CLINICAL TRIAL PROTOCOL

Protocol Title - Long:	Microbial contamination rates on the back surface of soft contact lenses in short-term, randomized, contralateral non-dispensing studies.
Protocol Title - Short:	Smart Touch non-dispensing handling studies
Protocol ID Number:	SOVS-2017-050
Amendment Number:	N/A
Version Date:	18th December 2018

CONFIDENTIALITY

APPROVALS

[redacted], Author/Sub-investigator	Date
[redacted], Sub-investigator	Date
[redacted] Principal Investigator	Date
[redacted]	Date

SPONSOR	
Sponsor:	[redacted]
Address:	[redacted]

CO-SPONSOR	
Co-Sponsor:	[redacted]
Address:	[redacted]

SUMMARY OF FINAL PROTOCOL & AMENDMENTS

Initial/ Amend #	Version Date	Author	Main Changes
Final	**1st September 2017**	[redacted]	N/A
A1	10th October 2017	[redacted]	Section 3 Medical Expert and Section 12.6 Referrals – changed to "Emergency Department" Section 4.1 Table 4 –contact lens details corrected Section 6 Trial Design – clarification in regards to "aseptic lens removal" has been added Section 6.1.2 Randomization and masking and Section 10.1 Administration of study lenses – changed the lens handling technique for lenses extracted from the conventional blister pack, and added practice for participants to familiarize themselves with the lens handling technique to remove a contact lens from the Smart Touch Technology blister pack
A2	18th December 2018	[redacted]	Addition of evaluation of the impact of EDTA in the packaging solution on microbial contamination rates. Revisions made to Tables 4 and 5, Sections 1, 4, 5, 6,
A3			

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1. PROTOCOL SYNOPSIS

Table 1

Protocol Title	Microbial contamination rates on the back surface of soft contact lenses in short-term, randomized, contralateral non-dispensing studies.	
Protocol ID Number	SOVS2017-050	
Trial Classification	Evaluation	
Investigator(s)/Site(s)	Eye Research Group @ SOVS The University of New South Wales Sydney, Australia	
Overall Duration of Trial	4 months	
Number of Trial Participants Planned	25 to complete each arm	
Planned Start Date	May 2017	
Primary Objective	To compare the microbial contamination rates on the back surface of hydrogel and silicone hydrogel contact lenses extracted from Smart Touch Technology blister packs versus conventional lens packaging, and the impact of EDTA in the packaging solution after short-term placement on the eye.	
Secondary Objectives	○ To compare the microbial contamination rates of the worn contact lenses to those on the participants' hands/fingers used to conduct lens insertion ○ To determine the sample size required to conduct Phase 2 of the study (a randomized, bilateral cross-over, dispensing study to evaluate ocular redness, comfort and lens contamination rates) based on the detection limits for microbial contamination rates on the back surface of worn contact lenses	
Primary Safety Variable(s)	Visual acuity Biomicroscopy: ocular redness, corneal details and staining	
Primary Efficacy/Performance Variable	Level of microbial contamination of on the back surface of worn soft contact lenses	
Experimental design	☐ Retrospective ☒ Prospective ☒ Single group ☐ Multiple group ☐ Parallel group ☐ Cross over ☐ Contralateral	☐ Single masked (Trial Participant) ☒ Single masked (Investigator) ☐ Double masked ☐ Sponsor masked ☐ Open label ☐ Other
Study product details	**Name**	Smart Touch Technology
	Manufacturer	Menicon Co. Ltd.
Inclusion criteria	Participants enrolled in the trial must be: ▪ Able to read and comprehend English and give informed consent as demonstrated by signing a record of informed consent; ▪ Be at least 18 years old;	

	▪ Experienced soft contact lens wearer; ▪ Willing to refrain from wearing contact lenses for 24 hours prior to the scheduled study visits.
Exclusion criteria	Participants enrolled in the trial must NOT: ▪ Have any active corneal infection, ocular disease or systemic disease that would affect wearing of contact lenses; ▪ Use or have a need for any systemic or topical medications which may alter normal ocular findings/are known to affect a participant's ocular health/physiology either in an adverse manner or risk providing a false positive; ▪ Have had eye surgery within 12 weeks immediately prior to enrolment for this trial; ▪ Have contraindications to contact lens wear; ▪ Have a greater than 2 line reduction in habitual visual acuity while wearing the study contact lenses; ▪ Be currently enrolled in another clinical trial; ▪ Be pregnant (verbal self-report); The Investigator may, at his/her discretion, exclude anyone else who they believe may not be able to fulfil the study requirements, or if it is believed to be in the participant's best interests.
Human Research Ethics Committee Status / **Regulatory Status**	This trial requires Human Research Ethics Committee approval prior to study initiation, any advertising, and participant consent/enrolment. This trial requires approval from the Therapeutic Goods Administration.

