Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

MiBo ThermoFlo Lid Temperature Evaluation

Protocol CR-6281

Version: 2.0, Amendment 1.0

Date: 15 November 2018

Investigational Products: MiBo ThermoFlo; Bruder mask

Key Words: Meibomian glands, eyelid temperature, Bruder mask, hot compress, lipid layer, tear break up time

Statement of Compliance to protocol, GCP and applicable regulatory guidelines:
This trial will be conducted in compliance with the protocol, ISO 14155,[1] the International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP),[2] the Declaration of Helsinki,[3] and all applicable regulatory requirements.

TABLE OF CONTENTS

SPONSOR NAME AND ADDRESS 6
MEDICAL MONITOR 6
AUTHORIZED SIGNATURES 7
CHANGE HISTORY 8
SYNOPSIS 9
1.1. Inclusion Criteria 10
COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS 13
1. INTRODUCTION AND BACKGROUND 14
1.2. Name and Descriptions of Investigational Products 15
1.3. Intended Use of Investigational Products 15
1.4. Summary of Findings from Nonclinical Studies 15
1.5. Summary of Known Risks and Benefits to Human Subjects 15
1.6. Relevant Literature References and Prior Clinical Data Relevant to Proposed Clinical Study 15
2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES 16
2.1. Objectives 16
2.2. Endpoints 16
2.3. Hypotheses 16
3. TARGETED STUDY POPULATION 17
3.1. General Characteristics 17
3.2. Inclusion Criteria 17
3.3. Exclusion Criteria 17
3.4. Enrollment Strategy 18
4. STUDY DESIGN AND RATIONALE 18
4.1. Description of Study Design 18
4.2. Study Design Rationale 18
4.3. Enrollment Target and Study Duration 18
5. TEST ARTICLE ALLOCATION AND MASKING 19
5.1. Test Article Allocation 19
5.2. Masking 19
5.3. Procedures for Maintaining and Breaking the Masking 19
6. STUDY INTERVENTION 19
6.1. Identity of Test Articles 19
6.2. Ancillary Supplies/Products 20

6.3. Administration of Test Articles 20
6.4. Packaging and Labeling 20
6.5. Storage Conditions 20
6.6. Accountability of Test Articles 20
7. STUDY EVALUATIONS 20
7.1. Time and Event Schedule 20
7.2. Detailed Study Procedures 21
VISIT 1 21
FINAL EVALUATION 24
7.3. Unscheduled Visits 25
7.4. Laboratory Procedures 26
8. SUBJECTS COMPLETION/WITHDRAWAL 26
8.1. Completion Criteria 26
8.2. Withdrawal/Discontinuation from the Study 26
9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION 26
10. DEVIATIONS FROM THE PROTOCOL 26
11. STUDY TERMINATION 27
12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS 27
13. ADVERSE EVENTS 27
13.1. Definitions and Classifications 27
13.2. Assessing Adverse Events 29
13.2.1. Causality Assessment 30
13.2.2. Severity Assessment 30
13.3. Documentation and Follow-Up of Adverse Events 30
13.4. Reporting Adverse Events 32
13.4.1. Reporting Adverse Events to Sponsor 32
13.4.2. Reporting Adverse Events to the Responsible IEC/IRB and Health Authorities 33
13.4.3. Event of Special Interest 33
13.5. Reporting of Pregnancy 33
14. STATISTICAL METHODS 33
14.1. General Considerations 33
14.2. Sample Size Justification 34
14.3. Analysis Populations 34
14.4. Level of Statistical Significance 34

14.5. Primary Analysis 34
14.6. Secondary Analysis 35
14.7. Other Exploratory Analyses 35
14.8. Interim Analysis 35
14.9. Procedure for Handling Missing Data and Drop-Outs 35
14.10. Procedure for Reporting Deviations from Statistical Plan 35
15. DATA HANDLING AND RECORD KEEPING/ARCHIVING 35
15.1. Electronic Case Report Form/Data Collection 35
15.2. Subject Record 36
16. DATA MANAGEMENT 36
16.1. Access to Source Data/Document 36
16.2. Confidentiality of Information 36
16.3. Data Quality Assurance 37
17. MONITORING 37
18. ETHICAL AND REGULATORY ASPECTS 37
18.1. Study-Specific Design Considerations 37
18.2. Investigator Responsibility 38
18.3. Independent Ethics Committee or Institutional Review Board (IEC/IRB) 38
18.4. Informed Consent 39
18.5. Privacy of Personal Data 39
19. STUDY RECORD RETENTION 41
20. FINANCIAL CONSIDERATIONS 41
21. PUBLICATION 42
22. REFERENCES 42
APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES) 43
APPENDIX B: PATIENT INSTRUCTION GUIDE 44
APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT) 45
APPENDIX D: [redacted] 46
[redacted], BIOMICROSCOPY SCALE 47
[redacted], DISTANCE AND NEAR VISUAL ACUITY EVALUATION 53
[redacted], DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS 58
[redacted] OCULUS KERATOGRAPH 65
[redacted] THERMOGRAPHY 72
[redacted] BRUDER MASK 77

[redacted]_EYELID PHOTOGRAPHY 80
[redacted]_LIPIVIEW II LIPID LAYER THICKNESS 82
[redacted] MIBOFLO 84
PULT MEIBOSCALE 86
[redacted] THERMAL CAMERA 510(K) SUMMARY 87
[redacted] THERMAL CAMERA SCIENTIFIC SPECIFICATIONS 95
PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE 97

TABLE OF CONTENTS

Figure 1: Study Flowchart 12

TABLE OF CONTENTS

Table 1: Test Articles 19
Table 2: Ancillary Supplies 20
Table 3: Time and Events 21

PROTOCOL TITLE, NUMBER, VERSION

Title: MiBo ThermoFlo Lid Temperature Evaluation
Protocol Number: CR-6281
Version: 2.0, Amendment 1.0
Date: 15 November 2018

SPONSOR NAME AND ADDRESS

Johnson & Johnson Vision Care (JJVC)
7500 Centurion Parkway
Jacksonville, FL 32256

MEDICAL MONITOR

Name: Chantal Coles-Brennan, OD
Title: Principal Research Optometrist
Address: Johnson & Johnson Vision Care (JJVC)
7500 Centurion Parkway
Jacksonville, FL 32256
[redacted]

The Medical Monitor must be notified by the clinical institution/site by e-mail, fax, or telephone within 24 hours of learning of a Serious Adverse Event. The Medical Monitor may be contacted during business hours for adverse event questions. General study related questions should be directed towards your assigned clinical research associate.

The Medical Monitoring Plan is maintained as a separate document and included in the Trial Master File.

AUTHORIZED SIGNATURES

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations,[8] ICH guidelines,[2] ISO 14155,[1] and the Declaration of Helsinki.[3]

Author	Eric Ritchey, OD, PhD Assistant Professor, University of Houston	15 Nov 2018 DATE
Study Responsible Clinician	*See Electronic Signature Report* Chantal Coles-Brennan, OD Principal Research Optometrist	DATE
Clinical Operations Manager	*See Electronic Signature Report* [redacted] Clinical Operations Department	DATE
Biostatistician	*See Electronic Signature Report* [redacted] Biostatistician II, Clinical Sciences	DATE
Biostatistics Reviewer	*See Electronic Signature Report* [redacted]. Senior Manager of Biostatistics, Clinical Sciences	DATE
Data Management	*See Electronic Signature Report* [redacted] Clinical Project Manager – Data & Systems, Clinical Operations	DATE
Approver:	*See Electronic Signature Report* [redacted] Director of Global Medical Affairs	DATE

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Date
1.0	E. Ritchey & C. Coles-Brennan	Original Protocol	01 OCT 2018
2.0	C. Coles-Brennan	• Clarification for treatment of Bruder Mask • Update to Section 2.2 • Topography added to Table 3	15 NOV 2018

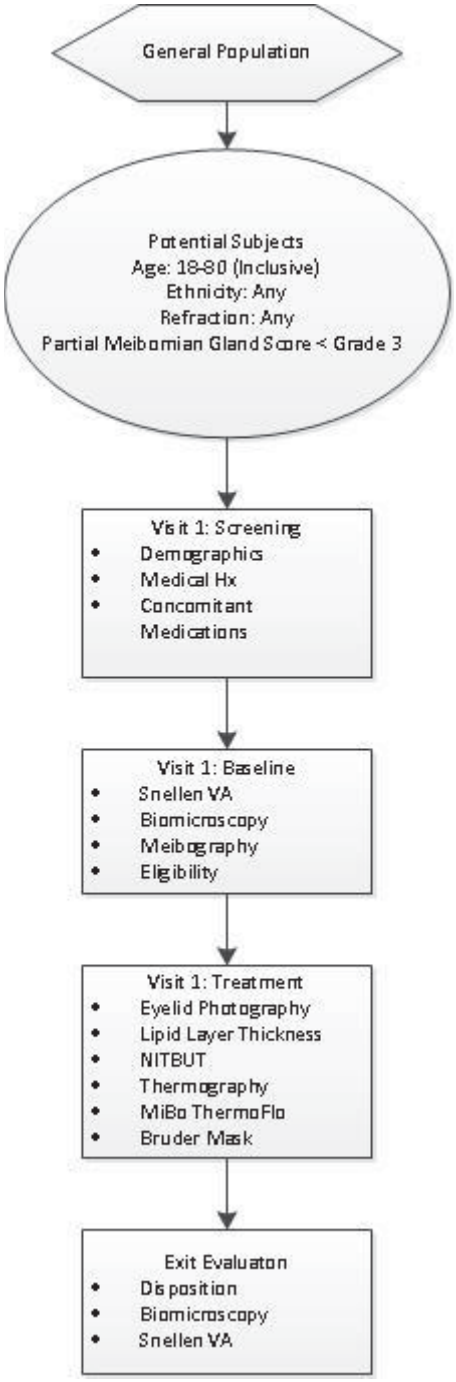
SYNOPSIS

Protocol Title	MiBo ThermoFlo Lid Temperature Evaluation
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Phase 4
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor
Test Article(s)	Investigational Product: MiBo ThermoFlo Control Product: Bruder Moist Heat Single Eye Compress
Wear and Replacement Schedules	N/A
Objectives	Determine anterior and posterior eyelid temperature after use of the MiBo ThermoFlo following standard clinical protocol and evaluate changes to the tear film with one MiBo ThermoFlo treatment session. Primary Objective: Determine the temperature of the palpebral conjunctiva after MiBo ThermoFlo treatment and Bruder Mask (i.e. hot compress) treatment using the ICI-7320 infrared camera (Infrared Cameras Inc., Beaumont, TX) Secondary Objectives: Tear Film Lipid Layer Thickness and Non-Invasive Tear Break Up Time post treatment
Study Endpoints	Primary endpoint(s): Palpebral Conjunctival Temperature Secondary endpoint(s): Tear Film Lipid Layer Thickness, Non-invasive tear break up time (NITBUT)
Study Design	This study is a prospective, contralateral, single-site, single-visit unmasked evaluation of external and internal eyelid temperature after treatment with the MiBo ThermoFlo. Approximately 20 subjects will be evaluated for enrollment in the study, with a goal of a minimum of 12 subjects completed. Subjects will be randomly assigned to receive 12 minutes of MiBo ThermoFlo treatment (treatment) on 1 eye and 10 minutes of Bruder mask treatment (control) on the fellow eye. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).
Sample Size	Up to 20 subjects will be enrolled with a goal of a minimum of target of 12 subjects to complete
Study Duration	The study will last approximately 1.5 months and include a 1-month enrollment period
Anticipated Study Population	Individuals between the ages of 18-80 years old (inclusive) with less than grade 3 partial Meibomian glands on the Pult 5-point grading scale.

Eligibility Criteria	Potential subjects must satisfy all the following criteria to be enrolled in the study: 1.1. **Inclusion Criteria** Potential subjects must satisfy all the following criteria to be enrolled in the study: 1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol 3. Between 18 and 80 (inclusive) years of age at the time of screening 4. Subjects must possess a functional/usable pair of spectacles and bring them to the visit (only if applicable - to the investigators discretion) Potential subjects who meet any of the following criteria will be excluded from participating in the study: 1. Currently pregnant or lactating 2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with participation in the study 3. Clinically significant (Grade 3 or 4 on the FDA classification scale) slit lamp findings (e.g. corneal edema, neovascularization or staining, tarsal abnormalities or bulbar injection) 4. Grade 3-4 Percentage of Partial Meibomian Glands on the Pult 5-point grading scale 5. Significant conjunctivitis (Grade 3 or greater) 6. Active Ocular Infection or Inflammation (Grade 3 or greater) 7. Any history of eyelid surgery or abnormality 8. History of Metal Implants in the Eyelids 9. Any known hypersensitivity or allergic reaction to ultrasound coupling gel 10. LASIK Surgery within 2 weeks of the Baseline Visit 11. Participation in any contact lens or lens care product clinical trial within 14 days prior to study enrollment 12. History of MiBo ThermoFlo or Lipiflow treatment Within the Last 6 months 13. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician)

Disallowed Medications/Interventions	History of MiBo ThermoFlo or Lipiflow treatment within the last 6 months
Measurements and Procedures	ICI-7320 infrared camera (Infrared Cameras Inc., Beaumont, TX) Tear Film Lipid Layer (Lipiview) Non-invasive Tear Break Up Time
Microbiology or Other Laboratory Testing	None
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	Aquasonic 100 Ultrasound Transmission Gel, Bruder Moist Heat Single Eye Compress
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

ADD	Plus Power Required For Near Use
ADE	Adverse Device Effect
AE	Adverse Event/Adverse Experience
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COAS	Complete Ophthalmic Analysis System
COM	Clinical Operations Manager
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LC	Limbus Center
LogMAR	Logarithm of Minimal Angle of Resolution
MedDRA©	Medical Dictionary for Regulatory Activities
MGD	Meibomian Gland Dysfunction
MOP	Manual of Procedures
NIH	National Institutes of Health
OD	Right Eye
OHRP	Office for Human Research Protections
OHSR	Office for Human Subjects Research
OS	Left Eye
OU	Both Eyes
PD	Protocol Deviation
PHI	Protected Health Information
PI	Principal Investigator

PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRO	Patient Reported Outcome
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SOP	Standard Operating Procedure
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VA	Visual Acuity

1. INTRODUCTION AND BACKGROUND

Several approaches have been used to treat Meibomian Gland Disease (MGD), including physical expression of the Meibomian glands alone or in conjunction with the use of various devices to heat the eyelids. The methods used to heat the eyelid tissue, colloquially referred to as hot compresses, include using hot water soaked cloths, exothermic chemical reactions (EyeGeine Wafers), heated flax seeds (MGDRx), heated rice, and proprietary bead technology (e.g. Bruder MediBeads).[4-7] Reports in the scientific literature indicate that for effective liquefaction of meibum in eyes with Meibomian Gland Dysfunction (MGD), a minimum temperature of approximately 40°C must be reached at the inner eyelid. Traditional treatments for MGD fail to reach this internal eyelid temperature, while therapy that applies sufficient heat to the inner eyelid surface can reach this temperature threshold.[6]

One device that attempts to liquefy inspissated meibum in patients with MGD is the MiBo ThermoFlo. The MiBo Thermoflo uses a thermoelectric probe coupled to the eyelid using ultrasound transmission gel after a system initiation/warm up period that heats a silver eye pad to a temperature of approximately 42°C. Upon starting treatment, the MiBo ThermoFlo eye pad is moved along the eyelid surface using a gentle circular motion, combining eyelid massage with controlled heat to the eyelid. Per the manufacturer, typical treatment duration ranges from 5 minutes to 12 minutes per session, with 3 treatment sessions over 2 weeks recommended to obtain maximum therapeutic effect (http://www.mibomedicalgroup.com/miboThermoFlo.html). Using the MiBo ThermoFlo Elite Eye Pad, upper and lower eyelids can be treated simultaneously.

