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One-month Clinical Evaluation of Oté Sensation Multi-Purpose Solution Care System

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One-month Clinical Evaluation of Oté Sensation Multi-Purpose Solution Care System

OTES-3301

PERSONNEL AND FACILITIES

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One-month Clinical Evaluation of Oté Sensation Multi-Purpose Solution Care System

OTES-3301

SYNOPSIS

OBJECTIVES: To test whether the Oté Sensation multi-purpose solution is substantially equivalent to another multi-purpose solution (Bausch & Lomb BioTrue® multipurpose solution).

STUDY DESIGN: One-month, approximately 200-subject, double-masked (care product), bilateral, randomized, comparative study. Subjects will be randomly assigned to use either the test or control solution.

TEST PRODUCT: Oté Sensation multi-purpose solution care system and Oté storage case (Oté Pharma, Uden, Nederland)

Constituents: PHMB 0.00002%, Polyquaternium-2 0.0001%, Sodium hyaluronate

The user instructions will include a rub and rinse step.

CONTROL PRODUCT: Bausch & Lomb BioTrue multipurpose solution and B&L storage case.

A sterile, isotonic solution that contains hyaluronan, sulfobetaine, poloxamine, boric acid, sodium borate, edetate disodium and sodium chloride and preserved with a dual disinfection system: polyaminopropyl biguanide 0.00013% and polyquaternium 0.0001%.

This will be used with a rub and rinse step.

CONTACT LENSES: The following six lens types will be used to represent a cross-section of lenses in use: ACUVUE® 2, ACUVUE® VITA® (Johnson & Johnson Vision Care), Air OPTIX® (Alcon), Biofinity®, Clariti (CooperVision), PureVision® (Bausch & Lomb)

Approximately 33 subjects will be allocated to use each lens type: 22 using the test MPS product and 11 using the control product. Each site will use four lens types.

NO. OF SITES: Approx. 10 (3-5 UK and 5-6 US) sites. Each site will enroll approx. 20 subjects.

NO. OF SUBJECTS: Total approx. 200 subjects (400 eyes), approx. 20 subjects/site. The aim is for at least 180 subjects to complete the study; 30 in each lens group (20 using the test solution and 10 using the control solution).

	Test Group	Control Group	Total Subjects
Site 1 to 10	~14	~7	~20
Total	133	67	200

STUDY POPULATION: Volunteer subjects will be currently adapted soft contact lens wearers (>1 month of lens wear), be at least 18 years of age with contact lens sphere power requirement in the range +4.00 to -8.00D and refractive astigmatism of less than or equal to 0.75D in each eye.

VARIABLES:
Comfort (0-10)
Average wearing time (WT), comfortable WT (hrs.)
Visual acuity (Snellen/logMAR)
Slit lamp findings, including corneal edema, limbal and bulbar hyperemia, vascularization, palpebral hyperemia and roughness, corneal staining, conjunctival staining, etc. (0-4)
Lens surface wettability (0-4)
Lens surface deposits (0-4, no. of spots)
Adverse events

IN VITRO MEASUREMENTS: Deposit analysis in dark field illumination using a modified version of the method of Lowther *et al* (ICLC 1991;18:219-26) on approx. 60 lenses.

VISITS/SCHEDULE: There will be four scheduled visits (visit 1a and 1b may be conducted on the same day):

Visit 1a: Baseline

Visit 1b: Lens issue

Visit 2: 1 week follow-up (7 days ±3 days) – WT 1-3 hours

Visit 3: 1 month follow-up (30 days ±4 days)

STUDY END POINTS

a) Safety Endpoints: Non-inferiority of slit lamp findings: limbal hyperemia, bulbar hyperemia, and corneal staining.

b) Efficacy Endpoints: Non-inferiority of comfort, visual acuity, surface wettability, lens deposits.

1 INTRODUCTION

The contact lens (CL) care product Oté Sensation is a multi-purpose soft contact lens solution applicable to all soft contact lenses and is intended for cleaning, disinfection, rinsing and storage of lenses.

The product is CE-marked and has been marketed in Europe since January 2011. The product contains constituents already used in FDA-approved multipurpose solutions. The disinfecting agents are polyheximethylene biguanide (PHMB) and polyquaternium which are widely used in other multi-purpose solutions, including BioTrue® (Bausch & Lomb).

There has been extensive pre-clinical testing to demonstrate sufficient safety and efficacy of the test solution, and scientific justification for conducting this clinical study (see Investigator Brochure).

The purpose of this study is to evaluate the clinical performance of the contact lens care product Oté Sensation in a representative population of soft contact lens wearers. For comparison, the widely used soft lens multipurpose solution, BioTrue (Bausch & Lomb) will be used as a control. This control product has been tested in previous clinical trials.[2-4]

2 STUDY OBJECTIVES

To test whether the Oté Sensation multi-purpose solution is substantially equivalent to another multi-purpose solution (Bausch & Lomb BioTrue).

2.1 Primary Hypotheses

2.1.1 Efficacy Hypotheses

The Oté Sensation multi-purpose solution will be non-inferior to the Bausch & Lomb BioTrue solution in terms of:

Comfort (0-10), a non-inferior bound of 1.0 will be used.

Visual acuity (logMAR VA), a non-inferiority bound of 0.05 will be used

Wettability (0-4), a non-inferior bound of 0.5 will be used.

Deposits (*in situ* 0-4), a non-inferior bound of 0.5 will be used.

2.1.2 Safety Hypotheses

The Oté Sensation multi-purpose solution will be non-inferior to the Bausch & Lomb BioTrue solution in terms of:

Corneal staining – type (mean grade, 0-4), a non-inferior bound of 0.5 will be used.

Limbal hyperemia (grade, 0-4), a non-inferior bound of 0.5 will be used.

Bulbar hyperemia (grade, 0-4), a non-inferior bound of 0.5 will be used.

3 STUDY DESIGN & RATIONALE

This will be a 1-month, 200-subject, double-masked (care product), bilateral, randomized, comparative study. Subjects will be clinically evaluated at the initial baseline visit (Visit 1), then after 1 week and 1 month of lens wear having been randomly assigned to use one of six lens types and either the test or control solution.

The risks and benefits to the subjects taking part in this study are detailed in the Informed Consent Form.

3.1 Masking

To prevent bias, several steps will be taken to keep the investigators and subjects masked to the identity of the assigned solution:

- Subjects will be identified by subject numbers, which are unrelated to study solution assignments.
- Solution bottles will be over-labelled ('A', 'B' or 'C') and packaged in kit-boxes so that the identity of the study solution is not revealed. Therefore, investigators must only dispense solutions for the study that have been provided by the sponsor or clinical research organisation (CRO).
- If for any reason the investigator needs to be unmasked to the solution type that the study subject is using, they should follow the decoding procedures which will be present in the investigator study binder.

If required, for purposes of a subject's safe clinical management, the investigators will be able to learn the identity of the solution being used by contacting the study Clinical Research Associate (CRA).

3.2 Randomization

Subjects will be randomly assigned to use either the test or control solution. Two codes will be used for the test product and one code for the control so there are equal numbers of bottles of each code ('A', 'B' or 'C'). Subjects will also be randomly assigned to a lens type.

A random number generator (Microsoft Excel) will be used to determine the randomization of solutions and lens types. Each eligible subject will randomly be assigned to one of the lens care products and lens types using a blocking method and stratified by site. All sites will use both the test and control solutions. Each site will only use four of the six study lens types.