2. INVESTIGATOR(S)

Table 2

Name:	[redacted]
Title:	[redacted]
Site Address:	[redacted]
Telephone:	[redacted]

Name:	[redacted]
Title:	[redacted]
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Title:	[redacted]
Site Address:	[redacted]
Telephone:	[redacted]

Name:	[redacted]
Title:	[redacted]
Site Address:	[redacted]
Telephone:	[redacted]

3. MEDICAL EXPERT

Table 3

Name:	[redacted]
Title:	[redacted]
Address:	[redacted]
Telephone:	[redacted]

4. BACKGROUND INFORMATION

4.1. Product

Following lens manufacture, disposable soft contact lenses are packaged in blister packs, with lenses free floating in solution. Extracting the contact lens from the blister pack involves removing the lens and manipulating the lens with both hands to ensure the lens is of the correct orientation prior to inserting the lens on the eye.

Contact lens manufacturer Menicon have developed Smart Touch Technology blister packaging designed to minimize the amount of lens handling prior to lens insertion. Contact lenses are pinched from the blister pack such that only the front surface of the lens is handled for insertion directly onto the eye.

The potential benefits of reduced handling of contact lenses during insertion include: minimizing the transfer of microbes to the eye, which may reduce the incidence of contact lens-related adverse events, reduced ocular redness and improved ocular comfort.

Details of the contact lenses to be evaluated in this trial are shown in Table 4.

Table 4

Visit	Contact Lenses	Material Type	Material	Power (D)	Diameter (mm)	Base Curve (mm)	TGA Approved *(for sale in Australia)*	EDTA
1 or 2	Miru 1day UpSide in Smart Touch™	Silicone hydrogel	midafilcon A	-0.50	14.2	8.4	No	Yes
1 or 2	Miru 1day UpSide in conventional	Silicone hydrogel	midafilcon A	-0.50	14.2	8.4	No	Yes
1 or 2	Miru 1day Menicon Flat Pack in Smart Touch™	Hydrogel	hioxifilcon A	-0.50	14.2	8.4	Yes	No
1 or 2	Miru 1day Menicon Flat Pack in conventional	Hydrogel	hioxifilcon A	-0.50	14.2	8.4	Yes	No
3	Miru 1day UpSide in Smart Touch™	Silicone hydrogel	midafilcon A	-0.50	14.2	8.4	No	No
3	Miru 1day Menicon Flat Pack in Smart Touch™	Hydrogel	hioxifilcon A	-0.50	14.2	8.4	Yes	Yes

4.2. Summary

4.2.1. Risks and Benefits

Risks of the Clinical Trial

As this will be a short-term non-dispensing study with three visits, all participants will be fitted with the same lens power (-0.50D) in each eye. This low power has been selected such that study participants with a habitual spectacle correction can wear their regular spectacles over the study contact lenses and still achieve similar vision. For study participants who do not require any habitual spectacle correction, this low power optical correction should still provide comparable and adequate vision for the short duration of lens wear (45 minutes). However, to ensure safety, participants' vision will be measured and only those who can achieve visual acuity within 2 lines with the study contact lenses compared to their habitual visual acuity without the contact lenses will be included in the study.

It is possible but unlikely that study participants will experience minor headaches associated with visual fatigue while wearing the low power contact lenses, unless they are engaging in highly visually demanding tasks. Therefore, participants will be advised to refrain from engaging in highly visually demanding tasks for the short duration of lens wear (45 minutes).

Potential problems associated with normal contact lens wear, such as discomfort, redness of the eyes, light sensitivity or blurry vision still apply and may occur during this study. However, any risks associated with the study are very minor given the short-term duration of contact lens wear in this non-dispensing study.

Benefits of the Clinical Trial

There is no guarantee or promise that the participants will receive any benefits from this clinical trial.

However, understanding microbial contamination rates of contact lenses extracted from Smart Touch Technology blister packaging compared to conventional contact lens packaging, and the impact of EDTA in the packaging solution, will provide vital information as to the potential benefits of reduced handling of contact lenses during insertion to: minimize the transfer of microbes to the eye; reduce the incidence of contact lens-related adverse events; reduce ocular redness and; improve ocular comfort.

4.2.2. Treatment Rationale

Contact lens manufacturer Menicon have developed Smart Touch Technology blister packaging designed to minimize the amount of lens handling prior to lens insertion. Contact lenses are pinched from the blister pack such that only the front surface of the lens is handled for insertion directly onto the eye.

The purpose of this randomized, contralateral, investigator-masked non-dispensing study, is to investigate the microbial contamination rates on the back surface of soft hydrogel and silicone hydrogel contact lenses extracted from Smart Touch Technology blister packs versus conventional lens packaging, and the impact of EDTA in the packaging solution after short-term placement on the eye, and to

compare the microbial contamination rates of the worn contact lenses to those on the participants' hands/fingers used to conduct lens insertion.

The detection limits for microbial contamination rates on the back surface of worn soft contact lenses will be determined, in order to calculate the sample size which would be required to conduct a dispensing study to evaluate the effect on ocular redness, ocular comfort and lens contamination rates in a bilateral, randomized cross-over study.

