |
| Pupil size at 40 cm under mesopic conditions | | | X |
| SLE | X | | X |
| i-Trace‡ | X | | X |
| Halo and glare simulator | X‡‡ | | X‡‡ |
| Dilated fundus exam | X | | X† |
| Cataract density / type | X | | |
| Intraoperative data | | X | |
| Toric IOL position | | X | X† |
| Questionnaires | X | | X |
| AE/Device deficiencies | | X | X |

X To be performed as scheduled
* Monocular and binocular testing
** Binocular testing only
‡ To be performed at one site only (CEP)
‡‡ With and without correction
†To be performed as deem necessary by the investigator.
DC: distance corrected.

## D. Study endpoint criteria

1. Patient Completion of Study: If a study patient has completed the final visit (Visit 5) of the study, he/she is considered to have completed the study.

2. Patient Discontinuation: Each study patient may voluntarily discontinue the study at any time they choose. Study patients who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study. Study patients discontinued during the enrollment phase (prior to surgery) of the study will be replaced.

3. Patient Termination: A study patient will be terminated if the study patient develops any severe adverse event that may be related to the study. A study patient will receive appropriate treatment at the discretion of the investigator. Notification of termination will be clearly documented. These study patients are considered to have completed the study and will not be replaced.

4. Study Termination: The investigator with appropriate notification may terminate the study. If, after clinical observations, the investigator feels that it may be unwise to continue the study, he may stop the study.

5. Study Completion: The study will be complete when all enrolled patients have completed Visit 5 or have been terminated from the study.

## 3. STATISTICAL CONSIDERATIONS

### A. Sample size

The sample size estimates depend in large part on the standard deviation (SD) for logMAR UCIVA. Assuming a SD of 0.122 for the two-sided t-test (alpha =0.05) for the intermediate visual acuity endpoint, we will need 32 subjects in each group (Symfony with Optiblue/ Vivity) to detect differences of 0.1 logMAR (1 line difference) with 90% power. Total sample size = 64.

### B. Statistical Analysis

All data will be collected by the site and entered into a database. Subjects will be assigned an ID number. Data analysis will be performed without patient identification. Statistical analysis will be performed using standard descriptive statistics and other tests as deemed appropriate based on the characteristics of the data to be analyzed. All statistical tests will be two-sided and interpreted at a 5% significance level. Comparisons between the groups will be made. Data analysis will be conducted by a third-party consultant.

### C. Study Endpoints

1. **Primary Endpoint:**
   Binocular distance corrected intermediate visual acuity at 66 cm under mesopic conditions.
2. **Secondary Endpoints:**
   a. Defocus curve under mesopic conditions
   b. Binocular low contrast distance visual acuity under mesopic conditions
   c. Uncorrected and distance-corrected near (40 cm) visual acuity under mesopic conditions.
   D. Uncorrected intermediate (66 cm) visual acuity under mesopic conditions

E. Uncorrected and best-corrected distance (4 m) visual acuity
F. Non-directed complaints
G. To evaluate patient's overall satisfaction of their vision
H. To evaluate patient's spectacle independence
I. To evaluate visual symptoms using a questionnaire
J. To evaluate the functional vision questionnaire
K. Residual mean spherical equivalent refraction
L. Residual refractive sphere
M. Residual refractive cylinder
N. Percentage of eyes with postoperative MRSE accuracy to target ≤ 0.5D

3. Exploratory endpoints:
   a. Effect of pupil size at 66 cm
   b. Effect of pupil size at 40 cm
   c. Angle alpha effect on visual disturbances
   d. i-Trace evaluation of depth of focus, modulation transfer function (MTF), visual function analysis, and point spread function (PST) among others.

### D. Safety Analyses

The type, severity, duration, and frequency of reported ocular adverse events will be tabulated for each group. Adverse events will also be summarized for events that were considered treatment-related. Comparison of treatment groups with respect to the proportion of study patients reporting adverse events will be made using Fisher's Exact Test.