The randomization will be performed in stages. Firstly, the sites will be randomly assigned to four of the six study lens types. Secondly, subjects will be randomly allocated, by site, to one of the four lens types in blocks of four subjects. Thirdly, subjects within each site and lens type will be randomly allocated to one of the three solution codes (2 x Test, 1 x Control) in blocks of three subjects.

Subject ID numbers will be assigned consecutively to maintain randomization.

4 STUDY POPULATION

4.1 Number of Sites

Approximately ten sites located in the UK and the US each recruiting approximately 20 subjects/site (up to a maximum of 24 subjects/site). Investigators will be contact lens practitioners with at least three years' post-registration experience of contact lens practice.

4.1.1 Investigator Recruitment

Investigational sites will be identified by Visioncare Research. The Investigators will be required to fulfil the following criteria:

- Appropriately licensed eye care practitioner or contact lens optician
- At least three years, post-registration contact lens fitting experience.
- In-office email.
- Willingness to follow the study protocol and to co-operate with the study monitors.
- Experienced investigators trained in Good Clinical Practice (GCP) and the study protocol prior to commencing the study.
- Computers available to complete CRFs using electronic data capture (EDC).

All of the investigational sites will be trained and evaluated by on-line training modules before enrolling subjects.

This clinical study is designed to be in conformance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for GCP and all applicable local regulations.

4.2 Number of Subjects

Approximately 200 subjects will be enrolled in the study. Of these, approximately 133 subjects will use the test solution (Oté Sensation) and 67 subjects will use the control solution (Bausch & Lomb BioTrue).

Each subject will be required to attend up to four scheduled study visits over a period of approximately 1 month.

Subjects will be currently adapted soft contact lens wearers and will be recruited from the sites' existing patient database or via REC/IRB approved recruitment material. The anticipated enrolment period for the study is approximately 5 weeks.

The study population has been chosen to represent the range of patients that may use this multipurpose solution type.

4.3 Inclusion Criteria

Subjects must satisfy the following conditions prior to inclusion in the study:

i. Be a currently adapted soft contact lens wearer (>1 month of lens wear).

ii. Be at least 18 years of age.

iii. Refractive astigmatism ≤0.75D in both eyes.

iv. Have clear corneas and be free of any anterior segment disorders.

v. Be correctable through spherocylindrical refraction to 6/12 (20/40) (0.30 LogMAR) or better in each eye.

vi. Contact lens sphere requirement between +4.00D and -8.00D (inclusive).

vii. Require visual correction in both eyes (monovision allowed, no monofit).

viii. Have normal eyes with no evidence of abnormality or disease. For the purposes of this study a normal eye is defined as one having:
   a. No amblyopia
   b. No strabismus
   c. No evidence of lid abnormality or infection
   d. No conjunctival abnormality or infection that would contraindicate contact lens wear
   e. No clinically significant slit lamp findings (i.e. corneal staining, stromal edema, staining, scarring, vascularization, infiltrates or abnormal opacities)
   f. No other active ocular disease.

4.4 Exclusion Criteria

Any of the following will render a subject ineligible for inclusion:

i. Require toric or multifocal contact lenses.

ii. Previously shown a sensitivity to any of the study solution components.

iii. Any systemic or ocular disease or allergies affecting ocular health.

iv. Using systemic or topical medications that will in the investigator's opinion affect ocular physiology or lens performance.

v. Clinically significant (≥Grade 3) corneal staining, corneal stromal edema, corneal vascularization, tarsal abnormalities, bulbar hyperemia, limbal hyperemia, or any other abnormality of the cornea that would contraindicate contact lens wear.

vi. Any corneal infiltrates or any corneal scarring or neovascularization within the central 5mm of the cornea.

vii. Keratoconus or other corneal irregularity.

viii. Aphakia or amblyopia.

ix. Have undergone corneal refractive surgery or any anterior segment surgery.

x. Abnormal lacrimal secretions.

xi. Has diabetes.

xii. Known/reported infectious disease (e.g., hepatitis, tuberculosis) or an immunosuppressive disease (e.g., HIV).

xiii. History of chronic eye disease (e.g. glaucoma).

xiv. Pregnant or lactating or planning a pregnancy at the time of enrolment.

xv. Participation in any concurrent clinical trial or in last 30 days.

4.5 Subject Identification

Subjects will be identified by a four-digit code made up of the site number and their enrolment number.

The enrolment ID **must** be assigned to the subjects sequentially. Enrolment numbers will be in ascending order for each site. Thus, the first subject to be enrolled at Site 1 will be 01/01, the second 01/02 and so forth. The first subject to be enrolled at Site 2 will be 02/01, the second 02/02 and so on. No ID can be used more than once and enrolment is recorded on the Enrolment Log (Appendix 1).

4.6 Study Withdrawal Criteria

If during the study it becomes evident to either the Sponsor or the Clinical Research Organisation (Visioncare Research) that the study test solution (Oté Sensation) poses a threat to subject well-being, the study will be terminated. The REC/IRB will be advised of the reason for termination.

4.7 Subject Replacement

Subjects that are discontinued or drop out of the study will not be replaced.

4.8 Subject Compliance

To track compliance, subjects will be questioned at each of the follow-up visits about: their lens cleaning regimen, average contact lens wearing times (typical insertion and removal times), average number of days lenses are worn per week and their contact lens solution usage.

Subjects will also be asked to return their remaining solution at the end of the study.

5 MATERIALS

5.1 Study Solutions

The contact lens care systems that will be used in this study are recorded in Table 1. The solutions will be over-labelled and secured in kit-boxes.

Table 1: Care Product Details

	Test	Control
Brand	Oté Sensation	Bausch & Lomb BioTrue®
Manufacturer	Oté Pharma, Vluchtoord 38 5406 XP Uden Nederland	Bausch & Lomb U.K., Ltd. 106 London Road Kingston-Upon-Thames Surrey KT2 6TN UK
Disinfectant	polyaminopropyl biguanide 0.00002%, polyquaternium-2 0.0001%	polyaminopropyl biguanide 0.00013%, polyquaternium-1 0.0001%
Wetting and other agents	sodium hyaluronate	hyaluronan, sulfobetaine, poloxamine, boric acid, sodium borate, EDTA
Bottle size	300 or 360 ml	
Lens case	Oté lens case	B&L lens case
CE Mark	Yes	Yes

Subjects will be given a leaflet explaining the care system regimen and instructions. A rub and rinse step is included in the required regimen for both the test and control multipurpose solutions.

The solution bottles will be over-labelled and the subjects and investigators will be masked to the solution type.

Both solutions will be provided to the sites in sealed kit-boxes by the sponsor's representative (Visioncare Research) and all boxes containing the study care solutions must be fully accounted for.

5.2 Concomitant Care Products and Medications

Subjects must only use the care products issued by the Investigator. Subjects will be instructed to use no other lens care products (e.g. daily cleaner solution or protein remover), unless absolutely necessary. If rewetting drops are required, investigators should dispense preservative-free, unit dose wetting drops (e.g. AMO Blink™ Contacts Vials). All unused solutions (empty, unopened or partially used bottles) will be returned to the investigator during Visit 3.

All medications (prescription and over the counter) that the subjects are taking at enrolment will be documented on the eCRF at baseline, including supplements such as vitamins and minerals, and/or herbs taken by the participant.

5.3 Study Contact Lenses

Subjects will be randomly allocated to use one of six lens types (Table 2). Approximately 33 subjects will be allocated to use each lens type: approximately 22 using the test MPS product and 11 using the control product.