Previous pilot data (TearScience; JJVC Confidential) suggests that treatment with the MiBo ThermoFlo does not adequately raise Meibomian gland temperature at the inner eyelids to therapeutic levels. This study will evaluate inner and outer eyelid temperature obtained with use of the MiBo ThermoFlo, as well as look at changes in the tear film after 1 treatment session. Temperature will be measured via thermography (see SOP_C31_Thermography_v1.0).

1.2. Name and Descriptions of Investigational Products

This study will evaluate the MiBo ThermoFlo, a therapeutic medical device for dry eye therapy. It uses a proprietary thermoelectric heat pump to help liquefaction of meibum in the Meibomian glands. The contralateral control article is the Bruder Moist Heat Eye Compresses. The Bruder mask uses MediBead technology, which absorbs water from the air and stores it inside the beads. When microwaved, the absorbed water is released as moist heat.

1.3. Intended Use of Investigational Products

The intended use of the MiBo ThermoFlo is the treatment of chronic dry eye by heating inspissated Meibomian glands, combined with gentle lid massage. Subjects will receive 12 minutes of treatment. The Bruder Moist Heat Eye Compresses is intended for the treatment of chronic dry eye and MGD and will be applied for 10 minutes.

1.4. Summary of Findings from Nonclinical Studies

Not Applicable – Marketed product only.

1.5. Summary of Known Risks and Benefits to Human Subjects

The risks of treatment with the MiBo Lipiflow are minimal. These risks include discomfort or sensation of pressure on the eyelids related to the procedure or irritation secondary to use of ultrasound coupling gel. These risks are self-limiting and typically resolve without treatment.

The risk of thermal burn with normal use of the MiBo Lipiflow or the Bruder mask is minimal. The temperature of the MiBo ThermoFlo treatment paddle is 108 degrees Fahrenheit (42 degrees Celsius), under the temperature required to cause a thermal burn with prolonged exposure to heat. The Bruder mask utilizes proprietary beads heated using a microwave oven to provide heat to the eyelid surface. The instructions for use limit the heating time to 20 seconds, with 2 additional 5 second heating sessions (maximum 30 seconds total) to achieve the required treatment temperature. Subjects will be educated to inform the study personnel if the device becomes too warm or if the treatment becomes painful.

The benefit to either treatment is that the surface heating treatments of the eyelid and Meibomian glands may lead to increase of available lipid to the tear film. This could transiently increase the thickness of the tear lipid layer or transiently increase tear break up time.

1.6. Relevant Literature References and Prior Clinical Data Relevant to Proposed Clinical Study

Selected references regarding the inner eyelid temperature required to effectively liquefy meibum can be found in the following peer reviewed literature:

Olson MC, Korb DR, Greiner JV. Increase in Tear Film Lipid Layer Thickness Following Treatment with Warm Compresses in Patients with Meibomian Gland Dysfunction. Eye Contact Lens 2003; 29:96-9.

Kenrick CJ, Alloo SS. The Limitation of Applying Heat to the External Lid Surface: A Case of Recalcitrant Meibomian Gland Dysfunction. Case Rep Ophthalmol 2017;8:7-12.

Murakami DK, Blackie CA, Korb DR. All Warm Compresses Are Not Equally Efficacious. Optom Vis Sci 2015;92: e327-33.

Wang MT, Jaitley Z, Lord SM, Craig JP. Comparison of Self-Applied Heat Therapy for Meibomian Gland Dysfunction. Optom Vis Sci 2015;92: e321-6.

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

The primary study objective of this pilot study is to measure posterior eyelid temperature (palpebral conjunctiva) to determine the ability of the MiBo ThermoFlo to raise posterior eyelid temperature to levels sufficient to provide a therapeutic effect in the treatment of MGD.

Other observations in this study include testing whether the MiBo ThermoFlo treatment can induce a change in tear lipid layer thickness and/or non-invasive tear break up time after (1) 12-minute treatment session.

2.2. Endpoints

The primary study endpoint is posterior eyelid temperature (palpebral conjunctiva) using the ICI-7320 infrared camera (Infrared Cameras Inc., Beaumont, TX). This metric has been selected as the ICI-7320 is FDA-approved [510(k) clearance] for use in medical imaging of any part of the body's surface. Collection of surface temperature with infrared video will allow for capture of the inner eyelid temperature while eyelids are inverted to access the palpebral conjunctiva. Other observations endpoints are Topography, Tear Lipid Layer thickness and Non-invasive Tear Break Up Time after treatment.

2.3. Hypotheses

1. After 12 minutes of treatment, the MiBo ThermoFlo will not heat the posterior eyelid palpebral conjunctiva to a temperature of 40°C.

   Background: Ocular surface temperature is usually 34.03 ±0.51 ºC in the 'normal' eye. The temperature required to melt obstructive secretions in the Meibomian glands ranges from 32-45°C but the more severely obstructed glands present in MGD would require a temperature of >40°C, for effective treatment. there is an approximate 5°C difference in temperature between heat applied on the external eyelid surfaces and that which reaches the inner surface of the lids (palpebral conjunctiva), where the meibomian glands are located. This difference is due to both dissipation of heat while passing through the lid tissues and to constant movement of blood through vasculature wicking heat away from the lids. Therefore, achieving the desired temperature of 40°C at the palpebral conjunctiva requires a constant heat of at least 45°C be maintained on the outer lid surface, a temperature which may be both uncomfortable and risk causing thermal injury to the eyelid skin.

Other Observations

1. After 10 minutes of treatment, the Bruder Mask will not heat the posterior eyelid palpebral conjunctiva to a temperature of greater than 40°C.
2. There is no difference in posterior eyelid palpebral conjunctiva between the Bruder Mask and the MiBo ThermoFlo

3. TARGETED STUDY POPULATION

3.1. General Characteristics

The study population are individuals between the ages of 18 to 80 years old (inclusive) with sufficient Meibomian gland anatomy to qualify for MiBo ThermoFlo treatment. This is defined as having Grade 0-2 Percentage of Partial Meibomian Glands on the Pult 5-point grading scale. Subjects with Grade 3-4 Percentage of Partial Meibomian Glands will be excluded.

3.2. Inclusion Criteria

Potential subjects must satisfy all the following criteria to be enrolled in the study:

1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol
3. Between 18 and 80 (inclusive) years of age at the time of screening
4. Subjects must possess a functional/usable pair of spectacles and bring them to the visit (only if applicable - to the investigators discretion)

3.3. Exclusion Criteria

Potential subjects who meet any of the following criteria will be excluded from participating in the study:

Exclusion Criteria after Screening and Baseline:

1. Currently pregnant or breastfeeding
2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with participation in the study
3. Clinically significant (Grade 3 or 4 on the FDA classification scale) slit lamp findings (e.g. corneal edema, neovascularization or staining, tarsal abnormalities or bulbar injection)
4. Grade 3-4 Percentage of Partial Meibomian Glands on the Pult 5-point grading scale
5. Giant Papillary Conjunctivitis (Grade 3 or greater)
6. Active Ocular Infection or Inflammation (Grade 3 or greater)
7. Any history of eyelid surgery or abnormality
8. History of Metal Implants in the Eyelids

9. Any known hypersensitivity or allergic reaction to ultrasound coupling gel
10. LASIK Surgery within 2 weeks of the Baseline Visit
11. Participation in any contact lens or lens care product clinical trial within 14 days prior to study enrollment
12. History of MiBo ThermoFlo or Lipiflow treatment Within the Last 6 months
13. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician)

3.4. Enrollment Strategy

Study subjects will be recruited from the Institution/clinical site's subject database and/or utilizing Independent Ethics Committee (IEC) or Institutional Review Board (IRB) approved materials.

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This study is a prospective, contralateral, single-site, single-visit unmasked evaluation of external and internal eyelid temperature after treatment with the MiBo ThermoFlo. Approximately 20 subjects will be evaluated for enrollment in the study, with a goal of a minimum of 12 subjects completed. If a subject meets all eligibility criteria then the subject will be randomly assigned to 1 of 2 treatment sequences in a contralateral fashion, (1) MiBo ThermoFlo (left eye) / Bruder mask (right eye) or (2) Bruder mask (left eye) / MiBo ThermoFLo (right eye). Subjects will undergo each treatment for a period of 12 minutes for the MiBo ThermoFlo and 10 Minutes for the Bruder mask, per the manufacturer recommendations.

The study visit is expected to last approximately 2.5 hours. Subjects will undergo Meibography, tear lipid layer measurements, non-invasive tear break-up time, eyelid photography and the study treatments (MiBo ThermoFlo and Bruder mask).

4.2. Study Design Rationale

Previous work suggests that treatment with the MiBo ThermoFlo does not adequately raise Meibomian gland temperature at the inner eyelids to therapeutic levels therefore, this study explores the ability of the MiBo ThermoFlo to increase posterior eyelid temperature over 1 treatment session. A contralateral design was considered the most efficient design to assess the primary endpoint of the study. Given the nature of the treatment, masking of the investigator and the subjects is not feasible.

4.3. Enrollment Target and Study Duration

The target enrollment is 20 subjects, with a minimum of 12 subjects completing the 1-visit study, which will last for approximately 2.5 hours.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

A computer-generated randomization scheme will be used to randomly assign subjects, in blocks of 2, to one of the two possible treatment sequences (left eye: MiBo ThermoFlo/ right eye: Bruder mask or right eye: Bruder mask/ left eye: MiBo ThermoFlo). The random scheme will be generated by site using the PROC PLAN procedure from SAS Software Version 9.4 or higher (SAS Institute, Cary, NC).

The study site must follow the randomization scheme provided and complete enrollment according to the randomization list and not pre-select or assign subjects. The randomized assignment of subjects will be performed at the first visit prior to the first fitting. The following must have occurred prior to randomization:

- Informed consent has been obtained
- Subject meets all the inclusion / exclusion criteria
- Subject history and baseline information has been collected.

5.2. Masking

Given the medical device being evaluated, masking is not possible. As such, this is an unmasked, open label trial. Subjects will be aware of the identity of the investigational product. Investigators and clinical site personnel involved in the data collection will not be masked as to the identity of the investigational product. Given the nature of the treatment, it is unlikely that the lack of masking will affect the study outcomes.

5.3. Procedures for Maintaining and Breaking the Masking

N/A

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following devices will be used in this study:

Table 1: Test Articles

	Test 1	Control
Name	MiBo ThermoFlo	Bruder Moist Heat Single Eye Mask
Manufacturer	MiBo Medical	Bruder

6.2. Ancillary Supplies/Products

The following ancillary supplies will be used in this study:

Table 2: Ancillary Supplies

	Ultrasound Gel
Solution Name/Description	Aquasonic 100 Ultrasound Transmission Gel
Manufacturer	Parker Laboratories, Inc.

6.3. Administration of Test Articles

Test article will not be dispensed to subjects. Upon completion of treatment with the Bruder mask, the mask will be disposed and a new mask used per subject.

6.4. Packaging and Labeling

N/A

6.5. Storage Conditions

No samples will be collected as part of the study procedures.

6.6. Accountability of Test Articles

JJVC will provide the Investigator with sufficient quantities of study articles and supplies to complete the investigation. Test article must be kept in a locked storage cabinet, accessible only to those assigned by the Investigator for dispensing. The Investigator may delegate this activity to authorized study site personnel listed on the Site Delegation Log. All test articles must be accounted.

[redacted] Site Instructions for Test Article Receipt and Test Article Accountability for additional information.

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 3: Time and Events

Visit Information	Visit 1 Screening & Treatment
Time Point	Day 1
Estimated Visit Duration	2.5 hours
Statement of Informed Consent	x
Demographics	x
Medical History/Concomitant Medications	x
Habitual Contact Lens Information	x
Inclusion/Exclusion Criteria	x
Entrance Visual Acuity	x
Slit Lamp Biomicroscopy	x
Meibography	x
Tear Lipid Layer Measurement	x
Non-Invasive Tear Break Up Time	x
Topography	x
Eyelid Photography	x
MiBo ThermoFlo	x
Bruder Mask	x
Exit Snellen Distance Visual Acuity	x

7.2. **Detailed Study Procedures**

VISIT 1

Note: The subjects should present to Visit 1 wearing spectacles (if necessary), not having worn contact lenses on the day of the visit.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. **Note**: The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's year of birth, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.4	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible. If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms are not required.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.5	Entrance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with their habitual correction in place (if required). Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
1.6	Slit Lamp Biomicroscopy (White Light)	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. Note: If the white light appearance of the cornea reveals significant findings which require the use of NaFl to evaluate, the subject cannot continue and proceed to F.1 Final Evaluation If any of these slit lamp findings are grade 3 or higher, discontinue and complete the final examination.	[redacted]
1.7	Meibography	Image the Meibomian glands of the upper and lower lid with the Oculus Keratograph 5. If the subject displays a significant percentage of partial Meibomian glands (Grade 3 or 4 on the Pult 5-point grading scale), proceed to the subject final evaluation.	SOP_C12_Oculus Keratograph_V2
1.8	Eligibility after Baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.	

Visit 1: Treatment			
Step	Procedure	Details	[redacted]
1.9	Eyelid Photography	The upper and lower eyelid margins of the subject will be photographed, OD, OS	Work Aid: Eyelid Photography
1.10	Tear Lipid Layer Thickness (LLT)	Measure the pre-treatment tear film LLT using the TearScience Lipiview, (OD, OS)	Work Aid: TearScience LipiView II Lipid Layer Thickness Measurement
1.11	Non-Invasive Tear Break Up Time (NITBUT)	Perform pre-treatment NITBUT using Oculus Keratograph 5 (OD, OS)	SOP_C12_Oculus Keratograph_V2
1.12	Corneal Topography	Perform pre-treatment corneal topography with the Oculus Keratograph	SOP_C12_Oculus Keratograph_V2
1.13	Thermography	Perform pre-treatment measurement of the external eyelid and palpebral conjunctival temperature for the upper and lower lids, (OD and OS)	SOP_C31_Thermography_V1.0
1.14	Randomization	Randomize treatment to eye using the randomization schedule	
1.15	MiBo ThermoFlo	Perform 12-minute MiBo ThermoFlo treatment on the eye indicated on the randomization schedule using the ThermoFlo Elite Eye Pad.	Work Aid: MiboFlo
1.16	Thermography	Immediately perform post-treatment measurement of the external eyelid and palpebral conjunctival temperature for the upper and lower lids, collecting data for the lower lid first.	SOP_C31_Thermography_V1.0
1.17	Bruder Mask	Heat the Bruder Mask per the manufacturer's instructions, measure the mask surface temperature and perform 10 minute Bruder Mask treatment on the contralateral eye.	Work Aid: Bruder Mask_V2

Visit 1: Treatment			
Step	Procedure	Details	[redacted]
		Note: The Bruder Mask should be placed gently on the closed eyelids. No not apply pressure on the mask and eye.	
1.18	Thermography	Perform post-treatment measurement of the external eyelid and palpebral conjunctival temperature for the upper and lower lids	SOP_C31_Thermography_V1.0
1.19	Tear Lipid Layer Thickness (LLT)	Measure the post-treatment tear film LLT using the TearScience Lipiview, OD, OS	Work Aid: TearScience LipiView II Lipid Layer Thickness Measurement
1.20	Corneal Topography	Perform post-treatment corneal topography with the Oculus Keratograph	SOP_C12_Oculus Keratograph_V2
1.21	Non-Invasive Tear Break Up Time (NITBUT)	Perform post-treatment NITBUT using Oculus Keratograph 5 (OD, OS)	SOP_C12_Oculus Keratograph_V2
1.22	Eyelid Photography	The upper and lower eyelid margins of the subject will be photographed, OD,OS	Work Aid: Eyelid Photography

FINAL EVALUATION

The final evaluation will ordinarily take place immediately following the last scheduled follow-up visit per the study protocol. It may also take place at any point the subject discontinues the study or is terminated from the study.