4.2.3. Guidelines and Regulations

The clinical trial will be conducted in accordance with the protocol, the Declaration of Helsinki (see Appendix 1), ICH GCP and local regulations as applicable including TGA and NH&MRC guidelines.

4.2.4. Trial Population

25 participants are required to complete each arm of the study.

5. TRIAL OBJECTIVES AND CLINICAL HYPOTHESIS

5.1. Trial Objective

The objective of this study is to investigate the microbial contamination rates on the back surface of hydrogel and silicone hydrogel contact lenses extracted from Smart Touch Technology blister packs versus conventional lens packaging, and the impact of EDTA in the packaging solution after short-term placement on the eye (45 minutes), in a randomized, contralateral, investigator-masked non-dispensing study comprising of two visits.

5.2. Clinical Hypothesis

The microbial contamination rates on the back surface of soft contact lenses extracted from Smart Touch Technology blister packs will be lower compared to the microbial contamination rates on the back surface of contact lenses extracted from conventional lens packaging.

6. TRIAL DESIGN

This will be a prospective, single centre, randomized, contralateral, investigator-masked non-dispensing study. This study requires three visits of approx. 1 hour duration each.

At the first visit, if possible, the order in which the hydrogel and silicone hydrogel contact lenses are allocated to the study participants will be randomized. At the second visit, participants will be crossed over to the alternate lens type (hydrogel or silicone hydrogel).

At each visit, participants will be instructed to:

- Wash their hands prior to handling the contact lenses;
- Swab their thumb and two index fingers of the hand routinely used to conduct contact lens insertion using a sterile cotton swab moistened with sterile preservative free saline for the evaluation of skin microbiota;
- Follow the manufacturer's guidelines for lens insertion;
- Open the blister pack and insert the contact lens randomly assigned for the right eye;
- Open the blister pack and insert the contact lens assigned for the left eye;
- Contact lenses will be removed aseptically by a masked investigator wearing sterile latex gloves, who is experienced in this technique, after 45 minutes of lens wear. All contact between the contact lens with the eyelids and eyelashes during lens removal will be avoided.

Lenses and finger swabs will be analysed for microbial contamination using established routine microbiology protocols. The number and species of organisms will be determined.

A minimum washout period of 48 hours will occur between the two study visits.

All proposed procedures conform to the NHMRC Statement on Human Experimentation.

Participants are considered enrolled when they have signed the informed consent form and are regarded as part of the clinical trial population.

6.1. Methodology / Study Visits

6.1.1. Data Requirements per Visit

This study requires three visits of approx. 1 hour duration each. The data requirements for this visit are shown in Table 5.

Table 5

Procedure	Visit 1	Visit 2	Visit 3
Informed Consent	X		X
Demographics, ocular and medical history	X		
Update ocular and medical history		X	X
Spectacle vision	X	X	X
Slit lamp examination including fluorescein assessment	X	X	X
Randomization to contact lens material type*	X		
Randomization – assign eye in which to insert contact lenses retrieved from the two types of lens packaging	X	X	
Randomization – assign eye in which to insert each contact lens material extracted from the Smart Touch Technology blister packs			X
Study participant to wash hands and undergo finger swab	X	X	X
Study participant to insert contact lenses (including practice removing the contact lenses from the lens packages)	X	X	X
Vision with spectacles worn over contact lenses	X	X	X
Aseptic contact lens removal	X	X	X
Adverse event	*	*	*

* If applicable

6.1.2. Randomisation and Masking

Prior to initiation of study treatment, each subject who provides informed consent will be assigned to a subject number that will serve as the subject identification number on all study documents. Subject numbers will be assigned in ascending order and should not be omitted or reused.

Participants will be randomly assigned to the lens packaging type to be inserted on each eye. A randomization scheme will be prepared in advance. In addition, if possible (dependent upon lens availability), participants will also be randomized as to the order in which the hydrogel and silicone hydrogel contact lenses are allocated at the first and second study visits.

Participants will practice the lens handling technique to remove a contact lens from the Smart Touch Technology blister pack. Once the participant is proficient with this technique, they will be instructed to follow the manufacturer's guidelines for insertion of the Smart Touch Technology contact lens, and to open the blister pack of the contact lens in the conventional lens packaging, scoop the lens out of the blister pack by placing a finger on the lens and sliding the lens up the side of the lens package until it is free of the container, and insert the contact lens on their eye.

The Investigator will provide instructions to the study participants as to the lens insertion technique but will not be cognizant to the randomisation schedule and will not be present during the lens insertion procedure to maintain masking.

6.1.3. Clinical Trial Population

A total of 25 experienced soft contact lens wearers (hydrogel or silicone hydrogel) will be required to complete each arm of the study.

Trial participants will be recruited from the local population at the investigational site. An e-mail invitation will be circulated to all SOVS staff, the Brien Holden Vision Institute, the Centre for Eye Health, SOVS post-graduate students, and previous study participants and/or Optometry Clinic patients who have indicated their willingness to be contacted to participate in future research studies. Advertisements may also be posted in University newsletters, notice boards, websites, local newspapers, social media (e.g. Facebook), on the SOVS clinic TV screen and other local advertising and community websites. .