Each investigational site will use four of the six lens types (e.g. Types 1,2,3,4 or Types 1,2,5,6 or Types 3,4,5,6). Each site will utilise a stock of lenses so that, where possible, subjects may be dispensed lenses at the first visit. However, if the appropriate lenses are not immediately available, a second visit (Visit 1b) will be scheduled.

One of the lenses (Acuvue 2) is recommended for 2-weekly replacement. For these subjects, spare lenses will be issued during the Baseline visit with instructions for replacement.

In the event of lens loss or damage, replacement lens(es) will be issued at an unscheduled visit.

Table 2: Contact Lens Details

	Type 1	**Type 2**	**Type 3**	**Type 4**	**Type 5**	**Type 6**
Brand	ACUVUE® 2	PureVision®	Clariti	ACUVUE® VITA®	Air OPTIX®	Biofinity®
Manufacturer	Johnson & Johnson Vision Care	Bausch & Lomb	CooperVision	Johnson & Johnson Vision Care	Alcon	CooperVision
Material type	Conventional hydrogel	SH ionic, plasma oxidation surface treatment	SH non-ionic, not surface treated, high water	Silicone hydrogel (SH) non-ionic, not surface treated; contains PVP	SH non-ionic, surface modification by plasma polymerization	SH non-ionic, not surface treated; contains monomer n-vinyl pyrrolidone
Material	etafilcon A	balafilcon A	somofilcon A	senofilcon C	lotrafilcon B	comfilcon A
Water content	58%	36%	56%	41%	33%	48%
FDA Group	Group 4	Group 5A	Group 5B	Group 5Cr	Group 5Cm	Group 5C
Base curve / Diameter (mm)	8.30, 8.70 / 14.0	8.60 / 14.0	8.40 / 14.1	8.40 / 14.0	8.60 / 14.2	8.60 / 14.0
Replacement period	2-weekly	Monthly	Monthly	Monthly	Monthly	Monthly
Powers (D)	+4.00 to -8.00					

5.4 Care Product Accountability

Kit-box (containing study care product) Accountability forms and Lens Foil Logs will be kept by each site. A sample Kit-box Accountability form is shown in Appendix 2.

To monitor care product usage, any remaining unused study solution will be returned to the investigator at Visit 3 (empty, unopened or partially used). The returned kit-boxes will be recorded on the Kit-box Accountability Logs.

5.5 Study Document and Case Report Forms

The following forms will be completed where appropriate:

eCRFs:

- Baseline Visit
- Eligibility Checklist
- Dispensing Visit
- Follow-up Visit (1 week, 1 month)
- Unscheduled Visit
- Adverse Event Form
- Study Exit Form

Additional Forms

- Statement of Informed Consent
- Participant Information Sheet
- Enrolment Log
- Participant Information Guide
- Kit-box Accountability Log
- Source Document Record Label

Any corrections that need to be made to the essential study documents should be neatly crossed through such that the original entry can still be seen, the new entry written in, and the correction initialed and dated.

6 TREATMENT

6.1 Study Product Formulations

The study solutions are to be used in place of habitual contact lens care solutions and will be randomly assigned to the study subjects in labelled kit-boxes.

6.2 Device Administration

The lenses will be used on a daily wear re-usable, monthly or 2-weekly replacement basis, i.e. lenses worn during the day, removed at night and cleaned and stored with appropriate contact lens care products.

The care systems will be used according to the Patient Information Guide.

7 METHODS AND ASSESSMENTS

7.1 Subject Recruitment

Recruitment materials (adverts, letters, etc.) must be approved by the Research Ethics Committee (REC) or Investigational Review Board (IRB). VCR will provide an approved advertisement, letter and telephone script for recruitment purposes. Any changes to these must be submitted back to the REC/IRB via VCR.

The procedures listed below will be conducted on all subjects. Variables must be collected in the order they are listed on the eCRF.

To participate in this clinical study, the Investigator will explain the Statement of Informed Consent to the subject, ensure each subject understands the subject instructions and determine subject eligibility.

The Investigator is required to answer any questions the subject has concerning the study or the information contained in the Statement of Informed Consent and Patient Information Sheet.

A subject is considered enrolled when he or she signs the Statement of Informed Consent. Other study-related may not be activities undertaken prior to obtaining informed consent.

All subjects enrolled should be accounted for, even if they are not dispensed lenses or study product. A signed Statement of Informed Consent constitutes enrolment. After enrolment, a subject is considered active and should be accounted for at every visit until the completion of or discontinuation from the study.

Each site will be expected to enroll approximately 20 subjects, up to a maximum of 24 subjects.

7.2 Study Visits

7.2.1 Visit Schedule

There will be a maximum of four scheduled visits as follows:

Visit 1a: Baseline

Visit 1b: Lens issue (may be combined with Visit 1a)

Visit 2: 1 week follow-up (7 days ±3 days) – WT 1-3 hours

Visit 3: 1 month follow-up (30 days ±4 days)

A visit schedule form will be supplied to all sites which will list the visit windows and this can assist in arranging visits within the acceptable visit window.

The investigator should confirm with the subject that they are able to attend the follow-up visits within the visit window before enrolling them in the study. If, in extreme situations (sickness, unforeseen circumstances), the subject can only attend outside the visit window, the investigator should discuss with the CRA whether this visit can be considered a scheduled visit.

The 1-week, and 1-month follow-up visits may only take place when the subject attends wearing their lenses. If this is not the case and the subject is not experiencing any problems with their lenses or the study solutions, the appointment will be rescheduled, ideally within the visit window unless they are experiencing difficulty.

7.3 Questionnaire

At the 1 month visit, subjects will be asked a small number of questions about their experience with the study care product. The responses will be entered by the investigator into the eCRF.

7.4 Visit 1a: Baseline

The subjects should attend the first visit wearing their habitual lenses.

If they are not wearing their lenses, reschedule the visit.

The following procedures will be conducted on all subjects:

i. Allow the subject to read the Participant Information Sheet and Informed Consent and explain the nature, purpose, risks of the study etc. If he/she is agreeable, ask the subject to sign the Informed Consent Form and initial where appropriate. The investigator (or person taking the consent) should also sign the consent form. Provide the subject with a copy and retain the original.

ii. The subject is assigned with a Subject ID number according to the Enrolment Log. Subjects must be enrolled sequentially. Enter details on Enrolment Log as outlined on the form.

Baseline Measurements and Eligibility:

The following baseline measurements will be recorded on the Baseline eCRF:

i. Subject demographics (age, sex, medications and associated medical history, allergies)

ii. Habitual lens comfort (on insertion, during the day and prior to removal, 0-10)

iii. Symptoms, problems and complaints

iv. Vision
- Subjective vision quality: distance (0-10 scale)
- Monocular high contrast (HC) visual acuity (VA) with CLs (Snellen/logMAR to the nearest letter)
- Spherical over-refraction (SOR)
- Monocular and binocular HC DVA with SOR

v. Wearing times – habitual lenses:
- Wearing time at visit
- Typical insertion time
- Typical removal time
- Typical time CL comfort deteriorates
- Maximum wearing time in last month (hrs.)
- Days worn per week

vi. Details of habitual lenses and care system:
- Lens brand
- Care system brand

vii. Rewetting drop usage (type and frequency),

viii. Lens surface characteristics - habitual lenses
- Lens surface wetting (0-4)
- Lens deposits (film: 0-4; no. of white spots)

ix. Lens fit - habitual lenses
- Centration (0-2)
- Corneal coverage (Y/N)
- Post-blink movement (0-4)
- Tightness on push-up (0-4)
- Overall fit acceptance (0-4) and reason if Grade 2 or less.

x. Remove habitual lenses

xi. Full ocular health

xii. Monocular sphero-cylindrical refraction and monocular HC distance VAs (logMAR or Snellen to the nearest letter)

xiii. Biometry: Horizontal visible iris diameter (HVID), palpebral aperture (PA), keratometry (D/mm)

xiv. Slit lamp examination
- Limbal hyperemia (0-4)
- Bulbar hyperemia (0-4)
- Stromal edema (0-4)
- Vascularization (0-4)
- Palpebral conjunctival hyperemia (0-4)
- Upper palpebral roughness (0-4)
- Corneal staining by sector (type 0-4)
- Conjunctival fluorescein staining by quadrant (0-4)
- Other findings (0-4)

See Appendix 4 for grading scales and measurement instructions.

xv. Complete the eligibility checklist

If at this point the subject is found to be ineligible, then complete an Exit eCRF and exit the subject from the study.