Final Evaluation			
Step	Procedure	Details	[redacted]
F.1	Final Exam Form	Indicate if the subject completed the study successfully. If subject discontinued from the study, indicate the reason.	
F.2	Exit Slit Lamp Biomicroscopy (White Light)	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. Note: If the white light appearance of the cornea reveals significant findings, use NaFl to evaluate.	[redacted]
F.3	Snellen Exit Acuity	Record the corrected <u>distance</u> visual acuity to the nearest letter (OD, OS, and OU).	[redacted]

7.3. **Unscheduled Visits**

If, during the investigation, a subject requires an unscheduled visit to the clinical site, the following information will be collected at a minimum:

- Chief complaint prompting the visit. If the reason is an adverse event, the applicable eCRF for the adverse event must be completed and subject record completed as appropriate
- Date and time of the visit and all procedures completed at the unscheduled visit
- Review of adverse event and concomitant medications
- Documentation of any test article dispensed or collected from the subject, if applicable
- Slit lamp findings (using the Slit Lamp Classification Scale)

If the Investigator withdraws a subject from the study, the final study visit case report forms must be completed indicating the reason(s) why the subject was withdrawn. The subject record must be completed documenting the date and primary reason for withdrawal and the study CRA notified.

Any ocular and non-ocular Adverse Events that are ongoing at the time of the study visit will be followed by the Investigator, within licensure, until they have resolved, returned to pre-treatment status, stabilized, or been satisfactorily explained. If further treatment i.e., beyond licensure is required, the subject will be referred to the appropriate health care provider.

The following information will be collected during an unscheduled visit.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.2	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.3	Entrance VA	Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]
U.4	Subjective Sphero-cylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, and OU).	[redacted]
U.5	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]8

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.6	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS, and OU) to the nearest letter.	[redacted]

7.4. Laboratory Procedures

N/A.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent
- they are eligible
- they complete the study procedures

8.2. Withdrawal/Discontinuation from the Study

A subject will be withdrawn from the study for any of the following reasons:

- Subject death during the study period
- Subject withdrawal of consent
- Subject not compliant to protocol
- Subject develops significant or serious adverse events causing discontinuation of treatment
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment)

For discontinued subjects, the Investigator will:

- Complete the current visit (scheduled or unscheduled)
- Complete the Final Evaluation, indicating the reason that the subject was discontinued from the study
- Collect used test article and discard them, unless otherwise stated in Section 7.2

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study.

10. DEVIATIONS FROM THE PROTOCOL

Investigator will notify study sponsor upon identification of a protocol deviation. Major protocol deviations must be reported to the sponsor within 24 hours after discovery of the protocol deviation. The Investigator will report deviations per IRB/IEC requirements. All deviations will be tracked and corrective actions implemented as appropriate.

If it becomes necessary for the Investigator to implement a deviation to eliminate an immediate hazard to the trial subject, the Investigator may implement the deviation immediately without notification to the sponsor. Within 24 hours after the implemented deviation, the Investigator must notify and provide the rationale to the Sponsor and, as required, the IEC/IRB.

11. STUDY TERMINATION

The occurrence of one or more Unanticipated Serious Adverse Device Effect (USADE), or any SAE where the relationship to study agent cannot be ruled out, may result in stopping further dispensing of test article. In the event of a USADE or SAE, the Sponsor may unmask the treatment regimen for the subject(s) and will discuss this with the Investigator before any further subjects are enrolled.

The Sponsor will determine when a study will be stopped. The Principal Investigator always has the discretion to initiate stopping the study based on patient safety or if information indicates the study's results are compromised.

JJVC reserves the right to terminate the study at any time for any reason. Additionally, the IEC/IRB reserves the right to terminate the study if an unreasonable risk is determined. The study can be terminated by the Principal Investigator at the individual clinical site due to specific clinical observations, if in their opinion, after a discussion with JJVC, it is determined that it would be unwise to continue at the clinical site.

JJVC (and the IEC/IRB and DMC, if applicable) will evaluate all adverse events. If it is determined that an adverse event presents an unreasonable risk, the investigation, or that part of the investigation presenting the risk, will be terminated, as soon as possible.

Should the study be terminated (either prematurely or as scheduled), the Investigator will notify the IEC/IRB and Regulatory Authority as required by local regulatory requirements.

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

N/A

13. ADVERSE EVENTS

13.1. **Definitions and Classifications**

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.
Note 1 to entry: This definition includes events related to the investigational medical device or the comparator.
Note 2 to entry: This definition includes events related to the procedures involved.
Note 3 to entry: For users or other persons, this definition is restricted to events related to investigational medical devices."[1]

An AE includes any condition (including a pre-existing condition) that:

1. Was not present prior to the study, but appeared or reappeared following initiation of the study
2. Was present prior to the study, but worsened during the study. This would include any condition resulting from concomitant illnesses, reactions to concomitant medications, or progression of disease states
3. Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event

Serious Adverse Event (SAE) – An SAE is any untoward medical occurrence that:

- Results in death
- Is life threatening
- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (e.g., a sight threatening event, a significant persistent or permanent change, impairment, damage, or disruption to the subject's body)
- Is a congenital anomaly/birth defect, or?
- Requires intervention to prevent permanent damage (the use of the test article resulting in a condition which requires medical or surgical intervention to preclude permanent impairment of the body structure or a body function). Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition

Diagnoses and conditions that are considered Ocular Serious Adverse Events include, but not limited to:

- Microbial Keratitis (MK)
- Iritis (including cells in the anterior chamber)
- Permanent decrease in best spectacle corrected visual acuity equivalent to 2 acuity lines or greater
- Central Corneal Opacity
- Central Corneal Neovascularization
- Uveitis
- Endophthalmitis
- Hypopyon
- Hyphemia
- Penetration of Bowman's Membrane
- Persistent Epithelial Defect
- Limbal cell Damage leading to Conjunctivization

Significant Adverse Events – Those events that are usually symptomatic and warrant discontinuation (temporary or permanent) of the test article (excluding Serious Adverse Events).

Diagnoses and conditions that are considered Ocular Significant Adverse Events include, but not limited to the following:

- Significant Infiltrative Events (SIE)
- Superior Epithelial Arcuate Lesions (SEALs)
- Any Temporary Loss of > 2 Lines of BSCVA
- Other grade 3 or higher corneal findings, such as abrasions or edema
- Non-contact lens related corneal events - e.g. Epidemic Keratoconjunctivitis (EKC)
- Asymptomatic Corneal Scar
- Any corneal event which necessitates temporary lens discontinuation > 2 weeks

Non-Significant Adverse Events – Those conditions that are usually asymptomatic and usually do not warrant discontinuation (temporary or permanent) of the test article. However, the Investigator may choose to treat as a precautionary measure.

Diagnoses and conditions that are considered Ocular Non-Significant Adverse Events include, but not limited to the following:

- Non-significant Infiltrative Event (NSIE)
- Superficial Punctate Keratitis (SPK)
- Conjunctivitis: Bacterial, Viral, Allergic
- Blepharitis
- Meibomianitis
- Contact Dermatitis
- Localized Allergic Reactions
- Any corneal event not explicitly defined as serious or significant adverse event, which necessitates temporary lens discontinuation < 2 weeks

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device.
Note 1 to entry: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
Note 2 to entry: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device."[1]

Unanticipated Adverse Device Effect (UADE) – Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, the test article, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, Investigator's Brochure or protocol, or any other unanticipated serious problem associated with the test article that relates to the rights, safety and welfare of subjects.

13.2. **Assessing Adverse Events**

In conjunction with the medical monitor, the Investigator will evaluate adverse events to ensure the events are categorized correctly. Elements of categorization will include:

- Seriousness/Classifications (see definition in Section 13.1)
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related; unlikely related; possibly related; related - see definition in Section 13.2.1)
- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild; moderate; severe for all events - see definition in Section 0)
- Outcome – not recovered or not resolved; recovering or resolving; recovered or resolved with sequelae; recovered or resolved; death related to adverse event; unknown
- Actions Taken – none; temporarily discontinued; permanently discontinued; other

13.2.1. Causality Assessment

Causality Assessment – A determination of the relationship between an adverse event and the test article. The test article relationship for each adverse event should be determined by the investigator using these explanations:

- Not Related- An adverse event that is not related to the use of the test article, study treatment or study procedures
- Unlikely Related – An adverse event for which an alternative explanation is more likely, e.g. concomitant treatment, concomitant disease(s), or the relationship of time suggests that a causal relationship is not likely
- Possibly Related – An adverse event that might be due to the use of the test article, or to the study treatment or study procedures. An alternative explanation, e.g. concomitant treatment, concomitant disease(s), is inconclusive. The relationship in time is reasonable. Therefore, the causal relationship cannot be excluded
- Related – An adverse event that is listed as a possible adverse effect (device) or adverse reaction (drug) and cannot be reasonably explained by an alternative explanation, e.g. concomitant treatment of concomitant disease(s). The relationship in time is very suggestive, e.g. it is confirmed by de-challenge and re-challenge

13.2.2. Severity Assessment

Severity Assessment – A qualitative assessment of the degree of intensity of an adverse event as determined by the Investigator or reported to him/her by the subject. The assessment of severity is made irrespective of test article, study treatment or study procedure relationship or seriousness of the event and should be evaluated according to the following scale:

- Mild – Event is noticeable to the subject, but is easily tolerated and does not interfere with the subject's daily activities
- Moderate – Event is bothersome, possible requiring additional therapy, and may interfere with the subject's daily activities
- Severe – Event is intolerable, necessitates additional therapy or alteration of therapy and interferes with the subject's daily activities

13.3. **Documentation and Follow-Up of Adverse Events**

The recording and documenting of adverse events (ocular and non-ocular) begins when the subjects are exposed to the test article, study treatment or study procedure. Adverse events reported before the use of test article, start of study treatment, or study procedures will be

recorded as medical history. However, if the condition deteriorates at any time during the study it will be recorded and reported as an AE. Untoward medical events reported after the subject's exit from the study will be recorded as adverse events at the discretion of the Investigator.

Upon finding an adverse event, the Principal Investigator will document the condition in the subject record and in the eCRFs. He/she will complete the Adverse Event /eCRF.

Complete descriptions of all adverse events must be available in the subject record. All Adverse Events including local and systemic reactions not meeting the criteria for "serious adverse events" shall be captured on the appropriate case report form or electronic data system. All adverse events occurring while the subject is enrolled in the study must be documented appropriately regardless of relationship.

It is the Investigator's responsibility to maintain documentation of each reported adverse event. All adverse events will be followed in accordance with applicable licensing requirements. Such documentation will include the following:

- Adverse event (diagnosis not symptom)
- Drawings or photographs (where appropriate) that detail the finding (e.g., size, location, and depth, etc.)
- Date the clinical site was notified
- Date and time of onset
- Date and time of resolution
- Adverse event classification, severity, and relationship to test articles, as applicable
- Treatment regimen instituted, including concomitant medications prescribed, in accordance with applicable licensing requirements
- Any referral to another health care provider if needed
- Outcome, ocular damage (if any)
- Likely etiology
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event

In addition, if an infiltrate(s) is present, he/she will complete the Corneal Infiltrate Assessment eCRF. Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature. If cultures are collected, the date of culture collection and laboratory utilized will be recorded.

Changes in the severity of an AE shall be documented to allow an assessment of the duration of the event at each level of intensity to be performed. Adverse events characterized as intermittent require documentation of the onset and duration of each episode. Changes in the assessment of relationship to the Test Article shall also be clearly documented.

Subjects who present with an adverse event shall be followed by the Investigator, within licensure, until all signs and symptoms have returned to pre-treatment status, stabilized, or been satisfactorily resolved. If further treatment beyond licensure is required, the patient will be referred to the appropriate health care provider. The Investigator will use his/her clinical judgment as to whether a subject reporting with an adverse event will continue in the study. If

a subject is discontinued from the study, it will be the responsibility of the Investigator to record the reason for discontinuation. The Investigator will also document the adverse event appropriately and complete the Adverse Event eCRF. Any subjects with ongoing adverse events related to the test article, study treatment or study procedures, as of the final study visit date, should be followed to resolution of the adverse event or until referral to an appropriate health care provider, as recommended by the Investigator. Non-ocular adverse events that are not related to the test article, study treatment, or study procedures may be recorded as "ongoing" without further follow-up.

13.4. **Reporting Adverse Events**

The Investigator will notify the Sponsor of an adverse event by e-mail, facsimile, or telephone as soon as possible and no later than 24 hours from discovery for any serious /significant adverse events, and 2 days from discovery for any non-significant adverse event. In addition, a written report will be submitted by the Principal Investigator to the IEC/IRB according to their requirements (Section 13.4.2). The report will comment whether the adverse event was considered to be related to the test article, study treatment or study procedures.

13.4.1. Reporting Adverse Events to Sponsor

Serious/Significant Adverse Events

The Investigator will inform the sponsor of all serious/significant adverse events occurring during the study period as soon as possible by e-mail, fax, or telephone, but no later than 24 hours following discovery of the event. The Investigator is obligated to pursue and obtain information requested by the Sponsor in addition to that information reported on the eCRF. All subjects experiencing a serious/significant adverse event must be followed up and all outcomes must be reported.

When medically necessary, the Investigator may break the randomization code to determine the identity of the treatment that the subject received. The Sponsor and study monitor should be notified prior to unmasking the test articles.

In the event of a serious/significant adverse event, the Investigator must:

- Notify the Sponsor immediately
- Obtain and maintain in the subject's records all pertinent medical information and medical judgment for colleagues who assisted in the treatment and follow-up of the subject
- Provide the Sponsor with a complete case history which includes a statement as to whether the event was or was not related to the use of the test article
- Notify the IEC/IRB as required by the IEC/IRB reporting procedure according to national regulations

Unanticipated (Serious) Adverse Device Effect (UADE)

In the event of an Unanticipated (Serious) Adverse Device Effect (UADE), the Investigator will submit a report of the UADE to the Sponsor and IEC/IRB as soon as possible, but no later than 24 hours after the Investigator first learns of the effect. This report is in addition to the immediate notification mentioned above.

The Sponsor must conduct an evaluation of the UADE and must report the results of the evaluation to FDA, the IEC/IRB and participating Investigators within 10 working days after the Sponsor first receives notification of the effect.

Non-Serious Adverse Events
All non-serious adverse events, including non-serious adverse device effects, will be reported to the sponsor by the Investigator no later than 2 days from discovery.

13.4.2. Reporting Adverse Events to the Responsible IEC/IRB and Health Authorities

Adverse events that meet the IEC/IRB requirements for reporting must be reported within the IEC/IRB's written guidelines. Each clinical site will refer to and follow any guidelines set forth by their Approving IEC/IRB. Each clinical site will refer to and follow any guidelines set forth by their local governing Health Authorities.