6.1.4. Trial Duration

This study requires three visits of approx. 1 hour duration each.

6.1.5. Enrolment

A study participant is considered enrolled when they have signed the Participant Information Statement and Consent Form.

6.2. Primary Endpoint

Microbial contamination rate of the back surface of worn soft contact lenses.

6.3. Secondary Endpoint(s)

Microbial contamination rate of participants' hand swabs compared to the worn contact lenses.

7. SELECTION AND WITHDRAWAL OF PARTICIPANTS

7.1. Participant Selection

Only experienced soft contact lens wearers will be enrolled. Informed consent will be obtained prior to any clinical trial procedures being conducted.

All participants will conform to the clinical trial entry criteria listed below:

7.1.1. Inclusion Criteria

- Able to read and comprehend English and give informed consent as demonstrated by signing a Participant Information Statement and Consent Form;
- Be at least 18 years old;
- Experienced soft contact lens wearer;
- Willing to refrain from wearing contact lenses for 24 hours prior to the scheduled study visits.

7.1.2. Exclusion Criteria

- Under 18 years old;
- Have any active corneal infection, ocular disease or systemic disease that would affect wearing of contact lenses;
- Use or have a need for any systemic or topical medications which may alter normal ocular findings/are known to affect a participant's ocular health/physiology either in an adverse manner or risk providing a false positive;
- Have had eye surgery within 12 weeks immediately prior to enrolment for this trial;
- Have contraindications to contact lens wear;
- Have a greater than 2 line reduction in habitual visual acuity while wearing the study contact lenses;
- Be currently enrolled in another clinical trial;
- Be pregnant (verbal self-report).

7.2. Participant Withdrawal

Participants may be permanently discontinued from the clinical trial for any of the following reasons:

- If, in the Investigator's opinion, it is in the best interest of the participant;
- Persistent clinical trial-related symptoms/complaints that are not correctable;
- Has a serious adverse event/serious adverse device event that is eye/lens related and/or which, in the Investigator's opinion, requires withdrawal of the participant;
- Participant voluntarily withdraws consent from the clinical trial (i.e. Revocation of Consent);
- If a participant is not compliant with the clinical trial requirements and instructions;
- Protocol violations/deviations.

7.3. Withdrawal and Follow-up Procedure

This study comprises two visits for each participant. Any participants who wish to be withdrawn from the study will be exited upon request.

7.4. Early Termination of Trial

The trial may be stopped early for any one or more of the following reasons:

- If the monitoring of the clinical trial reveals unacceptable levels of device-related adverse events, even though some of the participants may not be affected;
- If the Investigator does not adhere to the protocol or decides to stop the study for any reason, with appropriate notification.

In the event of early termination of the trial, the HREC will be notified.

8. NUMBERING

Participant numbering will occur sequentially commencing with '01'.

9. EQUIPMENT TO BE USED / STANDARD & NON-STANDARD PRACTICE PROCEDURES

9.1. Standard Equipment and Procedures:

- ***Visual Acuity:*** Measurement of the standard of vision achieved with spectacles or contact lenses using standard letter charts. Measurements are taken under monocular and/or binocular conditions.
- ***Slit-Lamp Biomicroscopy:*** A specialised microscope with its own light source is used to examine the anterior eye.
- ***Fluorescein Assessment:*** The ocular surface is assessed by instilling a harmless fluorescent dye called 'fluorescein' directly to the inferior bulbar conjunctiva using a sterile strip impregnated with fluorescein and moistened with sterile saline. The eye is assessed with the slit-lamp biomicroscope using a cobalt blue filtered light and a Wratten 12 filter.

9.2. Non-Standard Equipment and Procedures:

Non-standard procedures that may be performed include:

- ***Finger swabs for microbial evaluation:*** The thumb and two index fingers of the hand routinely used to conduct contact lens insertion will be swabbed by the study investigator using a sterile cotton swab moistened with sterile preservative free saline. The swab will be rolled over each finger twice – once in a forward direction, and once in the reverse direction.
- ***Collection of used contact lenses for microbial evaluation:*** Study lenses will be collected from participants' eyes aseptically using sterile powder-free gloves. The study lenses will be sent to the microbiology laboratory for analysis of microbial contamination rates on the back surface of lenses.
- ***Photography/Video:*** A photograph and/or video recording of any interesting/unusual findings may also be made for documentation and/or follow-up purposes.

9.3. Maintenance and Calibration of Equipment

Equipment will be monitored regularly for maintenance and calibration as per relevant company and product manuals.

10. TREATMENT OF PARTICIPANTS

10.1. Administration of Study Lenses

Participants will practice the lens handling technique to remove a contact lens from the Smart Touch Technology blister pack. Once the participant is proficient with this technique, they will be instructed to follow the manufacturer's guidelines for insertion of the Smart Touch Technology contact lens, and to open the blister pack of the contact lens in the conventional lens packaging, scoop the lens out of the blister pack by placing a finger on the lens and sliding the lens up the side of the lens package until it is free of the container, and insert the contact lens on their eye.