If eligible, the subject will be assigned to one of the four lens types allocated to the site and assigned to one of the study solutions.

7.5 Visit 1b: Lens Fitting and Dispensing

The subjects will undergo a trial fit with the randomly allocated study lens type. If the appropriate study lenses are not available, a dispensing visit will be scheduled for another day.

i. Slit lamp – confirm continued eligibility if on a different day

ii. Record the parameters of the lenses on the Dispensing eCRF (lens type / lot number, lens parameters, etc.).

The performance of the lenses should be assessed after 10-15 minutes settling time and the following variables will be assessed:

iii. Subjective comfort (0-10)

iv. Vision
- Monocular HC DVA (with CL)
- Spherical over-refraction (SOR)
- Monocular HC DVA with SOR
- Binocular distance VA with CLs (Snellen/logMAR to the nearest letter)

v. Surface characteristics
- Lens surface wetting (0-4) and reason if Grade 1 or less.

vi. Lens fit
- Centration (0-2)
- Corneal coverage (Y/N)
- Post-blink movement (0-4)
- Tightness on push-up (0-4)
- Overall fit acceptance (0-4) and reason if Grade 2 or less.

To be successfully dispensed, subjects must show >Grade 2 lens fit acceptance with the trial lens and must be correctable to 6/12 (20/40) (0.30 LogMAR) or better in each eye. Trial lenses must also show >Grade 1 wettability.

Modifications to optimize the lens power will be allowed.

If the lens fit is acceptable, the investigator will issue the care system (Kit-box containing solution, lens case and instructions) that the subject was randomized to, and complete the Kit-box Accountability Log. All kit-boxes must be accounted for, even if they are not dispensed.

vii. The subject will be instructed to wear the lenses on a daily wear basis (at least 8 hours a day, 6 days per week) until the 1-week follow-up appointment, unless they experience a problem which warrants lens removal. In this case the subject should contact the investigator.

viii. The investigator or a clinical assistant will review the Participant Information Guide with the subject, which describes the procedures for contact lens wear, lens care, handling, cleaning and disinfecting. Any subject, who does not follow instructions to a degree that, in the Sponsor or Investigator's opinion, jeopardizes the subject's wellbeing or the validity of the study, will be discontinued.

ix. The investigator will complete the Source Document Record (Appendix 3).

7.5.1 Study Contact Lens Care Products

Eligible subjects will receive a kit-box containing either the test or control multi-purpose solution as indicated during Randomization. The kit-boxes allocated to each subject must be recorded on the Kit-box Accountability Log.

If a subject proves intolerant to any of the products, then the subject will be discontinued and an Exit form will be completed.

7.5.2 Visit 2: 1-week Follow-up

The 1-week follow-up visit will be scheduled 1 week (7 days ±3 days) from the lens dispensing date. The subject should wear the lenses 1 to 3 hours prior to the appointment. This has been shown to be the time period when solution-induced corneal staining is most evident.[5] If the subject attends without lenses or with more than 3 hours of lens wear on that day and they are not having any problems with their lenses or the study solution, the visit should be rescheduled, if possible within the visit window.

The following clinical test variables will be recorded on the Follow-Up Visit eCRF:

i. Wearing times:
- Days worn since last visit
- Typical insertion time
- Typical removal time
- Typical time CL comfort deteriorates
- Maximum wearing time since last visit (hrs.)
- Wearing time today (hrs.)

ii. Rewetting drop usage (type and frequency)

iii. Symptoms, problems and complaints

iv. Subjective assessments
- Overall comfort on insertion, during the day and prior to removal (0-10)

v. Vision
- Subjective vision quality: distance (0-10 scale).
- Monocular VA (CL, Snellen/logMAR to the nearest letter)
- Spherical over-refraction (SOR)
- Monocular HC DVA with SOR
- Binocular distance VA with CLs

vi. Lens surface characteristics
- Lens surface wetting (0-4)
- Lens deposits (film: 0-4, no. of white spots)

vii. Lens fit
- Centration (0-2)
- Corneal coverage (Y/N)
- Post-blink movement (0-4)
- Tightness on push-up (0-4)
- Overall fit acceptance (0-4) and reason if Grade 2 or less

viii. Remove lenses and store in sterile saline

ix. Slit lamp examination
- Limbal hyperemia (0-4)
- Bulbar hyperemia (0-4)
- Stromal edema (0-4)
- Vascularization (0-4)
- Palpebral conjunctival hyperemia (0-4)
- Upper palpebral roughness (0-4)
- Corneal staining (type 0-4)
- Conjunctival fluorescein staining by quadrant (0-4)
- Other findings (0-4)

See Appendix 4 for grading scales and measurement instructions.

Rinse away fluorescein with non-preserved saline.

Re-insert study lenses.

7.5.3 Visit 3: 1-month Follow-up

The 1-month follow-up visit will be scheduled 4 weeks (30 ± 4 days) from the dispensing date. The subjects should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses or the study solution, the visit should be rescheduled, if possible within the visit window.

The subject will be asked a small number of questions relating to the study care solution.

The same assessments will be followed as at the 1-week visit and will be recorded on the Follow-Up Visit eCRF. At the UK sites (if requested) worn lenses will be retrieved for return to Visioncare Research for *in vitro* analysis.

The kit-boxes containing any remaining study solution will be collected from the subjects. The Kit-box accountability log will be completed and the kit-boxes returned to Visioncare Research at the end of the study.

7.5.4 Study Exit

The Study Exit Form must be completed when a subject exits the study. This will occur either at study completion, i.e. at the 1-month visit, or if the subject is discontinued from the study at another time. A Study Exit eCRF must be completed for all subjects who have signed a consent form. The exit date should also be recorded on the subjects named patient notes i.e. the Source Document Record.

At the study Exit Visit the following measurements are taken:

i. Monocular sphero-cylindrical refraction.

ii. Monocular distance high contrast visual acuity (Snellen/logMAR) with sphero-cylindrical refraction. If VA is 2 or more lines worse than at Baseline, the reason will be recorded on the Study Exit eCRF.

If the subject is being exited without completing the full study schedule, further details need to be recorded on the exit form. This is described in Section 7.6 below.

7.5.5 Study Lens Accountability

At the end of the study, worn study lenses will be returned to Visioncare Research (UK sites only) in cases labelled with the subject ID number and date of retrieval. Any remaining care solutions will be returned in the kit-boxes along with the completed Kit-box accountability form.

Accountability of kit-boxes, and lenses ordered, received, dispensed or otherwise disposed of will be conducted at the end of the trial.