The Sponsor will report applicable Adverse Events to the local health authorities according the written guidelines, including reporting timelines.

13.4.3. Event of Special Interest

None

13.5. Reporting of Pregnancy

Subjects reporting pregnancy (by self-report) during the study will be discontinued after the event is recorded as an Adverse Event. Once discontinued, pregnant participants and their fetuses will not be monitored for study related purposes. At the Investigator's discretion, the study participant may be followed by the Investigator through delivery. However, this data will not be collected as part of the clinical study database. Pregnant participants are not discontinued from device or solution related studies for safety concerns, but due to general concerns relating to pregnancy and device use. Specifically, pregnant women are discontinued due to fluctuations in refractive error and/or visual acuity that occur secondary to systemic hormonal changes, and not due to unforeseen health risks to the mother or fetus.

14. STATISTICAL METHODS

14.1. General Considerations

Statistical Analysis will be undertaken by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be implemented in this clinical trial is outlined below.

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 (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. Unscheduled visits will be summarized separately and will be excluded from the statistical analysis.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables as appropriate. Continuous variables will be

summarized with descriptive statistics (n, mean, standard deviation (SD), median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data.

14.2. **Sample Size Justification**

Inner eyelid palpebral temperature has not previously been collected with the ICI-7320 infrared camera (Infrared Cameras Inc., Beaumont, TX) and a search of the peer reviewed literature failed to show published results with the device. Previous evaluations of inner eyelid temperature have focused primarily on the lower eyelid using infrared pyrometers. Given the lack of previous data, a formal sample size calculation cannot be completed. The sample size selected approaches the sample size required to meet the Central Limit Theorem and provide data for future sample size calculations.

14.3. **Analysis Populations**

Safety Population:
All subjects who were administered any test article excluding subjects who drop out prior to administering any test article. At least one observation should be recorded.

Intent-to-Treat (ITT) Population:
All randomized subjects regardless of actual treatment and subsequent withdrawal from study or deviation from protocol. At least one observation should be recorded.

Per-Protocol Population:

All subjects who have successfully completed all visits and did not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock (Per-Protocol Population). Justification of excluding subjects with protocol deviations in the per-protocol population set will be documented in a memo to file.

14.4. **Level of Statistical Significance**

All planned analysis for this study will be conducted with an overall type I error rate of 5%.

14.5. **Primary Analysis**

Eyelid Temperature will be analyzed using a linear or generalized linear mixed model depending on the distribution of temperatures. Treatment sequence, treatment, eyelid location (inner and outer) and the interaction between treatment and eyelid location will be included as fixed effects. Age and gender may also be included as covariates when necessary. Subject will be included as a random effect. An appropriate covariance structure will be used to model the residual errors between measurements within same subject across eyes (R-side). The covariance structure will be selected based on the finite-sample corrected Akaike's Information Criterion. Covariance structures considered include:

- Unstructured Covariance Structure (UN)
- Homogenous Compound symmetry (CS)

Comparisons between the two treatments will be carried out using two-sided 95% confidence intervals constructed for least-square mean differences (MiBo ThermoFlo minus Bruder mask).

14.6. **Secondary Analysis**

N/A.

14.7. **Other Exploratory Analyses**

N/A.

14.8. **Interim Analysis**

There will not be an interim analysis performed on this study.

14.9. **Procedure for Handling Missing Data and Drop-Outs**

Missing or spurious values will not be imputed. The count of missing values will be included in the summary tables and listings.

14.10. **Procedure for Reporting Deviations from Statistical Plan**

The analysis will be conducted according to that specified in above sections. There are no known reasons for which it is planned to deviate from these analysis methods. If for any reason a change is made, the change will be documented in the study report along with a justification for the change.

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. **Electronic Case Report Form/Data Collection**

The data for this study will be captured on electronic case report forms (eCRFs) using an EDC system (Bioclinica). An authorized data originator will enter study data into the eCRFs using the EDC system. Data collected on equipment that is not captured in EDC will be formatted to the specification of the JJVC database manager and sent to JJVC for analysis. In the event that data is collected using paper Case Report Forms, double data entry will be utilized to prevent data entry error.

The clinical data will be recorded on dedicated eCRFs specifically designed to match the study procedures for each visit. Once completed, the eCRFs will be reviewed for accuracy and completeness and signed by the Investigator. The sponsor or sponsor's representatives will be authorized to gain access to the subject recordation for the purposes of monitoring and auditing the study.

Edit checks, electronic queries, and audit trails are built into the system to ensure accurate and complete data collection. Data will be transmitted from the clinical site to a secure central database as forms are completed or updated, ensuring information accuracy, security, and confidentiality. After the final database lock, the Investigator will be provided with Individual Patient Profiles (IPP) including the full audit trail on electronic media in PDF format for all of

the study data. The IPP must be retained in the study files as a certified copy of the source data for the study.

The content and structure of the eCRFs are compliant with ISO14155:2011.[1]

15.2. **Subject Record**

At a minimum, subject record should be available for the following:

- subject identification
- eligibility
- study identification
- study discussion
- provision of and date of informed consent
- visit dates
- results of safety and efficacy parameters as required by the protocol
- a record of all adverse events
- follow-up of adverse events
- medical history and concomitant medication
- study supplies receipt/dispensing/return records
- date of study completion
- reason for early discontinuation of subject or withdrawal from the study, if applicable

The subject record is the eCRF or an external record. The author of an entry in the subject record must be identifiable. The first point of entry is the source record.

Adverse event notes must be reviewed and initialed by the Investigator.

16. DATA MANAGEMENT

16.1. **Access to Source Data/Document**

The Investigator/Institution will permit trial-related monitoring, audits, IEC/IRB review and regulatory inspection(s) by providing direct access to source data/documents. Should the clinical site be contacted for an audit by an IEC/IRB or regulatory authority, JJVC must be contacted and notified in writing within 24 hours.

16.2. **Confidentiality of Information**

Information concerning the investigational product and patent application processes, scientific data or other pertinent information is confidential and remains the property of JJVC. The Investigator may use this information for the purposes of the study only. It is understood by the Investigator that JJVC will use information developed in this clinical study about the development of the investigational product and therefore may disclose it as required to other clinical investigators and to regulatory agencies. To allow the use of the information derived from this clinical study, the Investigator understands that he/she has an obligation to provide complete test results and all data developed during this study to the Sponsor.

16.3. **Data Quality Assurance**

Steps will be taken to ensure the accuracy and reliability of data, include the selection of qualified investigators and appropriate clinical sites and review of protocol procedures with the Principal Investigator. The Principal Investigator, in turn, must ensure that all Sub-Investigators and clinical site personnel are familiar with the protocol and all study-specific procedures and have appropriate knowledge of the study article.

Training on case report form completion will be provided to clinical site personnel before the start of the study. The Sponsor will review case report forms for accuracy and completeness remotely during the conduct of the study, during monitoring visits, and after transmission to data management. Any data discrepancies will be resolved with the Investigator or designee, as appropriate.

Quality Assurance representatives from JJVC may visit clinical sites to review data produced during the study and to access compliance with applicable regulations pertaining to the conduct of clinical trials. The clinical sites will provide direct access to study-related source data/documents and reports for monitoring and auditing by JJVC and for inspection by local and regulatory authorities.

17. MONITORING

The study monitors will maintain close contact with the Principal Investigator and the Investigator's designated clinical site personnel. The monitor's responsibilities will include:

- Ensuring that the investigation is being conducted according to the protocol, any subsequent amendments, and regulatory requirements are maintained
- Ensuring the rights and wellbeing of subjects are protected
- Ensuring adequate resources, including facilities, laboratories, equipment, and qualified clinical site personnel
- Ensuring that protocol deviations are documented with corrective action plans, as applicable
- Ensuring that the clinical site has sufficient test article and supplies
- Clarifying questions regarding the study
- Resolving study issues or problems that may arise
- Reviewing of study records and source documentation verification in accordance with the monitoring plan

18. ETHICAL AND REGULATORY ASPECTS

18.1. **Study-Specific Design Considerations**

Potential subjects will be fully informed of the risks and requirements of the study and, during the study, subjects will be given any new information that may affect their decision to continue participation. Subjects will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who are fully able to understand the

risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

18.2. **Investigator Responsibility**

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[3] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with Section 8 of the ICH E6 guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements.

18.3. **Independent Ethics Committee or Institutional Review Board (IEC/IRB)**

Before the start of the study, the Investigator (or Sponsor when applicable) will provide the IEC/IRB with current and complete copies of the following documents (where applicable):

- Final protocol and, if applicable, amendments
- Sponsor-approved informed consent form (and any other written materials to be provided to the subjects)
- Investigator's Brochure (or equivalent information) and amendments
- Sponsor-approved subject recruitment materials
- Information on compensation for study-related injuries or payment to subjects for participation in the study
- Investigator's curriculum vitae, clinical licenses, or equivalent information (unless not required, as documented by IEC/IRB)
- Information regarding funding, name of the Sponsor, institutional affiliations, other potential conflicts of interest, and incentives for subjects
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after IEC/IRB has given full approval of the final protocol, amendments (if any), the informed consent form, applicable recruiting materials, and subject compensation programs, and the Sponsor has received a copy of this approval. This approval letter must be dated and must clearly identify the documents being approved.

During the study, the Investigator (or Sponsor when applicable) will send the following documents to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments
- Revision(s) to informed consent form and any other written materials to be provided to subjects
- If applicable, new or revised subject recruitment materials approved by the Sponsor
- Revisions to compensation for study-related injuries or payment to subjects for participation in the study
- Investigator's Brochure amendments or new edition(s)

- Summaries of the status of the study (at least annually or at intervals stipulated in guidelines of the IEC/IRB)
- Reports of adverse events that are serious, unanticipated, and associated with the test articles, according to the IRB's requirements
- New information that may adversely affect the safety of the subjects or the conduct of the study
- Major protocol deviations as required by the IEC/IRB
- Report of deaths of subjects under the Investigator's care
- Notification if a new Investigator is responsible for the study at the clinical site
- Any other requirements of the IEC/IRB

For protocol amendments that increase subject risk, the amendment and applicable informed consent form revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).

At least once a year, the IEC/IRB will review and reapprove this clinical study. This request should be documented in writing.

At the end of the study, the Investigator (or Sponsor where required) will notify the IEC/IRB about the study completion. Documentation of this notification must be retained at the clinical site and a copy provided to the CRO or Sponsor as applicable.

18.4. **Informed Consent**

Each subject must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and ISO 14155[1] guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential subject the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects will be informed that their participation is voluntary and that they may withdraw consent to participate at any time.

The subject will be given sufficient time to read the informed consent form and the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by means of the subject's dated signature. After having obtained the consent, a copy of the informed consent form must be given to the subject.

18.5. **Privacy of Personal Data**

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site

personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA) and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

All information obtained during the course of the investigation will be regarded as confidential. All personal data gathered in this trial will be treated in strictest confidence by Investigators, monitors, Sponsor's personnel and IEC/IRB. No data will be disclosed to any third party without the express permission of the subject concerned, except for Sponsor personnel (monitor, auditor), IEC/IRB and regulatory organizations in the context of their investigation related activities that, as part of the investigation will have access to the CRFs and subject records.

The collection and processing of personal data from subjects enrolled in this study will be limited to those data that are necessary to investigate the efficacy, safety, quality, and utility of the investigational product(s) used in this study.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations.
The Sponsor ensures that the personal data will be:

- processed fairly and lawfully
- collected for specified, explicit, and legitimate purposes and not further processed in a way incompatible with these purposes
- adequate, relevant, and not excessive in relation to said purposes
- accurate and, where necessary, kept current

Explicit consent for the processing of personal data will be obtained from the participating subject before collection of data. Such consent should also address the transfer of the data to other entities and to other countries.

The subject has the right to request through the Investigator access to his personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps should be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of study subjects confidential.

19. STUDY RECORD RETENTION

In compliance with the ICH/GCP guidelines,[2] the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ICH/GCP[2] and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained until at least two (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 or until at least two (2) years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or instructed by the Sponsor. It is the responsibility of the Sponsor to inform the Investigator/Institution as to when these documents no longer need to be retained.

If the responsible Investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The Sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the Investigator relocate or dispose of any study documents before having obtained written approval from the Sponsor.

If it becomes necessary for the Sponsor or the appropriate regulatory authority to review any documentation relating to this study, the Investigator must permit access to such reports.
If the Investigator has a question regarding retention of study records, he/she should contact JJVC.

20. FINANCIAL CONSIDERATIONS

Remuneration for study services and expenses will be set forth in detail in the Clinical Research Agreement. The Research Agreement will be signed by the Principal Investigator and a JJVC management representative prior to study initiation.

JJVC reserves the right to withhold remuneration for costs associated with protocol violations such as:

- Continuing an ineligible subject in the study
- Scheduling a study visit outside the subject's acceptable visit range

JJVC reserves the right to withhold final remuneration until all study related activities have been completed, such as:

- Query resolution
- Case Report Form signature
- Completion of any follow-up action items

21. PUBLICATION

This study will be registered on ClinicalTrials.gov by the Sponsor.