The Investigator will provide instructions to the study participants as to the lens insertion technique but will not be cognizant to the randomisation schedule and will not be present during the lens insertion procedure to maintain masking.

10.2. Study Lens Storage and Accountability

10.2.1. Storage Requirements

Study lenses will be stored at room temperature in a secure storeroom/cupboard. The storage facility should be kept locked to prevent unauthorized access and to ensure accountability of the study lenses at all times.

10.2.2. Accountability

A Lens Tracking spreadsheet is used for keeping track of who, where and when lenses have been issued or dispensed to.

- ***Receipt of Lenses:*** Once invoice has been checked, the lenses will be entered into the Lens Tracking spreadsheet.
- ***Issue of Lenses to Clinical Trial Participants:*** The Optometrist is responsible for documenting the dispensing of the lenses on the Lens Tracking spreadsheet.
- ***Disposal of Unused Supplies:*** Instruction will be obtained from Menicon as to how to handle returned, unused lenses.

10.3. Concomitant Therapy

Whilst participating in this clinical trial participants are not permitted to enrol in other clinical trials.

Participants must not use or have a need for any systemic or topical medications which may alter normal ocular findings/are known to affect a participant's ocular health/physiology either in an adverse manner or risk providing a false positive.

Participants will be instructed to refrain from wearing contact lenses for 24 hours prior to the study visits.

10.4. Participant Instructions

General instructions to all participants

- Contact the clinic immediately if problems are experienced or if they have any questions or concerns.

11. ASSESSMENT OF EFFICACY

11.1. Parameters

- Microbial contamination rate on the back surface of worn soft contact lenses.

11.2. Methods

Used study contact lenses will be collected after 45 minutes of wear for evaluation of microbial contamination rates on the back surface of the lenses.

12. ASSESSMENT OF SAFETY

12.1. Parameters

- Visual acuity
- History
- Ocular redness: bulbar and limbal conjunctiva
- Corneal staining

12.2. Methods

Visual acuity will be measured using standard letter charts. The study participant's habitual visual acuity will be assessed as well as study contact lens acuity (with the study participant's habitual spectacle correction worn over the contact lenses where applicable).

History (including medical and general health) will be recorded at the study visit.

Ocular redness (bulbar and limbal), and corneal staining will be assessed and recorded using the CCLRU (Appendix II) and CIBA Grading scales (Appendix III).

An optometrist will be available for the duration of the study. Participants will be advised to contact the Optometrist immediately of any event not normal for lens wear e.g. unusual redness, pain, irritation, etc. At the clinic, the Optometrist will briefly assess the eye on a slit-lamp under low illumination to ascertain the nature of the condition, if any. If an adverse event occurs, the appropriate procedures will be conducted, including referral for medical treatment if necessary. Any adverse events will be followed until complete resolution to the reasonable satisfaction of the participant and the investigator.

12.3. Definitions

12.3.1. Adverse Events

Adverse Event: Any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not, that includes a clinical sign, symptom or condition and/or observation of an unintended technical performance or performance outcome of the device.

Adverse Events may be classified as Serious, Significant, Non-significant or Unanticipated as defined further on.

Adverse Device Event: A clinical sign, symptom or condition that is causally related to the device or the performance of the device system.

12.3.2. Serious Adverse Events

Any adverse medical occurrence that:

- led to death.
- led to a serious deterioration in health of a Participant user or other. This would include:
  - a life threatening illness or injury.
  - a permanent impairment of body function or permanent damage to a body structure.
  - a condition requiring hospitalisation or increased length of existing hospitalisation.
  - a condition requiring unnecessary medical or surgical intervention.
  - foetal distress, foetal death or a congenital abnormality/birth defect.
- might have led to death or a serious deterioration in health had suitable action or intervention not taken place. This includes:
  - a malfunction of a device such that it has to be modified or temporarily/permanently taken out of service.
  - a factor (a deterioration in characteristics or performance) found on examination of the device.

Specifically for the eye, Serious Adverse Events include but are not limited to:

- permanent decrease in best-corrected visual acuity (≥2 lines)
- central corneal opacities
- central corneal neovascularisation – in the central 4mm of the cornea
- central corneal opacities – in the central 4mm of the cornea
- infectious corneal ulcers
- uveitis
- iritis
- endophthalmitis
- hypopyon
- hyphema
- penetration of bowman's membrane
- persistent epithelial defect
- limbal cell damage leading to conjunctivalisation.

Serious adverse events are reportable.

12.3.3. Significant Adverse Events

Significant Adverse Events are those that are symptomatic and warrant discontinuation (temporary or permanent) of contact lens wear (excluding serious adverse events noted above). They include, but are not limited to:

- ***Peripheral and non-infectious corneal ulcer:*** Inflammatory reaction of the cornea characterised by peripheral or mid-peripheral corneal infiltrate with necrosis of the anterior stroma and excavation of the corneal epithelium. Bowman's layer is intact. Symptoms include moderate to severe pain, foreign body sensation, irritation, redness and tearing.