7.5.6 Clinical Variables

A full assessment of ocular health will be performed at the Baseline Visit.

Table 3 summarizes the clinical measurements to be taken at each visit:

Table 3: Summary of clinical measurements

	Baseline	**Dispensing**	**Follow-up (1-week, 1-month)**	**Exit**
	Visit 1a	**Visit 1b**	**Visits 2 & 3**	
Sphero-cylindrical refraction	✓			✓
Best corrected (sphero-cyl) Monocular VA	✓			✓
Keratometry/ Topography	✓			
Wearing time	✓		✓	
Comfort (on insertion, during the day, prior to removal)	✓		✓	
Symptoms, problems & complaints	✓		✓	
Vision quality	✓		✓	
Subjective assessments	✓		✓	
Monocular HC DVA	✓	✓	✓	
Spherical over-refraction (SOR)	✓	✓	✓	
Monocular HC DVA with SOR	✓	✓	✓	
Binocular distance VA with CLs	✓	✓	✓	
Lens fit assessments	✓	✓	✓	
Lens surface (wetting, deposits)	✓	✓	✓	
Slit lamp findings	✓	✓ if required	✓	✓

7.6 Subject Discontinuation

Subjects will be discontinued from the study in the event of any of the following occurring:

i. Unacceptable subjective discomfort (i.e. lens cannot be tolerated or worn)

ii. Unacceptable slit lamp findings (i.e. clinically significant, Grade 3 or 4)

iii. Unacceptable fit (i.e. lens too tight or too loose)

iv. At the discretion of the investigator or the subject

In the event of discontinuation, the Study Exit eCRF must be completed and the study exit date recorded on the source document record. The investigator will indicate the primary reason for discontinuation by selecting one of the boxes provided on the Exit eCRF. Further details can be provided in the 'comments' section if necessary.

7.7 Unscheduled Visits

An unscheduled visit is defined as any follow-up that occurs outside the visit window of the scheduled visit. A visit is also classified as unscheduled if the subject is seen a second time within the scheduled visit window.

Investigators should try as far as possible to schedule follow-up visits within the window. If this is not possible, and the visit falls outside the window, a protocol deviation eCRF will be completed to document. The investigator might also judge that a follow-up visit is in the best interest of the subject and schedule two visits within the same window, e.g. follow-up of an adverse event. Unscheduled visits are also made available anytime at the subject's request.

Unscheduled visits will be recorded on the follow-up eCRF. All variables listed on the Unscheduled Visit must be completed unless the subject exhibits a condition that prohibits the completion of a full visit. If this is the case, a written explanation is required in the comments section (e.g. not using solution due to discomfort after use).

Presenting VA and slit lamp variables must always be completed and the reason for the visit and any actions taken must be indicated in the 'comments' section.

7.8 Study Completion

The study is completed when all subjects have finished the 1-month Visit or have been discontinued.

Worn study lenses will be retrieved from the subjects and, if requested, returned to Visioncare Research in appropriately labelled cases. Lenses to be returned will be stored in saline and refrigerated until shipping. Similarly, any remaining care solutions will be returned in the kit-boxes along with the completed Kit-box Accountability Form.

7.9 Site Training and Visits

A site evaluation will take place during a visit to the site (with the exception for sites that have a valid onsite Site Evaluation Visit conducted within the past two years). Additional clinical training will be conducted by online training which will include an audio PowerPoint presentation and multiple-choice questions.

Monitoring visits will be documented in the Monitoring Plan which is a separate document.

8 ADVERSE EVENTS

An adverse event (AE) is defined as an undesirable clinical occurrence whether it is considered to be device-related or not. All adverse events regardless of whether device-related or not, will be monitored and reported on throughout the study. Possible adverse events are summarized in Table 4 below.

The investigator will be required to judge whether or not an adverse event is device-related. Reoccurring device-related events from the same subject are usually tabulated as separate events. In the case where more than one diagnostic finding is associated with an adverse

event, the event will be counted as one event and categorized under the most significant of the findings.

The investigator will be required to report all adverse events to the study CRO and all care product related adverse events to the REC/IRB. The seriousness of an adverse event is categorized as serious, significant, or non-significant (see Table 4).

Table 4: Adverse Events by Severity

Serious	Significant	Non-significant
Result in, or have the potential to cause either permanent impairment of a body function or damage to a body structure and may necessitate medical or surgical intervention. They include but are not limited to:	Symptomatic and warrant discontinuation of contact lens wear (temporary or permanent). They include but are not limited to:	Usually asymptomatic and do not warrant discontinuation of contact lens wear (temporary or permanent). However, as a precautionary measure the Investigator may decide to take action. They include but are not limited to:
MK – Microbial keratitis Permanent reduction in best spectacle corrected visual acuity (≥ 2 lines) Central (4mm) corneal opacity Central corneal neovascularization Iritis Hypopyon Hyphema Penetration of Bowman's membrane Any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect	CLPU – Contact lens peripheral ulcer CLARE – Contact lens associated red eye Significant Infiltrative Event (S.I.E) SEAL – Superior epithelial arcuate lesion Corneal warpage SLK – Superior limbic keratoconjunctivitis Other significant ≥Grade 3 corneal findings (e.g. edema or abrasions) Any corneal event which necessitates lens wear discontinuation of > 2 weeks Non-CL related anterior segment events e.g. EKC – epidemic keratoconjunctivitis Temporary loss of ≥ 2 lines of Best Spectacle Corrected Visual Acuity New corneal scar without positive history	CLPC – Contact lens associated papillary conjunctivitis SPK – Superficial Punctate Keratitis Non-significant infiltrative event Blepharitis Meibomitis Contact dermatitis Localized allergic reactions, including solution-related ocular toxicity Conjunctivitis: Bacterial, Viral, Allergic Keratoconjunctivitis Any corneal event not explicitly defined as a serious or significant event which necessitates lens wear discontinuation <2 weeks Other slit lamp findings requiring treatment

For additional information, questions or assistance in recording potential adverse events, contact Visioncare Research.

8.1 Adverse Event Categorization

The investigator will be required to rate the likelihood of an event being device-related (Possible, Probable, Highly Probable) or non-device-related (No) in their adverse event evaluation.

All device-related adverse events will be tabulated and reported in the final report.

8.2 Adverse Event Reporting

On finding an adverse event the investigator will complete an Adverse Event Form (AE eCRF) to document the condition.

The Investigator must notify Visioncare Research of any type of AE, so that they are able to provide advice and support to the Investigator on how to proceed.

The Investigator must do this by providing the information on the AE eCRF to Visioncare Research by eCRF, email, fax or telephone as soon as possible and no later than:

- 24 hours from discovery if event is Serious
- 2 working days from discovery if event is Significant or Non-Significant

Visioncare Research will advise the investigator to notify the REC/IRB no later than:

- Sterling IRB (US) reporting requirements, within 10 working days from the date of discovery.
- NRES REC (UK) reporting requirements, 15 working days from the date discovery.

Visioncare Research may notify the REC/IRB on behalf of the investigator.

To report to the REC/IRB send a covering letter with details as per the REC/IRB requirements. This usually includes the subject identifier and a brief description of how the AE was discovered, the subject's condition and any follow-up anticipated. The AE Form is also sent to the REC/IRB. These documents can be sent by fax or email depending on the individual REC/IRB facilities.

The investigator must also notify Visioncare Research in writing that the AE has been reported to the REC/IRB.