22. REFERENCES

1. ISO 14155:2011: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice. Available at: https://www.iso.org/standard/45557.html
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). Available at: http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
3. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
4. Olson MC, Korb DR, Greiner JV. Increase in Tear Film Lipid Layer Thickness Following Treatment with Warm Compresses in Patients with Meibomian Gland Dysfunction. Eye Contact Lens 2003;29:96-9.
5. Kenrick CJ, Alloo SS. The Limitation of Applying Heat to the External Lid Surface: A Case of Recalcitrant Meibomian Gland Dysfunction. Case Rep Ophthalmol 2017;8:7-12.
6. Murakami DK, Blackie CA, Korb DR. All Warm Compresses Are Not Equally Efficacious. Optom Vis Sci 2015;92:e327-33.
7. Wang MT, Jaitley Z, Lord SM, Craig JP. Comparison of Self-Applied Heat Therapy for Meibomian Gland Dysfunction. Optom Vis Sci 2015;92:e321-6.
8. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
9. *Health Information Portability and Accountability Act (HIPAA).* Available at: https://www.hhs.gov/hipaa/for-professionals/privacy/index.html
10. *Data Protection Act. Available at:* http://www.legislation.gov.uk/ukpga/1998/29/contents

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

Not applicable

APPENDIX B: PATIENT INSTRUCTION GUIDE

Not Applicable - no study lenses on eye.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Not Applicable

APPENDIX D: [redacted]

- [redacted]
- [redacted]
- [redacted]
- TOSI SOP_C12_Oculus Keratograph
- TOSI SOP_C31_Thermography
- TOSI Work Aid_Bruder Mask
- TOSI Work Aid_Eyelid Photography
- TOSI Work Aid_LipiView II Lipid Layer Thickness
- TOSI Work Aid_MiBoFlo
- Pult Meiboscale
- ICI 7320 Thermal Camera 510(K) Summary
- ICI 7320 Thermal Camera Scientific Specifications

[redacted], BIOMICROSCOPY SCALE

[redacted] **Biomicroscopy Scale**

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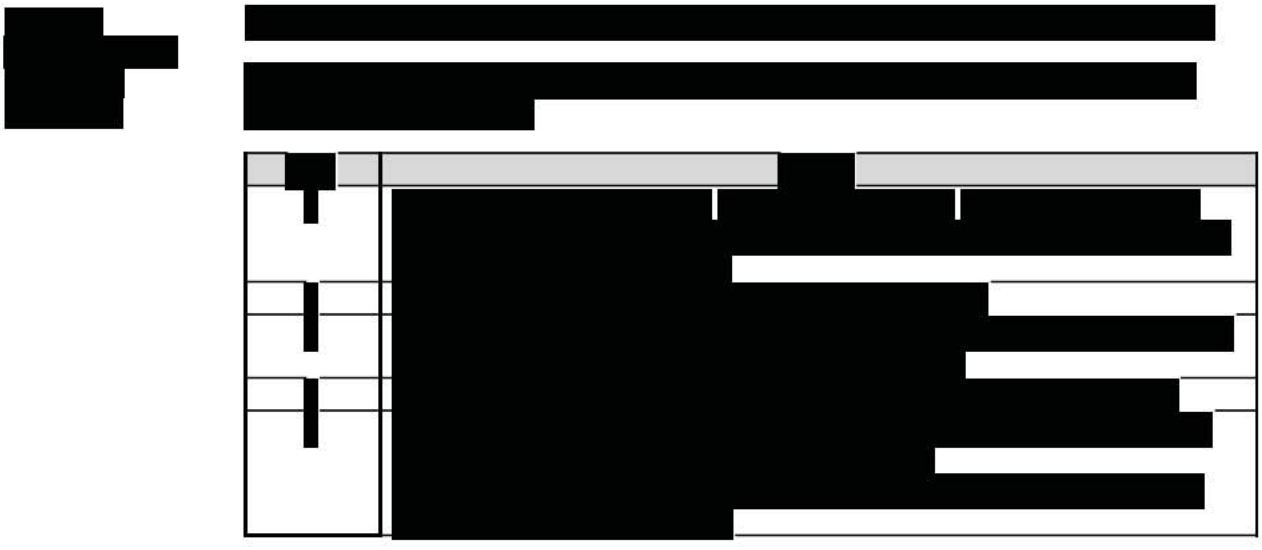

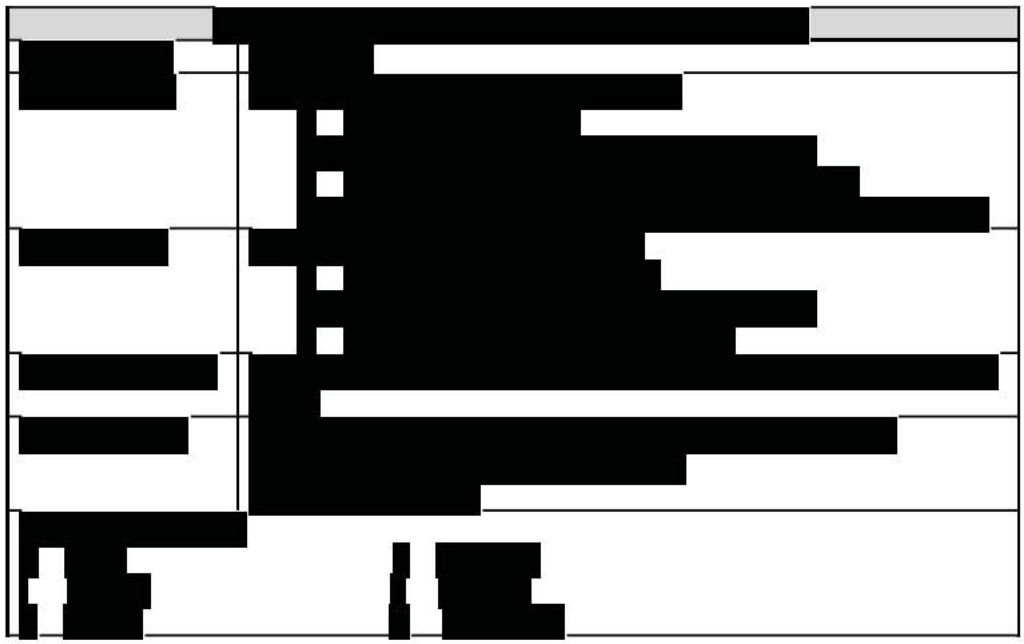

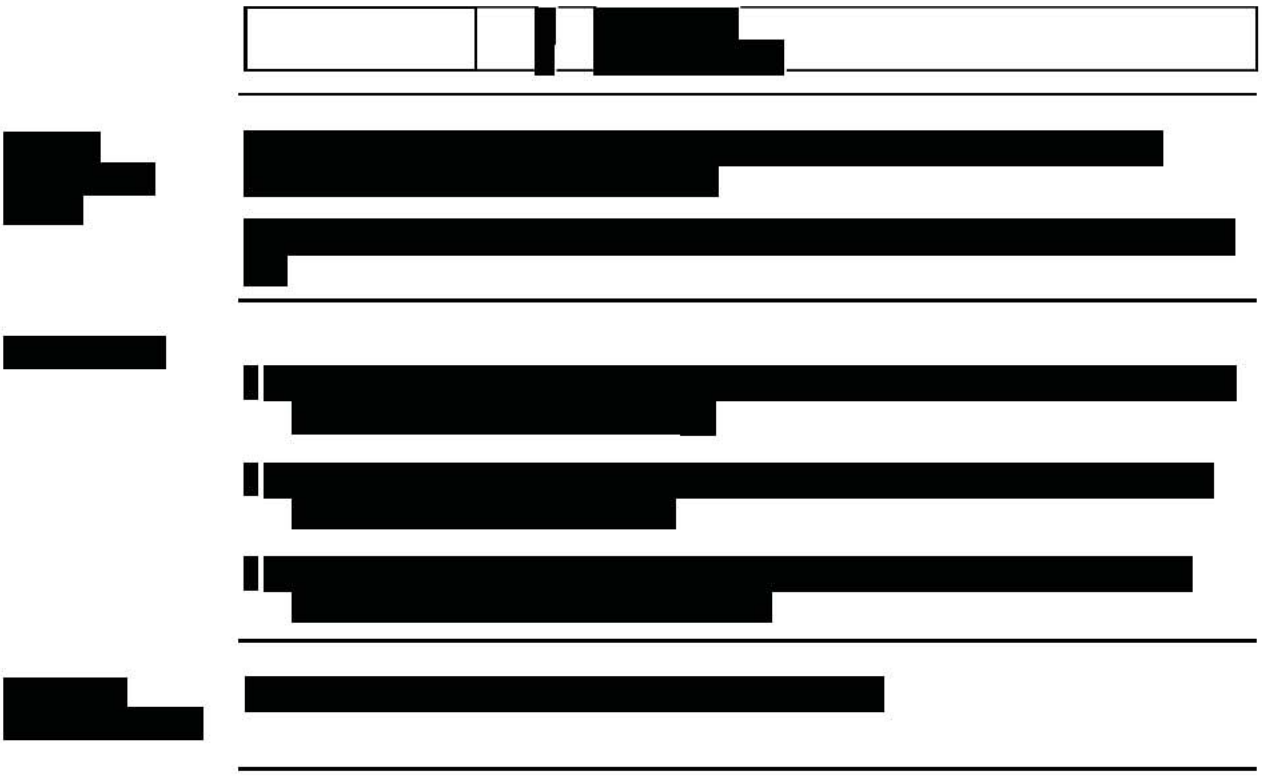

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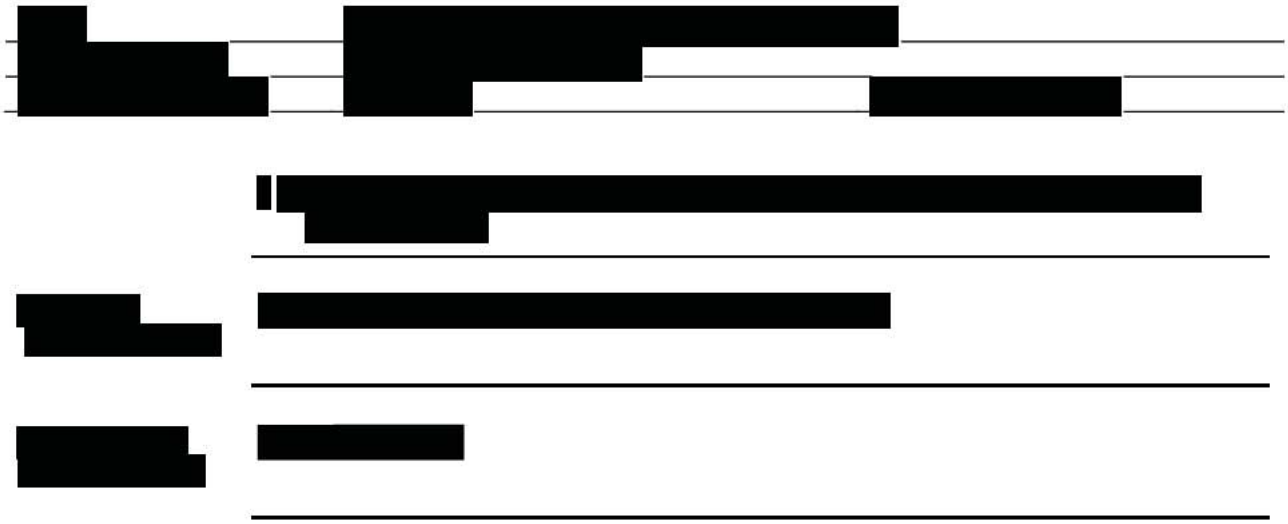

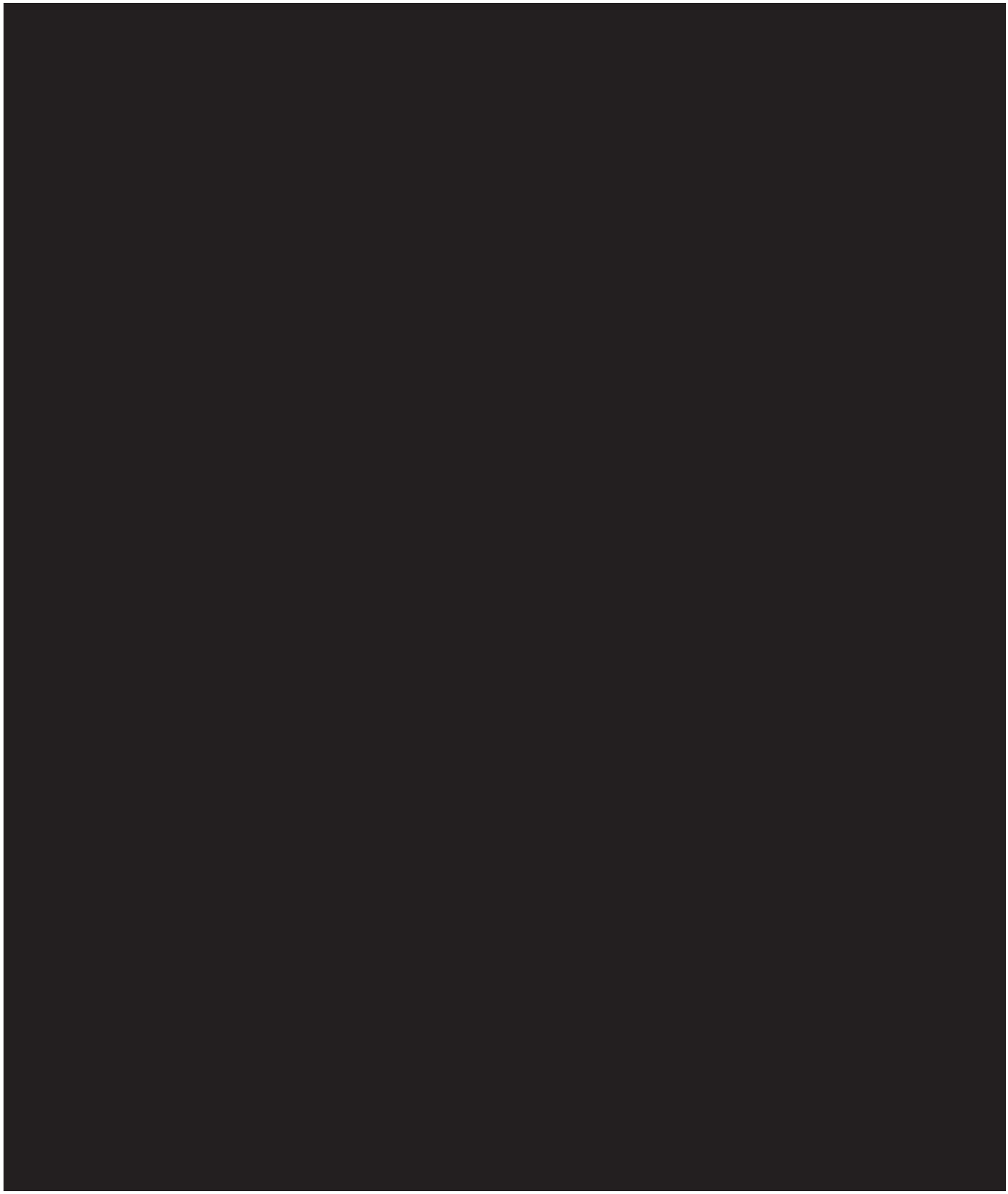

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted] **Determination of Distance Spherocylindrical Refractions**