- ***Acute red eye:*** Inflammatory reaction of the cornea characterised by small, focal and diffuse corneal infiltration with minimal or no epithelial involvement. Symptoms include irritation, pain, redness, tearing, and photophobia.

- ***Infiltrative keratitis:*** Inflammatory reaction of the cornea characterised by anterior stromal infiltrates with or without epithelial involvement. Symptoms include mild to moderate irritation, and redness. Staining may be slight to moderate.

- ***Conjunctivitis:*** Inflammatory reaction of the conjunctiva characterised by discharge, grittiness, redness and swelling.

- ***Contact Lens Induced Papillary Conjunctivitis:*** Inflammatory reaction of the palpebral conjunctiva characterised by raised, swollen papillae.

- ***Corneal Erosion:*** Full thickness epithelial loss over a discrete area.

- ***Superior Epithelial Arcuate Lesion:*** Mechanical injury to the cornea characterised by an arc-like lesion in the periphery of the superior cornea.

12.3.4. Non-Significant Adverse Events

Non-significant Adverse Events are those that do not warrant discontinuation of contact lens wear, but may cause a reduction in wear time. Treatment, if needed, is usually with over the counter products. They include, but are not limited to:

- asymptomatic infiltrative keratitis
- blepharitis
- meibomitis
- contact dermatitis
- localised allergic reactions.

12.3.5. Unanticipated Adverse Device Events

Adverse device events or serious adverse device events are considered "unexpected" or "unanticipated" if they do not appear listed in the device technical manuals to date. These events require expedited reporting.

12.3.6. Event Severity

Events should be rated by a study investigator according to their severity:

Mild:	No treatment required
Moderate:	Treatment required. May involve temporary interruption of contact lens wear.
Severe:	Requires referral to and treatment by an ophthalmologist.

12.4. Reporting

In the event of persistent irritation, redness, reduced visual acuity or any other unusual signs or symptoms, the participants will be advised to remove their lenses immediately.

Non-serious and anticipated device-related adverse events and adverse events should be recorded as part of Good Clinical Practice. Sponsors are expected to maintain up-to-date tabulations and/or line listings of all adverse device events.

All Serious Adverse Events should be reported to the HREC as per their reporting requirements. This should be followed by a more detailed written report commenting on potential confounding factors, results of investigations, treatment required and outcome. The Sponsor(s) and the Principal Investigator should review the events in conjunction with the known information about the device, and make a determination as to whether the event is device-related or not.

12.4.1. Expedited Reporting

UNSW, via the Principal Investigator (PI) of the clinical trial is required to report to the Therapeutic Goods Administration (TGA) single cases of serious and unanticipated device related adverse events.

- ***Fatal or life-threatening unexpected adverse events*** – the TGA should be notified as soon as possible but no later than 7 calendar days after first knowledge by the PI that the case qualifies, followed by a complete report as possible within eight additional calendar days.
- ***All other serious, unexpected adverse events*** – TGA notification as soon as possible but no later than 15 calendar days after first knowledge by the PI that the case meets the minimum criteria for expedited reporting.

In the case of an unexpected and serious adverse event that occurs outside Australia with use of the same product, the TGA and HREC should also be

notified. The time frame for this reporting should be within 72 hours of any significant safety issue which has arisen from an analysis of overseas reports or action which has been taken by another country's regulatory agency. This advice must include the basis for such action. Investigators should also be notified, who must in turn notify the HREC.

Reports should be on the 'Medical Device Incident Report Form' located on the TGA website (http://www.tga.gov.au/docs/html/forms/iris_mdir.htm) or similar format, and clearly marked 'Clinical Trial Adverse Device Event' and sent to:

The Medical Officer
Office of Devices, Blood and Tissues
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606

12.4.2. Foreseeable Adverse Events and Adverse Device Events

Risks associated with the use of the study lenses include:

- Eye discomfort (<1%)
- Eye redness (<1%)
- Blurry vision (<10%)
- Headaches (<10%)

12.4.3. Other Observations

There may be other situations that may necessitate rapid communication to regulatory authorities. Scientific and medical judgment should be applied for each situation. In general, information that might materially influence the benefit-risk assessment of a product or that would be sufficient to consider changes in product administration or in the overall conduct of a clinical investigation represent such situations.

12.5. Follow-up

Participants who experience an adverse response will be discontinued from the study and followed up until the condition resolves or the participant is referred to another practitioner.

12.6. Referrals

Participants will be referred to a medical expert when judged by the optometrist to be necessary. After hours, participants will be referred to [redacted] (Table 6).

Table 6

Title:	[redacted]
Address:	[redacted]
Telephone:	[redacted]

13. STATISTICS

13.1. Description

Data stored in relational databases will be imported into SPSS software for statistical purposes. Statistical analysis will initially be reported in Excel. Data will be investigated for quality using range checks and frequency distribution. Underlying distributions of variables will be tested. Details of statistical analysis are described in Section 13.1.3.