8.3 Device-Related Adverse Event Documentation

Investigators are required to document and follow-up all AEs.

All AEs are documented on an AE eCRF upon event discovery. One AE eCRF is used per eye.

Procedure:

The investigator has the responsibility to:

1. Complete as much information as possible on the AE eCRF upon event discovery. This includes:
   - A detailed description of the AE and a diagnosis, including a probable cause
   - Detailed drawings that detail size, location and depth or photographs (if necessary)
   - Likelihood of the AE being device-related and whether lens or care product-related.
2. If serious, collect any contact lenses worn, solutions, and the lens case used at the time.
3. Report the AE to the sponsor (via CRO, i.e. Visioncare Research) and the REC/IRB within the specified timelines (see Adverse Events section 8.2).
4. Follow study subject until resolution recording all information on an unscheduled visit eCRF, including VA, symptoms and slit lamp findings, resolution and permanent sequelae if any.

5. Complete all remaining information as required by the AE eCRF. If follow-up of the AE is required, the follow-up section can only be completed when all follow-up visits are done. Additional information that will be completed on the AE eCRF include:

    - Outcome, ocular sequelae if any
    - Whether the patient is discontinued from the study as a result of the AE

8.4 Adverse Event Follow-up

The Investigator will conduct follow-up examinations until the condition has either:

- Returned to pre-event status,
- Stabilized, or
- Been satisfactorily explained.

If the subject is referred for medical attention, they will be tracked by the investigator until the aforementioned conditions are met.

Follow-up data will be collected on Follow-up Visit eCRFs (marked as unscheduled visit) and on the AE eCRF.

If Corneal Staining is present of Grade 3 or more, another follow up visit should be scheduled within 24 hours.

The investigator should use his/her clinical judgement as to whether or not the subject reporting with an adverse event should continue in the study.

8.4.1 Sponsor Safety Responsibilities

The sponsor will ensure that all participating investigators are promptly informed of significant new safety information with respect to the device being studied as per regulatory bodies' requirements.

To comply with this, the sponsor is responsible for promptly advising (in writing, via Visioncare Research) all investigators conducting clinical studies using an investigational device, of any incidents of serious or unexpected adverse events/unanticipated adverse device effects reported for the devices/products involved in those studies.

9 DATA MANAGEMENT

9.1 Electronic Case Report Forms/Data Collection

The data for this study will be collected on electronic report forms (eCRFs) using an electronic data collection (EDC) system. Designated study site personnel will enter study data into the electronic CRFs (eCRFs) using the Medrio EDC system. Medrio is compliant with all relevant aspects of ICH/Good Clinical Practices and 21 CFR Part 11 (Electronic Records & Electronic Signatures) regulations.

9.2 Data Quality Assurance

When eCRFs are reviewed at Visioncare Research, they will be subjected to error checking and data queries will be raised electronically via the EDC system for resolution of omissions and discrepancies by the investigator.

Before the final closing of the database, the data will be checked and approved for analysis as per Visioncare Research SOPs. This includes checking for missing or erroneous data entries

9.3 Data Entry and Storage

All study data shall be entered into the study eCRFs. The statistical analyses will be completed by the CRO using SAS software (SAS Institute Inc., Version 9.4).

10 SAMPLE SIZE AND STATISTICAL METHODS

10.1 Sample Size Rationale

The sample size was selected to be in agreement with ISO 11980:2012. The sample size assumes a drop-out rate of <10% and was rounded up to allow for equal subject numbers and even enrolment at each site.

10.2 Statistical Analysis Plan

General considerations: All data summaries and statistical analyses will be performed using the SAS software Version 9.4 or higher (SAS Institute, Cary, NC). Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis. Missing data will be excluded from the analysis. Unscheduled visits will be excluded from the statistical analysis.

Descriptive statistics will be reported by solution type at baseline, dispensing, and each follow-up visit according to ISO 11980:2012. Continuous variables will be summarized using sample size (N), mean, standard deviation (SD), minimum and maximum, and categorical data variables will be summarized using the sample size, frequency distribution (count and percentage of subjects or eyes in each category), mean, median and SD.

Analysis Population: Statistical Analysis for hypothesis testing will be performed on all evaluable subjects. All inference will be carried out with an overall type I error rate controlled at 0.05.

Analysis of comfort: Results will be analyzed using a linear mixed model including the experimental design factors: solution type, visit and their interaction will be included as fixed effect factors and site and subject as random effects.

Comparisons between the test and control solutions will be carried out using pairwise one-sided confidence intervals constructed for least-square mean differences (mean difference calculated as Test minus Control). Non-inferiority will be concluded if the lower confidence limit is greater than -1.0.

Analysis of visual acuity: Results will be analyzed using a linear mixed model including the experimental design factors: solution type, visit and their interaction will be included as fixed effect factors and site and subject as random effects.

Comparisons between the test and control solutions will be carried out using pairwise one-sided confidence intervals constructed for least-square mean differences (mean difference calculated as Test minus Control). Non-inferiority will be concluded if the upper confidence limit is less than +0.05 logMAR.

Analysis of wettability: Results will be analyzed using a linear mixed model including the experimental design factors: solution type, visit and their interaction will be included as fixed effect factors and site and subject as random effects.

Comparisons between the test and control solutions will be carried out using pairwise one-sided confidence intervals constructed for least-square mean differences (mean difference calculated as Test minus Control). Non-inferiority will be concluded if the lower confidence limit is greater than -0.5.

Analysis of deposits: Results will be analyzed using a linear mixed model including the experimental design factors: solution type, visit and their interaction will be included as fixed effect factors and site and subject as random effects.

Comparisons between the test and control solutions will be carried out using pairwise one-sided confidence intervals constructed for least-square mean differences (mean difference calculated as Test minus Control). Non-inferiority will be concluded if the upper confidence limit is less than +0.5.

Analysis of slit lamp findings: First the results will be averaged across each sector. Average results will be analyzed using a linear mixed model including the experimental design factors: solution type, visit and their interaction will be included as fixed effect factors and site and subject as random effects.

Comparisons between the test and control solutions will be carried out using pairwise one-sided confidence intervals constructed for least-square mean differences (mean difference calculated as Test minus Control). Non-inferiority will be concluded if the upper confidence limit is less than +0.5.

Additional analyses:

- Overall occurrence of slit lamp findings of Grade 2 or higher
- Overall occurrence of lens VA findings worse than 6/12 (20/40)
- Overall occurrence of clinically significant lens surface deposits (>Grade 1)
- Ocular adverse events.

Any deviations from the above analysis will be documented in the report.

10.3 Interim Analysis

There will be no interim analyses and, therefore, there are no criteria for early termination of the clinical investigation on statistical grounds.

11 GENERAL STUDY MANAGEMENT

11.1 Relevant Standards

This protocol has been developed in accordance with the following:

- ISO 14155:2011 Clinical Investigation of Medical Devices for Human Subjects
- ISO 11980:2012 Ophthalmic Optics - Contact lenses and contact lens care products
- ICH Harmonised Tripartite Guideline for Good Clinical Practice
- Declaration of Helsinki

The study will also be carried out in accordance with the Visioncare Research Quality Management System (ISO 9001:2008, ISO 13485:2012)

11.2 Ethical Review

The study protocol, patient instruction sheet, questionnaire and Informed Consent Form will be submitted to the REC/IRB (UK – NRES, US - STERLING). A favorable opinion will be received prior to undertaking the study. The approval letter should clearly mention the approval/favorable opinion of the protocol, the patient information sheet and informed consent form, including respective version dates.