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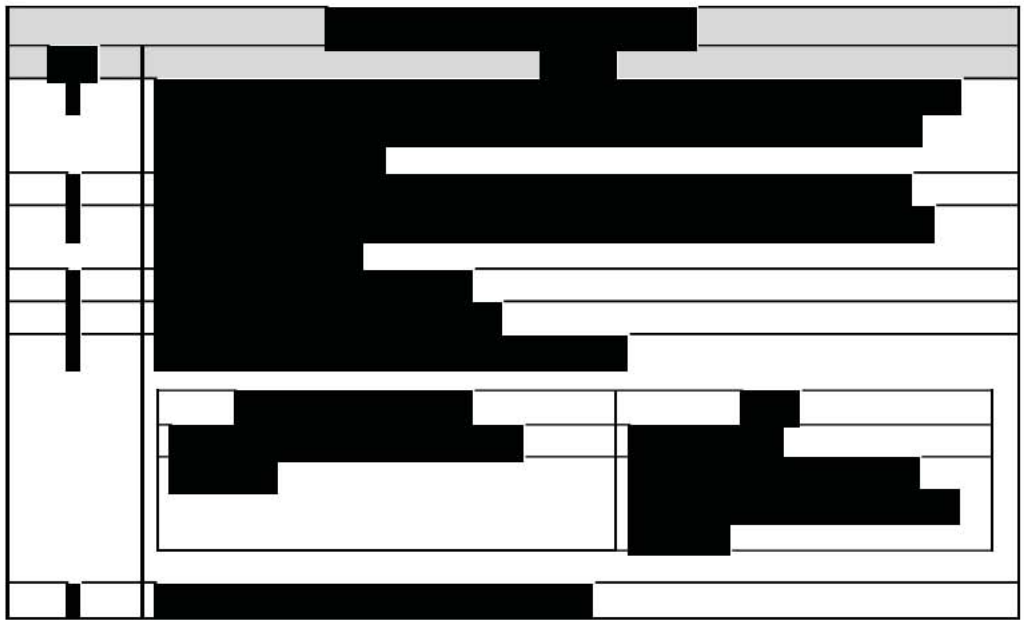
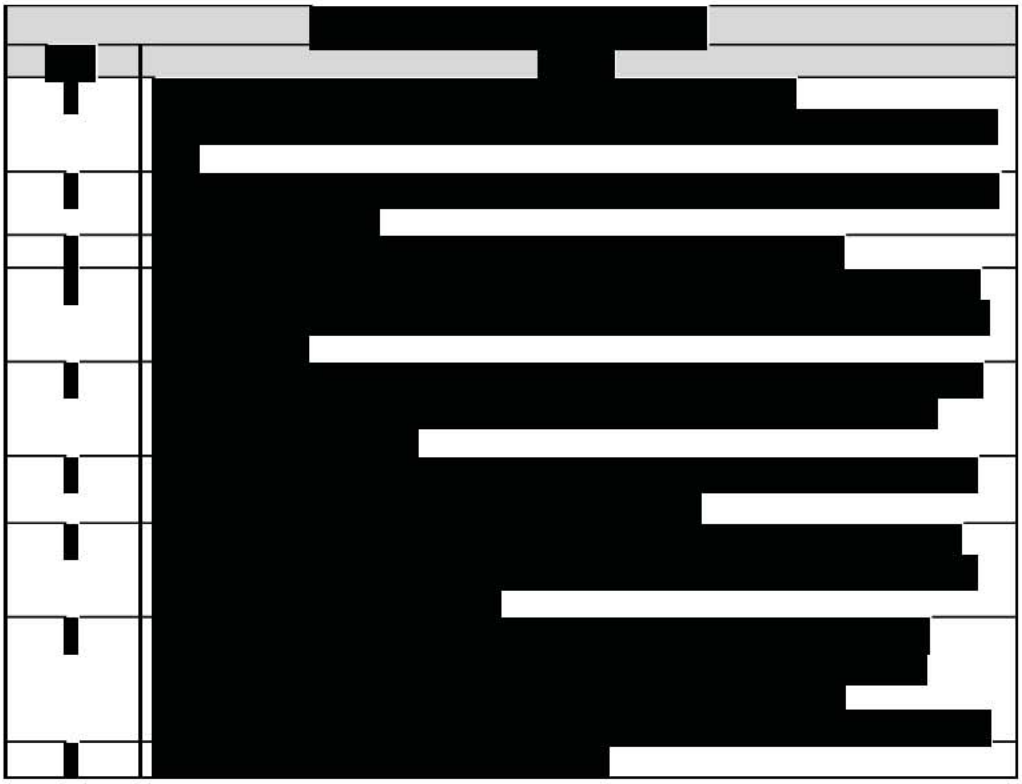
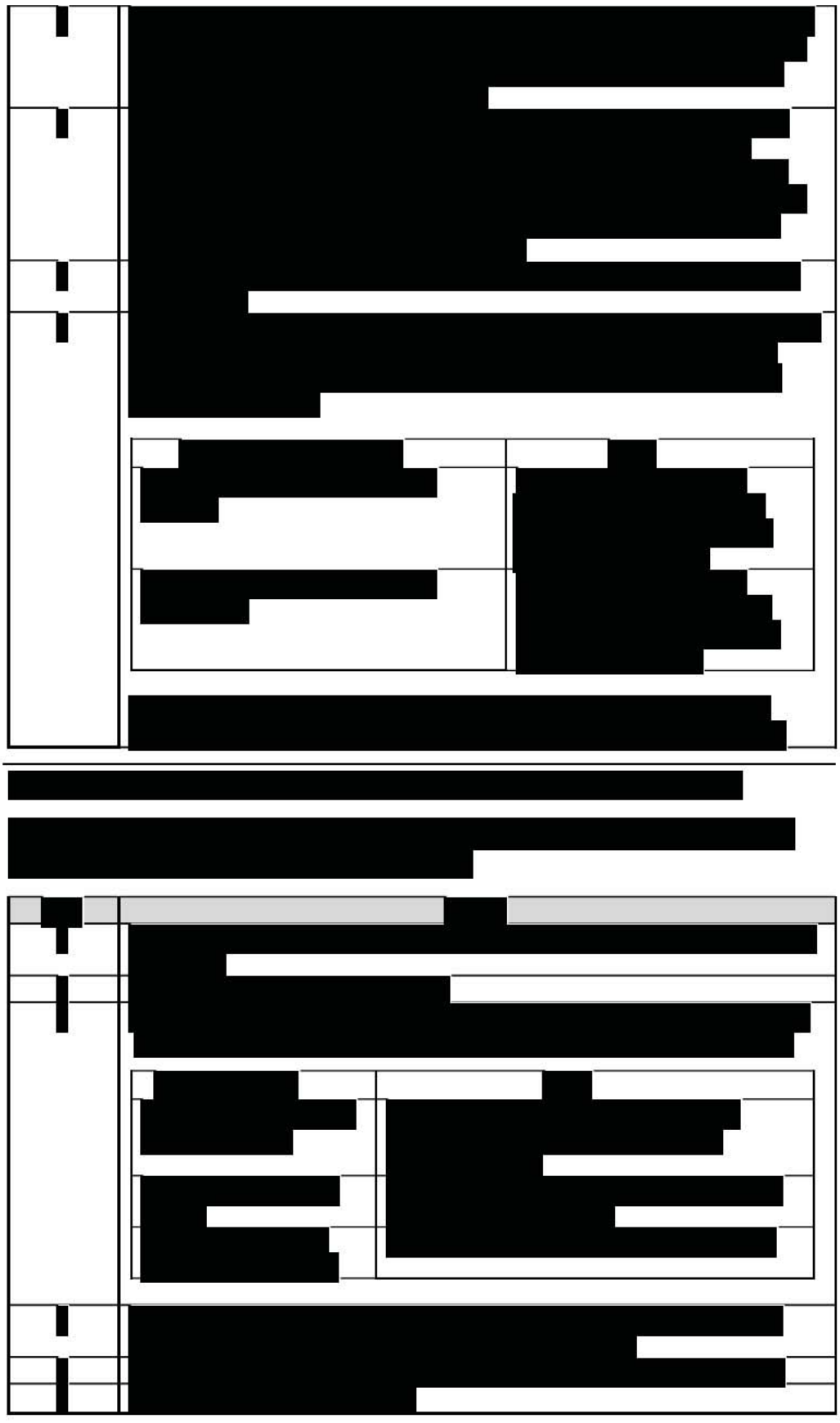
[redacted]







Standard Operating Procedure for Oculus Keratograph 5

DOCUMENT CHANGE SUMMARY

VERSION	DATE	SUMMARY
1.0	05/10/2011	SOP Finalized
2.0	08/17/2017	Revised for the Keratograph 5 (E. Ritchey)

A. Description

System for measuring and analyzing the cornea topography, including topographic measurement, near portion height measurement, lid angle measuring, imaging, pupillometry measuring, and measuring the back surface of a contact lens.

B. Procedure: Topographic Measurement

Note: If the Keratograph is moved to a different location, position the device so that direct light cannot influence measurements. The Keratograph should be operated in a dark room to ensure that the examination is conducted without interference from reflections.

1. Switch on the PC or laptop.
2. Switch on the Keratograph at the power supply (position ON). The LED on the switch will light up in green.
3. The PC will display the Keratograph icon on the desktop. Double click to open the program.
4. The program opens to “Patient Data Management”. A patient list is displayed on the left hand side.
5. If examining a new patient, enter the patient information into the “Patient” box above the patient list. The new patient will then appear in the patient list.
6. Select the patient to be examined from the list. (Clicking [Search] provides search function by first name, last name, date of birth, or by assigned ID number.)
7. This will transfer to the patient window. A list of any previous examinations for this patient is in the examination window on the bottom right.
8. Click [Keratograph] to start the Keratograph software.
9. Select the menu “Examination”.
10. Click on “New examination (eye)”.
11. The Measuring window appears. The keratograph starts the illuminated Placido ring system automatically.
12. Clean the chin and forehead rest of the keratograph with an alcohol pad. A clean chin rest paper can also be used.
13. Position the patient in the keratograph instrument. Adjust the height of the stage so that the chin and forehead rests are comfortable for the patient. The black ring marking should be used to gauge the required height of the patient’s eyes.

14. Instruct the patient to focus on the red light in the center of the Placido ring system for the whole examination.
15. Ask the patient to open his/her eye wide while looking into the red fixation spot.
16. Align the keratograph so that the patient's eye being examined appears sharply focused in the camera image. To do this, slide the slide rest toward the patient until the Placido rings that are projected onto the eye appear as sharply focused as possible. Focus the projected Placido rings by moving the joystick towards or away from the keratograph.
17. Adjust the keratograph according to the arrows shown in the measuring window.
18. A red cross replaces the directional arrow when the correct alignment position has been reached.
19. When all alignment positions are reached, the keratograph automatically initiates the measurement. *NOTE: If the measurement does not start automatically, it can be initiated by pressing the Return key.*
20. The overview display "Topography" appears on the screen.

C. Procedure: Near Portion Height Measurement (used to determine separator positions for bifocal spectacles and RGP lenses)

1. Start the Keratograph software.
2. Position the patient as in a normal topographic measurement.
3. Select the menu "Examination".
4. Click "New examination"
5. Enable the Near Portion Height radio button.
6. Center and focus the eye in the camera image
7. Enable the Ring Illumination radio button. The lighting will be brighter and the pupil size will decrease.
8. Press the Capture Image button or use the foot pedal to trigger the recording. The image is stored automatically.
9. Press the button in the left hand column that correspondes with the contact lens diameter (8.8, 9.2, 9.6 or 10.0)
10. Click on the Blue lens contour/outline and hold down the mouse button. Move the outline down until the lens truncation line aligns with the lower lid margin.
11. Move the cursor to the red-dashed line (the dividing line) until a vertical double arrow appears.
12. Press and hold the mouse button to place the red dividing line at the pupil margin.
13. Release the mouse button and read the suitable dividing line position. This is relative to the geometric center of the lens (in mm).

14. The correct position of the dividing line can be gauged according to the + or – readings, in relation to the desired lens diameter and its central axis.

D. Procedure: Lid Angle Measurement

1. Start the Keratograph software.
2. Position the patient as in a normal topographic measurement.
3. Select the menu “Examination”.
4. Enable the Eyelid Angle radio button.
5. Center and focus the eye in the camera image
6. Press the Capture Image button or use the foot pedal to trigger the recording. The image is stored automatically.
7. An overview image will appear on the screen.
8. Select the Eyelid Angle button in the left hand column
9. Select the lowest point of the lower lid margin by pressing the mouse button.
10. Move the cursor to the approximate position of the lacrimal point, which is approximately located at the highest point of the nasal course of the lid, and press the mouse button.
11. The angle measure appears. Record the angle.

E. Procedure: General Imaging Measurement

Note: The imaging software can be used to make video and image files of the contact lens on the eye.

1. Start the Keratograph software.
2. Position the patient as in a normal topographic measurement.
3. Select the menu “Examination”.
4. Click “New examination”.
5. Select the New Picture/Video radio button in the left hand column.
6. Adjust the Illumination settings in the right hand column per the study protocol (options include IR-Top, IR-Central, Blue for Fluorescein evaluation, White, Placido White, Placido IR, Inner Ring and Fixation). Refer to the Keratograph 5 Instruction Manual for Illumination details.
7. Adjust the Magnification Settings by selecting the appropriate radio button.
8. Adjust the Camera Exposure and Gain using the slider control in the right hand column.
9. Use the Image, Record and Stop buttons to record still/video images.
10. Both video recordings and single images are saved automatically.

***F.* Procedure: Meibography (Meibo-Scan Examination).**

1. Start the Keratograph software.

2. Position the patient as in a normal topographic measurement.
3. Select the menu “Examination”.
4. Click “New examination”.
5. Enable the Meibog. Upper/Lower Lid radio button. If a single image is desired, select the Meibography Single Image radio button
6. Evert the upper eyelid and position the camera so that the upper eyelid fits in the red-framed recording box
7. Press the Image button or use the foot pedal to start recording.
8. Repeat for the lower lid, if applicable.
9. Images are saved automatically, along with date and time information. To view previous images, choose the menu “Examination” and select “Load an old examination.”

G. Procedure: Pupillometry Measuring Procedure

1. Start the Keratograph software.
2. Position the patient as in a normal topographic measurement.
3. Select the menu “Examination”.
4. Select the appropriate measuring program in the “Pupillometer Programs” box:
   a. [Pupillogram] is the automatic, standard pupillometry program.
   b. [Asymmetric Test] is the automatic pupillometry program for detection of unequal pupils.
   c. Manual option for regulating glare intensity.
7. Adjust to view to the center of the pupil by moving the slide rest and joystick accordingly. Sharply focus the image of the pupil by moving the slide rest or joystick towards or away from the keratograph. (The blue bar indicates sharpness of the image; the higher the bar, the sharper the camera image.)
8. To perform an automatic measurement, click the desired program in the measurement menu. The measuring procedure starts automatically. (If performing manual pupillometry, click on the program [Manual] and adjust using “Glare” and “Min. glare”.)
9. The measuring procedure ends automatically when the measurement reaches the right-hand side of the graph. You can also end the automatic measurement procedure by pressing the “Stop” button.
10. The overview screen will automatically appear, and measured data can be analyzed.

H. Procedure: Measuring the Back Surface of a Contact Lens

Note: If unfamiliar with the mounting parts and the contact lens holder during set-up, see images on pages 29-30 in the Keratograph Instruction Manual.

1. Fill the contact lens holder with water:

a. To do this, open the contact lens holder by unscrewing the lock nut. Pour in the water and close the holder by screwing the lock nut back on. Make sure as little air as possible gets trapped inside.
b. Hold the CL holder so that the adjusting screw points downward.
c. Screw the adjusting screw into the holder until the top part of the CL holder is fully wetted with water.
d. Screw out the adjusting screw again until the surface of the water takes on a slightly concave curvature.

2. Clean and dry the CL that is to be measured with a soft cloth. There should be no moisture or residual dust, especially on the concave inside surface.
3. To secure the CL, place between your thumb and index finger and carefully lay it on the surface of the water on the CL holder. Screw the adjusting screw of the CL holder out until the CL sits securely in the holder. (Make sure no air bubbles are produced and no water gets onto the back surface.)
4. Fasten the mounted CL holder by screwing the reference sphere holder to the chin rest.
5. Plug the CL holder onto the mounting clip. Adjust the mounting arm so that the optical axes of the CL roughly coincide with those of the keratograph.
6. Start the Keratograph software.
7. Select New Examination
8. In the Topography field, enable the “CL Back Surface” radio button.

9. Measurement takes place in the same way as the topography measurement.

I. Procedure: Non-Invasive Keratograph Break Up Time (NIKBUT)

1. Switch on the PC or laptop.
2. Switch on the Keratograph at the power supply (position ON). The LED on the switch will light up in green.
3. The PC will display the Keratograph icon on the desktop. Double click to open the program.
4. The program opens to “Patient Data Management”. A patient list is displayed on the left hand side.
5. If examining a new patient, enter the patient information into the “Patient” box above the patient list. The new patient will then appear in the patient list.
6. Select the patient to be examined from the list. (Clicking [Search] provides search function by first name, last name, date of birth, or by assigned ID number.)
7. This will transfer to the patient window. A list of any previous examinations for this patient is in the examination window on the bottom right.
8. Click “Keratograph” to start the Keratograph software.