## 4. DATA HANDLING AND RECORD KEEPING

### A. Confidentiality

To ensure confidentiality in this study, records of the participants will be examined only by the principal investigator and research staff involved in the study. Study records will be kept on file. Any statistical analysis and publication will not include any subject identifiers. Medical records will be made available only for review by the investigators, Sponsor Company or Research Institution, the IRB, and other State or Federal Regulatory Agencies, if necessary. All information in these records will be kept confidential.

B. Records Retention

The PI is accountable for the integrity, retention, and security of all study related data. The investigator must maintain accurate, complete, and current records relating to the clinical
study. The investigator must maintain the required records during the investigation and for a period of 2 years after the date on which the investigation is terminated, completed, or published then records will be scanned and kept electronically on a secured server.

## 5. STUDY MONITORING, AUDITING, AND INSPECTING

A. The nature and location of all source documents will be identified to ensure that original data required to complete the case report forms (CRFs) exist and are accessible for verification. If electronic source records are maintained, these records must be 21 CFR Part 11 compliant and will be printed and certified for verification as needed.

B. The required examination must be recorded on the CRFs. CRFs will be used as source document. All data reported must have corresponding entries in the source documents. The principal investigator or sub-investigator must review the reported data and certify that the CRFs are accurate and complete. No subject identifiers should be recorded on the CRFs beyond subject number, subject initials, and study specific identifiers.

C. Data from CRFs will be entered into a database. Upon completion of the CRFs, the data will be reviewed by study designated personnel and statistician for accuracy and completeness. If corrections and/or any additions to the data are deemed necessary, queries will be generated. Designated research staff expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data in the database are reflected in the subjects' source documentation. Any changes will need to be initialed and dated by the authorized personnel making such changes.

D. Data will not be sold to third parties but collected data may be used for additional analysis in the future.

## 6. INVESTIGATIONAL PRODUCT

A. Description

The Symfony InteliLight IOL (DXR00V or DXW150 – 375 – Toric II IOL) combines an echelette design (to create an extended depth of focus) with an achromatic technology (to correct chromatic aberrations) and a violet-light filter that diminishes the perception of visual disturbances such as halo, glare, and starburst. The lens has been designed to provide high quality vision up to 26 inches so patients may still need to wear glasses for some activities mainly at near.

Acrysof® IQ Vivity Intraocular Lens is a non-diffractive aspheric IOL that provides an extended range of vision maintaining low incidence of visual disturbances when compared to a monofocal IOL. The extended vision ranging from distance to near is obtained by a Wavefront-shaping technology on the anterior surface of the lens.

B. Treatment/Dosing Regimen

The IOL will be implanted at time of uncomplicated routine cataract surgery. Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the patient.

C. Method for Assigning Subjects to Treatment/Dosing Groups

N/A

D. Subject Compliance Monitoring

Since the IOL is implanted at time of cataract surgery, subject compliance will not be an issue in this particular study.

E. Packaging, Receiving, Storage, Dispensing and Return

N/A

7. ETHICAL CONSIDERATIONS

This clinical trial will be conducted in accordance with the principles of the Declaration of Helsinki, and Good clinical practice. The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that all personnel involved in the conduct of the clinical trial are qualified to perform their

assigned duties through relevant education, training, and experience. Deviations from the clinical protocol must be documented in each subject's study records including the dates and reasons for each deviation. The PI must ensure that all aspects of the trial follow the applicable regulatory laws and conditions of approval imposed by the IRB.

## 8. IN CASE OF AN INJURY RELATED TO THIS RESEARCH STUDY

Every effort to prevent study-related injury will be taken by the study doctor and staff. In the event a patient is injured as a direct result of the study while following the study instructions and requirements, the patient will be instructed to immediately contact the principal investigator and/or study staff. Treatment will be provided as needed for those injuries caused directly by this research study. In the event of injury or illness caused by or occurring during the participation in this study, all charges for medical care provided will be billed to the patient's insurance company. The medical care costs for injuries or illnesses that are not caused directly by the research study will not be covered.

## 9. CONFIDENTIALITY/PUBLICATION OF THE STUDY

The existence of this Study is confidential and should not be discussed with people outside of the Study. Results will be submitted for publication and presentation at national and/or international meetings. A manuscript will be submitted to peer-review journals for publication but there is no guarantee of acceptance.

## REFERENCES:

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