If significant protocol changes which require the preparation of an amendment are necessary, written approval will be obtained prior to implementation.

11.3 Protocol Deviations

The investigators will not deviate from the protocol without written approval from Visioncare Research.

Any serious breaches of GCP that are likely to effect to a significant degree the safety, physical or mental integrity of the trial subjects or scientific value of the trial must be immediately notified to the Sponsor (and Visioncare, if reported by the investigator) to permit notification to the REC/IRB within 10 days after becoming aware of the breach.

In medical emergencies, the investigator will use their judgement and remove the subject from immediate hazard. Any significant changes or deviations in the protocol will be the subject of a protocol amendment and must be pre-approved by the REC/IRB.

If an unexpected deviation from the protocol occurs, the investigator must notify Visioncare Research immediately and the deviation from the protocol will be documented and resolved on a Protocol Deviation eCRF.

11.4 Premature Termination of the Study

The sponsor reserves the right to terminate the study at any time for any reason including adverse effects. The applicable authorities also have the right to terminate the study. If it is determined that an unanticipated adverse device effect presents an unreasonable risk, then the entire investigation or part of the investigation presenting the risk shall be terminated as soon as possible. A written statement fully documenting the reasons for such termination will be provided to the REC/IRB.

11.5 Source Documentation

The eCRFs will be considered the source document, unless otherwise documented. The sponsor's representatives (Visioncare Research) will be authorized to gain access to the source documentation for the purposes of monitoring and auditing the study (see sections 11.6 and 11.7).

The Source Document Record must be completed to comply with GCP guidelines. It is a permanent record within the patient's records/notes that documents the subject's involvement in a clinical research study.

Contents of the source document record:

- Study number
- Subject ID
- Confirmation that subject met eligibility criteria
- Confirmation that subject signed the informed consent
- Confirmation that subject received a signed and dated copy of informed consent
- Date enrolled
- Details of Solution (code) assigned
- Details of lenses worn on study
- General notes
- Adverse events
- Exit date
- Whether subject completed the study or discontinued
- Investigator's signature

The Source Document Record will be completed for each subject upon enrolment and then updated when required, e.g. when subject exits the study.

11.6 Monitoring

Investigational site monitoring will be performed by a qualified study monitor identified by the Sponsor or Visioncare Research. On-site visits will be completed at each site. The frequency and procedure of the monitoring visits will be documented in the monitoring plan which is in a separate document. The investigator will allow the study monitor and sponsor representatives or REC/IRB to observe procedures and inspect study records and subjects' medical records throughout the study to verify protocol compliance, case report completeness and investigational material accountability. Should the investigator be found to be non-compliant and unwilling or unable to convert non-compliant practices, Visioncare Research in consultation with the Sponsor will terminate the investigator's role in the investigation and the REC/IRB will be notified.

11.7 Audits

The Investigator shall permit Visioncare Research, the Sponsor, the REC/IRB and the appropriate regulatory authorities to inspect its facilities, equipment, and study-related records, data and other documents upon reasonable notice. In addition, the regulatory authorities or the REC/IRB may conduct such inspections as they deem necessary at any time whether or not advanced notice is given by them. The Investigator agrees to notify the Sponsor or Visioncare Research within 24 hours (or as soon as reasonably practicable) of the start of any unannounced inspection by the REC/IRB or the regulatory authorities or of the receipt from the REC/IRB or the regulatory authorities of a notice of inspection whether given in writing or orally. If such notice is in writing, a copy with any attachments thereto shall be provided to Visioncare Research or the Sponsor.

11.8 Records Retention

Investigators will be required to retain all records and the study file for a period of at least 10 years unless otherwise authorized by the Sponsor. As the clinical research organisation supervising the study, Visioncare Research will also retain the written records for the same period of time.

11.9 Confidentiality and Publication

By signing the Informed Consent form the subject authorizes the sponsor and the sponsor's representatives (Visioncare Research) to access their optometric clinical records. The authorization will be indefinite; however, subjects will have the right to reverse this authorization at any time.

All patient information will have the patient name (or any information that can identify the patient) removed before leaving the principal investigator's site.

In accordance with the VCR Confidentiality Policy, the data, information, and reports arising from this project are the property of the sponsor. VCR will not release to a third party any information arising from this study unless required to do so by a legal or regulatory body. The electronic records will also be handled in accordance with the UK Data Protection Act (1998).

The investigators will not be permitted to publish or present at scientific meetings results obtained from the clinical study without prior written consent from the sponsor.

12 REFERENCES

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13 ABBREVIATIONS

AE	Adverse event
CL	Contact lens
CRA	Clinical Research Associate
CRF	Case report form
CRO	Clinical Research Organisation
D	Diopter
eCRF	Electronic case report form
EDC	Electronic data collection
EDTA	ethylenediaminetetraacetic acid
GCP	Good Clinical Practice
HC	High Contrast
ICH	International Conference on Harmonization
IRB	Investigational Review Board
logMAR	Log of Minimum Angle of Resolution
MPS	Multipurpose solution
NRES	National Research Ethics Service
PHMB	polyheximethylene biguanide
REC	Research Ethics Committee
SH	Silicone hydrogel
SOP	Standard Operating Procedure
SOR	Spherical over-refraction
UK	United Kingdom
US	United States
VA	Visual acuity
VCR	Visioncare Research
WT	Wearing time

APPENDIX 1

Template Enrolment Log (Sample)

VISIONCARE RESEARCH

OTES-3301

ENROLMENT LOG

SITE: 01

A maximum of 24 subjects may be enrolled. All subjects must be enrolled sequentially.
Subjects should only be entered onto the Enrolment Log once they have signed study Informed Consent Form.

Subject ID Site -Sub	Subject Name	Enrolment Date (Consent signed) (dd/mm/yy)	Subject Eligible	Reason if not eligible
01-01	***John SMITH***	***10 / 06 / 17***	(Y) / N	
01-01		/ /	Y / N	
01-02		/ /	Y / N	
01-03		/ /	Y / N	
01-04		/ /	Y / N	
01-05		/ /	Y / N	
01-06		/ /	Y / N	
01-07		/ /	Y / N	
01-08		/ /	Y / N	
01-09		/ /	Y / N	
01-10		/ /	Y / N	
01-11		/ /	Y / N	
01-12		/ /	Y / N	
01-13		/ /	Y / N	
01-14		/ /	Y / N	
01-15		/ /	Y / N	
01-16		/ /	Y / N	
01-17		/ /	Y / N	
01-18		/ /	Y / N	
01-19		/ /	Y / N	
01-20		/ /	Y / N	
01-21		/ /	Y / N	
01-22		/ /	Y / N	
01-23		/ /	Y / N	
01-24		/ /	Y / N	

ENROLMENT LOG OTES-3301 v1 dated 24 May 2017

APPENDIX 2

Template Kit-Box Accountability Form (Sample)

OTES-3301
Kit-box Accountability Log

Site #

Instructions:

1. When Kit-boxes are received at site, check the Kit-box number and record date of receipt.
2. When the Kit-box is dispensed record subject ID and date dispensed.
3. Record the date the Kit-box is returned by the subject to the site.
4. Record the date the Kit-box is returned to Visioncare Research.