9. Select the menu “Examination”.
10. Click on “New examination”.
11. Enable the NIKBUT radio button in the left hand column.
12. Select IR or White lighting in the column on the right.
13. Clean the chin and forehead rest of the keratograph with an alcohol pad. A clean chin rest paper can also be used.
14. Position the patient in the keratographer. Adjust the height of the stage so that the chin and forehead rests are comfortable for the patient. The black ring marking should be used to gauge the required height of the patient’s eyes.
15. Instruct the patient to focus on the red light in the center of the Placido ring system for the whole examination..
16. Adjust the keratograph according to the arrows shown in the measuring window.
17. A red cross replaces the directional arrow when the correct alignment position has been reached.
18. When all alignment positions are reached, the keratograph automatically initiates the measurement. The screen will indicate for the examiner to direct the patient to blink 2 times.
19. Following the blinks, the patient should keep their eyes open for as long as possible or until the automatic measure is complete.
20. The keratograph automatically detects the blinks and begins recording tear break-up time across all sections of the cornea.
21. When the measure is complete, or the patient cannot keep their eyes open any longer, the measure is finished and the overview display appears on the screen.

J. References

Oculus Keratograph 5M User Guide

Oculus Keratograph 5M Instruction Manual

[redacted] THERMOGRAPHY

Noncontact Infrared Thermography

DOCUMENT CHANGE SUMMARY

VERSION	DATE	SUMMARY
1.0	12/17/2013	SOP Finalized (Daniel Powell)
2.0	05/17/2015	Minor changes to document (Daniel Powell)
3.0	04/28/2016	Added section for backup storage of captured data (Daniel Powell)

A. Description

Thermography is used to measure the surface temperature of objects, including the skin and ocular surface in humans and other animals. It is postulated that the overall ocular surface temperature in dry eye is greater than in non-dry eye states; this is most likely explained by the increased amount of inflammation in the region. In situations such as the evaporative form of dry eye, the corneal surface may actually be cooler than in non-dry eye cases because the increased evaporation allows for cooling.

B. Equipment/Camera

The device used to capture thermographic images is the ICI-7320 infrared camera (Infrared Cameras Inc., Beaumont, TX). This camera is FDA-approved [510(k) clearance] for use in medical imaging of any part of the body's surface. A USB cable connects the camera to a computer. Using a software program provided by the camera manufacturer, the examiner can adjust the camera settings as well as capture single or multiple images taken in series. In addition, the camera can send data to a computer where a software program can determine the overall surface temperature and other variables. The camera is mounted in an apparatus similar to a biomicroscope.

C. Procedure: Subject Alignment

1. Position the subject comfortably in the chin rest and direct them to place their forehead against the forehead rest.
2. Adjust the height of the chin rest so that the subject's lateral canthus is aligned with the black line on the upright bar.
3. If necessary, move the table to adjust for subject comfort.
4. On the computer desktop, click the IR Flash icon: 

5. Under the Video tab, depending on whether a single or series of images will be captured, select either "Capture Single Image" or "Capture Image Series" (yellow arrow, Fig. 1).
   Note: If "Capture Image Series" is selected, you must also specify how the images will be captured. To do this, select "Configure Series Image Capture" under the Video tab and make the appropriate selections.

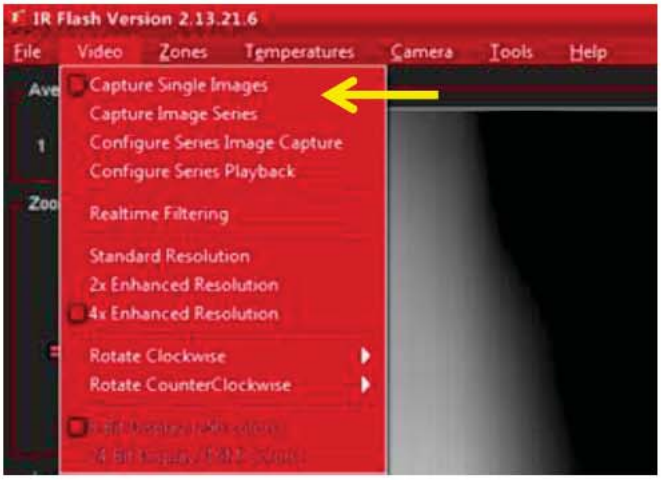


Figure 1

6. On the monitor, you will see an active image in the upper left hand corner. Position the camera using the joystick so the area of interest is centrally located and focused (i.e., the corneal surface/precorneal tear film as indicated by the blue asterisk, Fig. 2).
   Note: If thermographic images of the palpebral conjunctiva overlying the meibomian glands are to be obtained, use a Q-tip to evert the lids and to hold them into place (do not use your fingers).
7. At the upper right hand corner of the screen, use the scroll icon next to "palette" to select the output of the image (gray scale, rainbow, IR, iron, etc.). For studies within TOSI, generally select the "Rainbow" or "Gray Scale" palette from the dropdown menu in the upper right corner of the screen (green arrow, Fig. 2).

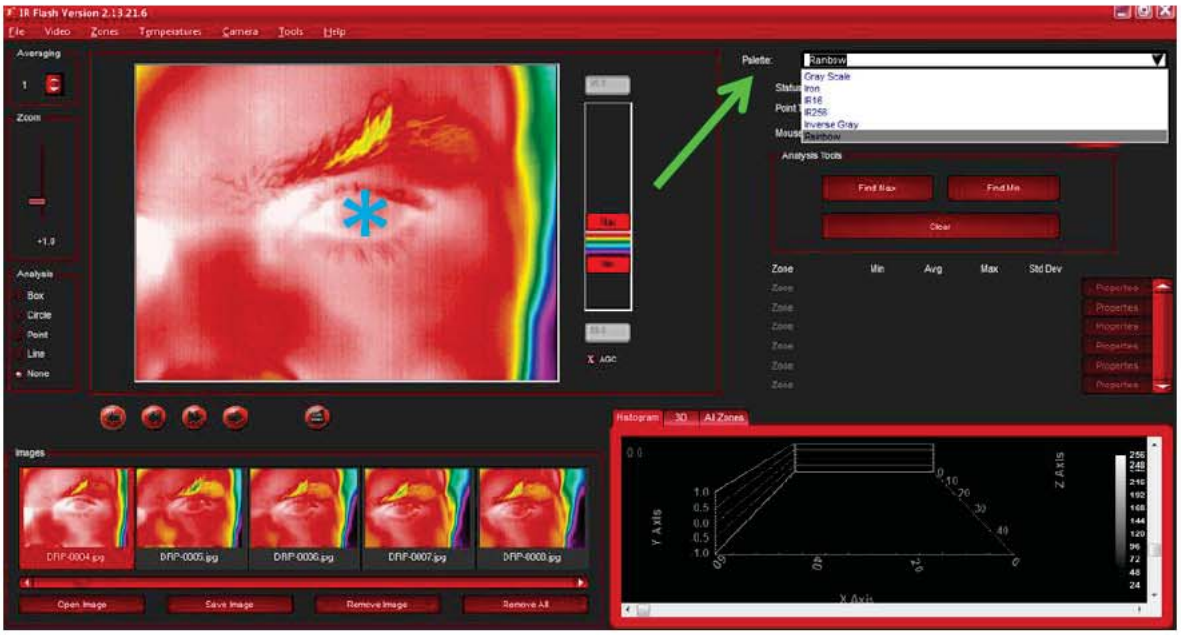


Figure 2

8. To the right of the image of the person in Figure 2, there are settings where you can set the maximum and minimum temperature range that you expect to find in the area of the eye you want to capture the reading. A preset setting is indicated if the box marked AGC is checked. If you want to insert your own maximum and minimum setting, deselect the AGC box and slide the max and/or min boxes up or down to adjust the ranges. You can also enter the temperatures in the gray boxes at the top (maximum temperature) and bottom (minimum) of the sliding scale figure. To measure the ocular surface temperatures, a recommended maximum and minimum setting would be 105 and 80 degrees Fahrenheit, respectively.
9. When you are ready to capture a single image or an image series click on the Camera icon  (for single image capture only) or the red recording icon  (for image series capture only) directly beneath the active image.
10. To exit the program, click on the File tab and then click "Exit".
    Note: If you are using the capture image series option and need to stop image capture, click on the black box icon immediately to the right of the red recording icon directly beneath the active image: 
11. Captured images will appear in the lower left-hand side of the screen. Click on the images to save and then click on "Save Image". To save all images, click on "Save All". Save images under a file name specific for the particular study and subject (and eye, if both eyes are evaluated).
12. Repeat Steps 6-9 above for the fellow eye.
    Note: DO NOT unplug the USB cable from the camera or computer as this may affect calibration, particularly the emissivity correction (which is set to 0.98 as the surface of the human skin has a emissivity of 0.97-1.00; a value of 1.00 is a perfect radiator, or black body). To check for this, click on the Temperatures tab and select "Emissivity Correction".

D. Procedure: Data Backup

1. Data should be backed up after each subject has been completed but at least once per day.
2. Copy files requiring backup: Click on the icon "Shortcut to My Passport" which is located on the desktop.
3. Check to be sure the files have indeed been transferred to the My Passport external hard drive.

E. Procedure: Image Analysis

1. Under the File tab, select the "Load Image" option.
2. Select the area of the image to be analyzed using the options (box, circle, point, line, or none) located in the Analysis box located at left-hand margin of the screen (yellow arrow, Fig. 3).

3. Click the image immediately to the right and click the area where you would like to evaluate the surface temperature. The option selected (i.e., box) will show up on the image. This is called a Zone. You can also click on other areas of the image to introduce new zones or select another analysis (i.e, circle) to introduce a new zone shape to the image for surface temperature analyses within separate areas of the image. Each Zone will be designated in numerical order (see Fig. 3).
4. Use the red boxes to widen the area of analysis as needed.
5. The results of the minima and maxima surface temperature along with the standard deviation in the designed area of analysis will show at the right-hand side of the screen about midway down (green arrow, Fig. 3). Transfer data points into an Excel spreadsheet for additional analyses (i.e., statistical analyses).
6. Repeat Steps 1-5 to analyze additional images from the same eye (i.e., images captured in series) or from the fellow eye.
7. To delete zones within the image, click on the "Zones" tab and then click "Clear All".

Figure 3

D. Reference

ICI 7430 Camera Manual, Infrared Cameras Inc., Beaumont, TX: 2012.

[redacted]**BRUDER MASK**

Work Aid: Bruder Mask

The following work aid to prepare a Bruder Mask for treatment of Meibomian Glands.

1. Shake the Bruder Mask to evenly distribute the MediBeads within the mask
2. Place the mask in a microwave and heat for 20 seconds
3. Remove the mask from the microwave, shake the mask to evenly distribute the MediBeads.
4. Measure the mask temperature
    a. If the temperature is greater than 42 degrees Celsius (108 degrees Fahrenheit), shake the Bruder Mask to redistribute the MediBeads and re-measure the temperature. If the temperature continues to be greater than 42 degrees Celsius, measure the temperature every 60 seconds until the target temperature of 42 degrees Celsius or less is obtained.
    b. If Bruder Mask temperature is under 37 degrees Celsius (100 degrees Fahrenheit), place in the microwave for an additional 5 seconds, remove from the Microwave and re-measure
        i. If the new temperature is between 37 and 42 degrees, proceed
        ii. If the temperature exceeds 42 degrees, go to step 4a
        iii. NOTE: Step 4b may be repeated one additional time. Total heating time of the Bruder Mask shall not exceed 30 seconds.
5. Place the Bruder Mask on/in the Bruder Mask Sleeve
6. Apply the Bruder Mask and Sleeve to the closed eye(s). The mask should not be applied tightly.
7. The mask should be applied for 10 minutes, or as specified in the protocol.

References:

1. Bruder Eye Compress Moist Heat Instruction Sheet

DOCUMENT CHANGE SUMMARY

VERSION	DATE	SUMMARY
1.0	06-July-2018	Original Work Aid (Eric Ritchey)

Sample Bruder Mask Temperature Log

Subject ID			
Date (DDMMMYYYY)	Time (24 Hr)	Microwave Time (sec)	Temperature (C)
Page _____ of _____			

[redacted]EYELID PHOTOGRAPHY

Work Aid: Eyelid Photography

Equipment: Haag-Streit BQ-900 Biomicroscope, Cannon EOS Digital Camera

1. Turn on computer and monitor
2. Turn on digital camera (lower right hand corner of camera, mounted above slit lamp oculars)
3. Double click on *EOS Utility*. Icon on computer desktop.
    a. Select "Camera Setting/Remote Shooting" option on menu
4. Turn on *Digital Photo Professional* software. Icon on computer desktop.

<u>EOS Utility Set Up</u>

1. Click on File Folder icon
2. Confirm Destination folder for the study
3. Click FILE NAME tab
4. Select file name format pull-down for the study
    a. Look at the example line to tell if the name string is for OD or OS
    b. Each eye (OD/OS) has it's own pull down selection.

<u>Camera Set Up</u>

1. Turn Room lights ON
2. Confirm aperture knob in front of slit lamp oculars is set to "2"
3. Set Slit Lamp Mag to setting specified by the project
4. Set Illumination tower 25-30 degrees temporal.
    a. Make sure tower is not visible in the right ocular.
    b. Illumination tower position may be changed to avoid excessive reflection off the tissue of interest
5. Set 5mm vertical beam
6. Place flip up diffuser in the beam path
7. Set tower illumination to "Half Open" illumination
8. Take photo by pressing blue button in front of the slip lamp joystick.