13.1.1. Number of Participants

25 participants will be required to complete the study.

This sample size is an estimate for this preliminary study, to determine whether differences in microbial contamination rates on the back surface of worn soft contact lenses can be detected.

The results of this study will be used to inform the detection limits for microbial contamination rates on the back surface of worn soft contact lenses between the two different types of lens packaging. This will assist to determine the appropriate sample size required to conduct a longer-term dispensing study.

13.1.2. Significance

A p-value less than or equal to 5% will be considered to be statistically significant.

13.1.3. Analysis

Participants who complete the study treatment will be included in the analysis dataset. Reasons and frequency distribution of participants discontinued will be reported.

Overall contamination rates, expressed as a binary variable, and contamination rates for type of organism will be compared between the worn contact lenses extracted from the two different types of lens packaging, as

well as between the hydrogel and silicone hydrogel lens materials extracted from the two different types of lens packaging.

Data will be summarised as means ± standard deviations for variables measured on an interval scale and median ± inter-quartile range for ordinal variables. Statistical tests will be employed to determine significant differences between the worn contact lenses extracted from the two different types of packaging. Commonly used tests of significance at each visit may include paired t-tests and group t-test for parametric data and Wilcoxon sign rank test and rank sum test for non-parametric data.

13.2. Criteria for Termination of the Trial

The trial will be terminated upon completion of the final study visit by the last participant or unless any of the conditions of Section 7.4 are met. An active participant is one who is enrolled in the study and has not been discontinued.

13.3. Accountability of Data

Individual data points that are missing will be excluded from analysis involving only those specific variables. A participant's complete visit data will not be excluded if some of the observations are missing. Inclusion of outliers in the analysis will be based on the magnitude of change in test statistic with and without the outliers. Outliers will preferably be retained unless there is significant change in test results.

14. DATA HANDLING AND RECORD KEEPING

14.1. Source Data

The Investigator/Institution is to maintain the trial documents as specified in ICH GCP guidelines and as required by the applicable local regulations. The Investigator/Institution is to also take measures to prevent accidental or premature destruction of clinical trial-related documentation.

Paper Case Report Forms are utilized for this clinical trial, and will be entered into Excel spreadsheets for importing into statistical software. For tests conducted that produce printed results, these should be included in the participant's file. Source data includes, but is not limited to printouts, diagrams, videos, photos, and any other paper, electronic or digital data that is the first recording of that information, and these must be maintained by the Investigator in the source files for the participant, or if unable to file (e.g. digital images), then reference should be made to their location. The clinic records will maintain a record of trial participation but will not be considered as the source.

14.2. Direct Access to Source Data/Documents

The Investigator will conduct this clinical trial under HREC review. As necessary the Investigator will provide the HREC and appropriate regulatory authorities direct access to source data/documents for review.

14.3. Data Management

The data will be accessible to study personnel only, secured and backed up regularly.

14.4. Data Archiving

Electronic data will be stored in a secure off-site storage facility. Paper records are archived approximately 3 months after study closeout. The records are initially kept on site in a secure location, and may later be transferred to a secure off-site storage facility.

14.5. Retention of Essential Documents

The Investigator/Institution is to retain essential documents until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region. However, these documents should be retained for longer if required by local regulatory agencies.

The Investigator/Institution must also retain essential documents for 15 years as per TGA requirements following the completion of a clinical trial. However, essential documents may need to be retained longer after consideration of the following: product liability and the potential need to produce records at any time during, and possibly beyond, the life of a product in the event of a claim as a result of an adverse outcome associated with the use of the product.

15. QUALITY CONTROL AND QUALITY ASSURANCE

15.1. Ethical Considerations

This trial requires HREC approval prior to start.

The Investigator is to ensure that the protocol, Participant Information Statement and Consent Form, available safety information, information about payment and compensation to participants, advertising or any clinical trial specific information provided to participants (including potential participants), the Investigator's CV and/or evidence of appropriate qualifications and any other documentation they may request are submitted, reviewed and approved. Any subsequent amendments will be reviewed and approved by an HREC prior to implementation.

The HREC must be appropriately constituted, and will perform its functions in accordance with the applicable local regulatory requirements (TGA and NHMRC) and GCP.

This trial will be conducted in accordance with local guidelines and requirements (including those of the NHMRC and TGA, as applicable).

15.1.1. Confidentiality

Confidentiality will be maintained throughout the clinical trial by all parties involved in accordance with guidelines under section 95 of the Privacy Act 1998, and guidelines approved under section 95a of the Privacy Act 1998 (December 2001). Data will be secured against unauthorised access.

Privacy and confidentiality of information about each clinical trial participant will be preserved in the reports and any publication of the clinical investigation data.

15.1.2. Informed Consent

The nature and purpose of the trial will be fully explained to each participant. Written informed consent must be obtained from each participant prior to any trial procedures being performed.