Kit-box Number	Solution (A, B or C)	Date Received	Subject ID #	Date Dispensed	Date Returned to Site	Date Returned to Visioncare Research

Investigator's name: _____

Investigator's Signature_____ Date:_____

[Page 1 of 2]

APPENDIX 3

Template Source Document Record (Sample)

Source Document Record

OTES-3301

Sub ID: ___ / _____ Met Inclusion/Exclusion Criteria: YES / NO

Signed consent: YES / NO Received sign/dated copy of consent: YES / NO

Enrolment Date: ____ / ___ / ____

Multi-Purpose Solution Code: _____

Lens Code:_____

General Notes:

Adverse Event Occurred? YES / NO (Record details of AE below)

Adverse Event Resolved? YES / NO

Exit Date: ____ / ___ / ____ Discontinued? YES / NO

Investigator signature: _____

APPENDIX 4

Grading Scales & Measurement Instructions

Variable	Assessment Method	Grading/Measurement System
Wearing Times		
Average Wearing Time	Typical time of day when lenses inserted and removed.	Time of day to nearest half hour
Comfortable Wearing Time	Typical time of day when subject first experiences lens awareness or irritation.	Time of day to nearest half hour when first aware of lenses OR 'Always comfortable' (tick-box)
Maximum Wearing Time	Maximum WT on a given day since last visit.	Hours to nearest half hour
Subjective Assessments		
Comfort	Assessed by subject.	0 to 10 scale 10 = cannot be felt
Vision		
Distance VA – High contrast	Measured using Snellen (or logMAR) chart.	Visual acuity (VA) to nearest letter
Vision Quality	Assessed by subject	0 to 10 scale 10 = perfect
Lens Fit **- assessed using slit lamp**		
Lens Centration	Lens centration will be recorded by degree and direction in the primary position.	0 Centered - optimal 1 Decentered slightly 2 Substantially decentered (≥0.5mm) If decentered, direction(s) will be recorded as: Superior, Inferior, Nasal, Temporal
Corneal Coverage	Assessed in primary gaze.	Y Yes, full corneal coverage at all times N No, incomplete corneal coverage
Post-Blink Movement	Assessed immediately after the blink - lower lid to be depressed only if necessary for observation.	0 Insufficient, unacceptable movement 1 Minimal, but acceptable movement 2 Optimal movement 3 Moderate, but acceptable movement 4 Excessive, unacceptable movement
Lens Tightness – Push-up test	Assessed by digital push-up test (gentle push of the lens upward using the lower lid) with eye in primary gaze position and observing ease of push-up and speed of return to original position.	0 Insufficient, unacceptable movement 1 Minimal, but acceptable movement 2 Optimal movement 3 Moderate, but acceptable movement 4 Excessive, unacceptable movement

Variable	Assessment Method	Grading/Measurement System
Overall Fit Acceptance	Assessed by the investigator based on lens fit alone (i.e. not comfort or vision).	0 Should not be worn 1 Borderline but unacceptable 2 Min. acceptable, early review 3 Not perfect but OK to dispense 4 Perfect
Biomicroscopy		
Stromal Edema	Assessed with indirect white light, medium-high magnification and observing any corneal haze against the pupil. More significant changes (e.g. striae, folds) can be observed with direct illumination.	0 NONE: No corneal haze, normal transparency 1 TRACE: Just detectable haze 2 MILD: Faint corneal striae (2 or fewer) 3 MODERATE: Pronounced corneal striae (3) 4 SEVERE: Folds in Descemet's membrane and ≥4 striae
Limbal & Bulbar Hyperemia	Assessed using slit lamp with white light, low-medium magnification	0 NONE: No injection present 1 TRACE: Slight limbal (mild segmented), bulbar (mild regional), and/or palpebral injection 2 MILD: Mild limbal (mild circumcorneal), bulbar (mild diffuse) injection 3 MODERATE: Significant limbal (marked segmented), bulbar (marked regional or diffuse) injection 4 SEVERE: Severe limbal (marked circumcorneal), bulbar (diffuse episcleral or scleral) injection
Corneal Vascularization	Assessed using slit lamp with diffuse white light, low-medium magnification. The depth and location of any vascularization should also be recorded.	0 NONE: No vascular changes 1 TRACE: Vessel penetration <1.0mm 2 MILD: Penetration of limbal vessels ≤1.5mm 3 MODERATE: Penetration >1.5mm to 2.0mm 4 SEVERE: Penetration more than 2.0mm inside the limbus
Upper Palpebral Conjunctival Roughness	Assessed using slit lamp with white light, low-medium magnification.	0 NONE: Uniform satin appearance of conjunctiva 1 TRACE: Slight conjunctival injection without loss of texture 2 MILD: Mild or scattered papillae/follicles less than 1mm in diameter 3 MODERATE: Significant papillae/ follicles less than 1mm in diameter and/or marked conjunctival injection 4 SEVERE: Localized or generalized papillae/ follicles 1mm or more in diameter
Palpebral Conjunctival Hyperemia	Assessed with diffuse white light, low-medium magnification using CCLRU images for reference	0 None 1 Slight injection of conjunctival vessels 2 Mild injection 3 Moderate injection 4 Severe injection

Variable	Assessment Method	Grading/Measurement System
Corneal Staining Type	Assessed by sector with fluorescein, blue light, yellow filter and full beam using medium magnification. Cornea will be assessed by sector (C, N, T, I, S)	0 NONE: No staining 1 Micropunctate – Superficial, minute/fine/pinpoint punctate staining, includes superficial stippling 2 Macropunctate – Focal, ball-like punctate staining, includes moderate stipple staining 3 Coalesced macropunctate 4 Patch (> 1 mm)
Conjunctival Staining	Assessed by quadrant using fluorescein, blue light, yellow filter, low-medium magnification. Ignore conjunctival indentation with no staining.	0 None 1 Minimal diffuse punctate 2 Coalescent punctate 3 Confluent 4 Widespread confluent
Other Significant Findings	Describe finding and grade severity	0 NONE 1 TRACE 2 MILD 3 MODERATE 4 SEVERE
Lens Surface Characteristics		
Lens Surface Wetting	Lens surface wettability rated on the appearance of the lens surface and the drying time viewed with a slit lamp under low magnification.	0 VERY POOR: Immediately displaying non-wetting areas on lens surface. 1 POOR: Irregular surface appearance; drying time <interblink period. 2 ACCEPTABLE: Smooth surface appearance immediately after the blink becoming irregular with time; drying time ≥ interblink period. 3 GOOD: Typical lens appearance with long drying time. 4 EXCELLENT: Appearance of a healthy cornea with very long drying time.
Film Deposits	Any film deposits (protein/lipid) attached to the front surface of the lens. Scan the entire lens surface (10- 20X) for the presence of deposits.	0 No film. 1 Slight film visible only under magnification. 2 Moderate film only under magnification. 3 Moderate film visible to the naked eye 4 Heavy film visible to the naked eye
White Spot Deposits	Assessed using slit lamp with white light, low-medium magnification	Number of white spot deposits

MEASUREMENT INSTRUCTIONS

DISTANCE VISUAL ACUITY

Measure Visual Acuity (VA) to the nearest letter.

If the subject reads more than half of the letters on a given line, ask them to attempt the next line. Then if the subject is able to read letters on the next line assume that the previous line was correctly read for the purposes of recording VA.

EXAMPLE 1: If all six of the letters on the 6/9 line were correctly identified and the subject then correctly identified all but one of the six letters on the 6/7.5 line, record the acuity as:

6 / 7.5 - 1

EXAMPLE 2: If the subject correctly identified four of the six letters on the 6/6 line and two of the six letters on the 6/5 line were correctly identified, record the acuity as:

6 / 6 + 2

If necessary, VA can also be recorded on the eCRF in logMAR