DOCUMENT CHANGE SUMMARY

VERSION	DATE	SUMMARY
1.0	07-June-2018	Original Work Aid (Eric Ritchey)

[redacted] LIPIVIEW II LIPID LAYER THICKNESS

Work Aid: TearScience LipiView II Lipid Layer Thickness Measurement

1. Turn on the LipiView II power button at the base of the unit
2. Log into the LipiView II
3. At the subject page, select “add patient”
4. To identify subjects
    a. Last name = study name; first name = subject number, Date of Birth = date of the examination **OR**
    b. Enter a subject ID in the Patient ID field.
5. Select the Lipid Imaging test from the Capture/View screen and press “new”
6. Make sure the chin rest is in the proper position. The position for lipid layer analysis is the position closest to the device. Clean with an alcohol pad.
7. Adjust chin rest height so that the lateral canthus of the subject is aligned with the marks on the LipiView II headrest.
8. Instruct the subject to look at the orange fixation light
9. Touch the side of the screen corresponding with the eye to be imaged
10. Using the touch screen, position the image of the eye so that the pupil is centered
11. Use the target icon on the touch screen to auto-focus the image
12. **Tell the patient to blink normally** and fixate on the orange light
13. Press “Capture” on the touch screen. The video will record for 20 seconds
    a. Use the play button to review the video quality
    b. If the video quality is unacceptable, use the “trash can” icon to delete and take another recording
14. Record the other eye using the procedure above
15. Press “Analyze”
16. Record the following values
    a. Average Lipid Layer Thickness (nm)
    b. Minimum Lipid Layer Thickness (nm)
    c. Maximum Lipid Layer Thickness (nm; this may reach a ceiling value of “100+nm”)
    d. C Factor
    e. Standard Deviation

References:

1. LipiView II Device Training Video

DOCUMENT CHANGE SUMMARY

VERSION	DATE	SUMMARY
1.0	06-July-2018	Original Work Aid (Eric Ritchey)

Work Aid: MiBoFlo

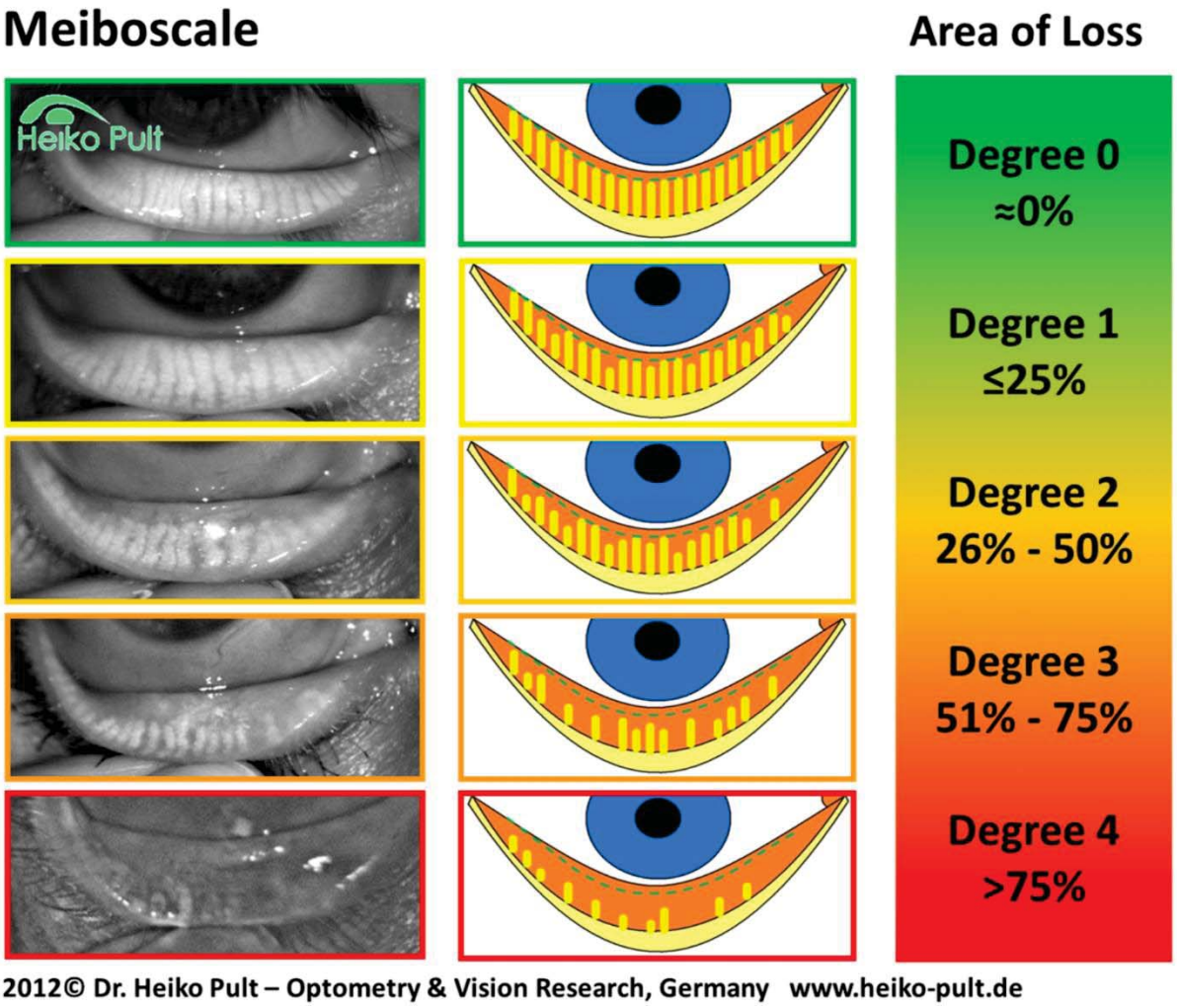
1. Verify that the appropriate treatment eyepad to be used per the study instructions is inserted in the unit
2. Clean the MiBoFlo Pad with an alcohol swab
3. Turn on MiBoFlo power key the on position and wait until the pre-treatment warm up timer is complete
4. Place some ultrasound transmission gel on the eyepad
5. Instruct the subject to close his/her eyes
6. Press start on the touchpad
7. Place the eyepad on the eye and slowly move side to side laterally to disperse the ultrasound transmission gel
8. With light pressure, massage the lids with a gentle circular motion.
9. Apply additional ultrasound transmission gel as needed, disrupting treatment as minimally as possible
10. End treatment when the timer expires
11. Using a facial tissue, remove any excess ultrasound transmission gel
12. Perform the procedure on the other eye, if needed.

References:
1. MiBoFlo Manual
2. MiBoFlo Training Video

DOCUMENT CHANGE SUMMARY

VERSION	DATE	SUMMARY
1.0	08-July-2018	Original Work Aid (Eric Ritchey)

PULT MEIBOSCALE



[redacted] THERMAL CAMERA 510(K) SUMMARY

K073581

510(K) SUMMARY
This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

510(k) number:

JUL 11 2008

1. Submitter's Identification:
Texas Infrared
2105 West Cardinal Drive
Beaumont, TX 77705
Contact: Gary Strahan
President/CEO
Phone: 409-861-0788
FAX: 409-866-7229
Date Summary Prepared: 7-27-2007

2. Name of the Device:
Common Name: Telethermographic System (Adjunctive Use)
Trade or Proprietary Name: ICI P and S Series IR Camera(s) and the IR Flash Software version 1.0
Device Class: 1
Product Code: LHQ
Regulation Number: 884.2980

4. Predicate Device Information:

Trade Name: A20M
FLIR Systems, Inc.
27700A SW Parkway Avenue
Wilsonville, OR 97070 USA
Phone: +1 800 322.3731
Fax: +1 503.498.3904
510(k) number: K033967

5. Device Description:

The ICI Series P and S IR Cameras, which provides capture of skin surface temperature of any part of the body, and the IR Flash Software version 1.0, which provides visualization and reporting functionalities, are intended for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of relative skin surface temperature.

Environment of use: hospitals, sub-acute healthcare settings, public areas, i.e., airport.

ICI P and S Series Cameras

Base IR Camera	***ICI P and S series Cameras***
Intended Use	The ICI Series P and S IR Cameras, which provides capture of skin surface temperature of any part of the body, and the IR Flash Software version 1.0, which provides visualization and reporting functionalities, are intended for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of relative skin surface temperature. Environment of use: hospitals, sub-acute healthcare settings, public areas, i.e., airport.
Technology	FPA uncooled Microbolometer
Material	Vanadium Oxide
Spectral Response	8 - 14 um
Contrast/Brightness	Software Controlled
Spatial Resolution IFOV	1.13 mrad
Data Output	Digital USB 2.0
Thermal Time Constant	14 ms
Thermal Sensitivity	0.038C @ 25C
Accuracy	+2C or 2%
Emissivity Correction	Computer Controlled
Performance	38 mK NETD
Frame Rate	S Series Camera 50-60fps P Series Camera < 9 fps
Pitch Size	25 um
Encapsulation	IP54
Optics	25mm with 22° FOV
Vibration	3G's
Shock	30G's
Array size	320 x 240 array
Weight	5.2oz (148g) w/lens
Tripod Mount	1/4" - 20 female thread
Operating Temperature	-20C to +50C
Storage Temperature	-40C to +70C
Dimensions	2.1"x3.2"x0.5"
Focus	Manual
Special Computer Hardware	USB 2.0 Compatible running Windows XP or Windows Vista. 64-bit operating systems are not supported at this time.
Power Supply	5 VDC @ 500ma max draw from USB. Systems with motorized focus have an additional 12 VDC supply @ 1A max.

Components of the system include:

ICI P or S Series IR Camera
USB Cable
Tripp-Lite model IS250HG isolation transformer

6. Intended Use:

The ICI Series P and S IR Cameras, which provides capture of skin surface temperature of any part of the body, and the IR Flash Software version 1.0, which provides visualization and reporting functionalities, are intended for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of relative skin surface temperature.

Environment of use: hospitals, sub-acute healthcare settings, public areas, i.e., airport.

7. Comparison to Predicate Devices:

Technical characteristics of the device(s) compared to the predicate device:

Base IR Camera	**ICI P and S Series IR Camera(s) and the IR Flash Software version 1.0**	**A20M (K033967)**
Intended Use	The ICI Series P and S IR Cameras, which provides capture of skin surface temperature of any part of the body, and the IR Flash Software version 1.0, which provides visualization and reporting functionalities, are intended for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of relative skin surface temperature. Environment of use: hospitals, sub-acute healthcare settings, public areas, i.e., airport.	The Flir devices are intended for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of differences in skin surface temperature changes. It can visualize, document temperature patterns and changes. Environment of use: hospital, sub-acute, public areas, i.e., airports
Technology	FPAuncooled Microbolometer	FPA uncooled Microbolometer
Material	Vanadium Oxide	Amorphus Silica
Spectral Response	8 -14 um	7.5 -13um
Contrast/Brightness	Software Controlled	Manual or Software Controlled
Spatial Resolution IFOV	1.13 mrad	2.7 mrad
Data Output	Digital USB 2.0	RS170 EIA/NTSC or CCIR/PAL composite
Thermal Time Constant	14 ms	Unknown
Thermal Sensitivity	0.038C @ 25C	0.120C @ 30C
Accuracy	+2C or 2%	+2C or 2%
Emissitivity Correction	Computer Controlled	Variable from 0.1 to 1.0
Performance	38 mK NETD	Under <80mK

Frame Rate	S Series Camera 50-60fps P Series Camera < 9fps	60 fps
Pitch Size	25 um	Unknown
Encapsulation	IP54	IP40
Optics	25mm with 22° FOV	25mm with 19° FOV
Vibration	3G's	2G's
Shock	30G's	25G's
Array size	320 x 240 array	320 x 240 array
Weight	5.2oz (148g) w/lens	1.7lbs (0.8 kg)
Tripod Mount	1/4" -20 female thread	1/4" -20 female thread
Operating Temperature	-20C to +50C	-15C to +50C
Storage Temperature	-40C to +70C	-40C to +70C
Dimensions	2.1"x3.2"x0.5"	6.2"x2.9"x3.1"
Focus	Manual	Manual or Software Controlled
Special Computer Hardware	USB 2.0 Compatible running Windows XP or Windows Vista. 64-bit operating systems are not supported at this time.	Ethernet connection, Video capture device to vonvert RS-170 video, Firewire 8/16-bit monochrome and 8-bit color
Power Supply	5 VDC @ 500ma max draw from USB. Systems with motorized focus have an additional 12 VDC supply @ 1A max.	AC adaptor 110/220 vac, 50/60hz input to 12/24vdc nominal, <6w output

8. Discussion of Non-Clinical Tests Performed for Determination of Substantial Equivalence are as follows:

The devices have been tested and found to comply with IEC-60601-1 and IEC 60601-1-2. Software validation was performed.

9. Discussion of Clinical Tests Performed:

Not applicable

10. Conclusions:

The subject device(s) has the same intended use and similar characteristics as the predicate device. Moreover, documentation supplied in this submission demonstrates that any difference in their technological characteristics do not raise any new questions of safety or effectiveness. Thus, the ICI P and S Series IR Camera(s) and the IR Flash Software version 1.0 are substantially equivalent to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 11 2008

Texas Infrared
% Mr. Daniel W. Lehtonen
Responsible Third Party Official
Intertek Testing Services NA, Inc.
2307 E. Aurora Rd., Unit B7
TWINSBURG OH 44087

Re: K073581
Trade/Device Name: ICI P and S Series IR Camera(s) and the IR Flash Software version 1.0
Regulation Number: 21 CFR 884.2980
Regulation Name: Telethermographic System
Regulatory Class: I
Product Code: LHQ
Dated: June 27, 2008
Received: June 30, 2008

Dear Mr. Lehtonen:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at one of the following numbers, based on the regulation number at the top of this letter.

21 CFR 876.xxxx	(Gastroenterology/Renal/Urology)	240-276-0115
21 CFR 884.xxxx	(Obstetrics/Gynecology)	240-276-0115
21 CFR 892.xxxx	(Radiology)	240-276-0120
Other		240-276-0100

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Nancy C Brogdon

Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE

510(k) Number (if known): K073581

Device Name : ICI P and S Series IR Camera(s) and the IR Flash Software version 1.0

Indications for Use:

The ICI Series P and S IR Cameras, which provides capture of skin surface temperature of any part of the body, and the IR Flash Software version 1.0, which provides visualization and reporting functionalities, are intended for use as an adjunct to other clinical diagnostic procedures in the diagnosis, quantifying, and screening of relative skin surface temperature.
Environment of use: hospitals, sub-acute healthcare settings, public areas, i.e., airports.

Prescription Use __X__ AND/OR Over-The-Counter Use
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE -CONTINUE ON ANOTHER PAGE IF NEEDED)

(Division Sign-Off)
Division of Reproductive, Abdominal and Radiological Devices
510(k) Number K073581

[redacted] THERMAL CAMERA SCIENTIFIC SPECIFICATIONS

ICI 7320 P Series

ICI 7320 Professional Series Radiometric Camera

Detector:	Microbolometer 320 x 240 UFPA VOX
Field of View:	18° with standard 25mm lens
Instantaneous Field of View:	Lens dependent
Spectral Response:	7 to 14 µm
Video Update Rate:	50-60 Hz (14 bit digital)
Focusing Distance:	4" to infinity
Focus Adjustment:	Manual / Electronic focus available
Temperature Dynamic Range:	16 Bits
Accuracy :	± 1° C or ±1%
Thermal Sensitivity:	<27 mk
Operating Temperature:	-20° C to 50° C
Storage Temperature:	-40° C to 70° C
Environmental Protection:	IP54
Shock:	30g
Vibration:	3g
Palettes:	8 palettes including color and B&W

InfraredCamerasInc.com
(866) 861-0788
(409) 861-0788

Includes IR Flash Professional Thermal Imaging Software.
Optional application software: DLL's-Labview & C++
Optional SDK available

Automatic or Manual Gain and Level
1 watt input powered by computer USB connection
Weight: 5.2 oz (148g) w/ lens
Dimensions: 2.1" x 3.2" x 0.5" (53mm x 81mm x 13mm)
Data Interface: USB2
Outputs: USB2

Optional Lenses Available

5mm	87° FOV
10mm	46° FOV
18mm	25° FOV
25mm	18° FOV
50mm	11° FOV
75mm	7.3°FOV
100mm	5.5°FOV
150mm	3.7°FOV

ICI 7320 shown with optional 35 Micron Microscopic Lens

PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6281 MiBo ThermoFlo Lid Temperature Evaluation

Version and Date: 2.0, Amendment 1.0 15 November 2018

I have read and understand the protocol specified above and agree on its content.

I agree to conduct this study according to ISO 14155,[1] GCP and ICH guidelines,[2] the Declaration of Helsinki,[3] United States (US) Code of Federal Regulations (CFR),[8] and the pertinent individual country laws/regulations and to comply with its obligations, subject to ethical and safety considerations. The Principal Investigator is responsible for ensuring that all clinical site personnel, including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

I will assure that no deviation from, or changes to the protocol will take place without prior agreement from the Sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants.

I am responsible for ensuring that all clinical site personnel including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

All clinical site personnel involved in the conduct of this study have completed Human Subjects Protection Training.

I agree to ensure that all clinical site personnel involved in the conduct of this study are informed about their obligations in meeting the above commitments.

I shall not disclose the information contained in this protocol or any results obtained from this study without written authorization.

Principal Investigator:

_____ _____

Signature Date

_____

Name and Professional Position (Printed)

Institution/Site:

_____

Institution/Site Name

_____

Institution/Site Address