The informed consent documentation to be used for the trial will include all the elements of informed consent per GCP, and TGA requirements as applicable, and will be reviewed and approved by the HREC prior to use.

15.1.3. Protocol Amendments

The Investigator will review deviations to determine the need to amend the protocol or to terminate the investigation. Justification for any changes will be provided.

Protocol amendments will be submitted to the HREC for review and approval prior to implementation, unless the change required is to eliminate an immediate hazard to trial participants, or involves only administrative and/or logistical aspects of the trial (e.g. Change in contact numbers).

15.1.4. Investigator Responsibilities

The Investigator is responsible for ensuring participant safety and data quality by: protocol compliance, adherence to GCP and local regulatory requirements, and the Declaration of Helsinki. The Investigator should be appropriately qualified and legally entitled to practice, and be trained in the proper method of obtaining informed consent.

The Investigator must have the appropriate resources to conduct the clinical trial, be familiar with the protocol and agree to adhere to it, support monitoring and auditing activities, make the necessary arrangements to ensure proper conduct and completion of the clinical trial, and ensure the protection and welfare of the participant, including arranging any emergency treatment as needed.

The Investigator must ensure written HREC approval is received prior to the start of the clinical trial, that the HREC is kept informed of the clinical trial progress, including serious/adverse events and deviations as required by them, and that any changes to the protocol are notified to the HREC and receive written approval prior to implementation.

The Investigator must try to ensure adequate participant recruitment; that all necessary and appropriate information is given to potential participants to ensure informed consent; to ensure informed consent is taken and documented; and that clinical records indicate the participant is enrolled in a clinical trial. The Investigator must ensure that clinical trial participants are provided with emergency contact details along with a procedure to follow in the case of an emergency, and that clinical trial participants are kept informed as pertinent new information becomes available that may affect their decision to participate.

The Investigator has primary responsibility for the accuracy, legibility and security of all clinical investigation data, documents and participant records at the investigator site during and after the clinical trial. Case Report Forms are to be signed by the Investigator, and any alterations to data are to be by authorised personnel, initialled and dated by same.

The Investigator must ensure that data be kept for the minimum time as specified by this protocol, investigational product must be accounted for (the quantity of the devices received must be reconciled with the quantities of the device used, discarded or returned), and must also be responsible for the supervision and assignment of duties to all responsible for the conduct and evaluation of the clinical trial for the investigator centre involved.

16. FINANCING AND INSURANCE

Memorandum of Agreement can be provided on request.

17. PUBLICATION POLICY

Please refer to Memorandum of Agreement.

INVESTIGATOR AGREEMENT

"I agree to conduct the trial outlined above according to the terms and conditions of the protocol, Good Clinical Practice Guidelines and with the applicable regulatory requirements. All information pertaining to the trial shall be treated in a confidential manner."

Principal Investigator's Signature: _____ Date:_____

Principal Investigator's Printed Name: _____

APPENDIX I

DECLARATION OF HELSINKI

APPENDIX I: WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles for Medical Research Involving Human Subjects

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association (WMA), the global representative body for physicians.

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996 and the
52nd WMA General Assembly, Edinburgh, Scotland, October 2000

A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.
9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.
11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.
12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

APPENDIX I: Declaration of Helsinki *(cont.)*

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.
15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.
19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
20. The subjects must be volunteers and informed participants in the research project.
21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.
27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.
29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

APPENDIX I: Declaration of Helsinki *(cont.)*

At the conclusion of the study, every patient entered into the study should be assured of access to the best
30. proven prophylactic, diagnostic and therapeutic methods identified by the study.
31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.
32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

APPENDIX II

CCLRU GRADING SCALES

APPENDIX II: CCLRU Grading Scales

The CCLRU Grading Scale uses a 0-4 scale in 0.5 steps, as shown in the following table:

Table 7

Grade	Description
0	Absent
1	Very Slight
2	Slight
3	Moderate
4	Severe

The scale is to be used in conjunction with the colour photographs as a standard to compare the observed finding and grade accordingly.

APPENDIX III

CIBA GRADING SCALES

APPENDIX III: CIBA Grading Scales

SLIT-LAMP QUANTIFICATION CHART

BIOMICROSCOPY SIGNS

Limbal Redness

0 = **None:** No injection
1 = **Trace:** Mild segmented injection
2 = **Mild:** Mild circumcorneal injection
3 = **Moderate:** Marked segmented
4 = **Severe:** Marked circumcorneal injection

Bulbar Redness

0 = **None:** White and clear
1 = **Trace:** Regional hyperemia
2 = **Mild:** Diffuse hyperemia
3 = **Moderate:** Marked regional or diffuse hyperemia
4 = **Severe:** Diffuse episcleral or scleral hyperemia

Epithelial Staining

0 = **None:** No staining
1 = **Trace:** Regional superficial stippling and/or foreign body tracks
2 = **Mild:** Regional or diffuse punctate staining and/or F.B. tracks
3 = **Moderate:** Dense coalescent staining and/or abrasions
4 = **Severe:** Epithelial loss, or full thickness abrasion