Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

Clinical Evaluation of Manufacturing Curing Processes for a Reusable Multifocal Optical Design in a Presbyopic Population

Protocol CR-6317

Version: 1.0

Date: 06 November 2018

Investigational Products: JJV Investigational senofilcon A Multifocal Contact Lenses manufactured with various curing processes

Key Words: Presbyopia, Multifocal, senofilcon A, Daily Wear, Reusable, Dispensing, Randomized

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.

Confidentiality Statement:

TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

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SPONSOR NAME AND ADDRESS

Johnson & Johnson Vision (JJV)
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MEDICAL MONITOR

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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.

[redacted]

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,[4] ICH guidelines,[2] ISO 14155,[1] and the Declaration of Helsinki.[3]

Author	See Electronic Signature Report [redacted] Sr. Principal Research Optometrist	DATE
Clinical Operations Manager	See Electronic Signature Report [redacted] Clinical Operations Manager	DATE
Biostatistician	See Electronic Signature Report [redacted] Biostatistician IV	DATE
Data Management	See Electronic Signature Report [redacted] Clinical Project Manager-Data and Systems	DATE
Reviewer	*Fellow Review Not Required*	
Approver	See Electronic Signature Report [redacted] Presbyopia Platform Sr. Manager	DATE

[redacted]

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Date
1.0	Tom Karkkainen	Original Protocol	06-Nov-2018

SYNOPSIS

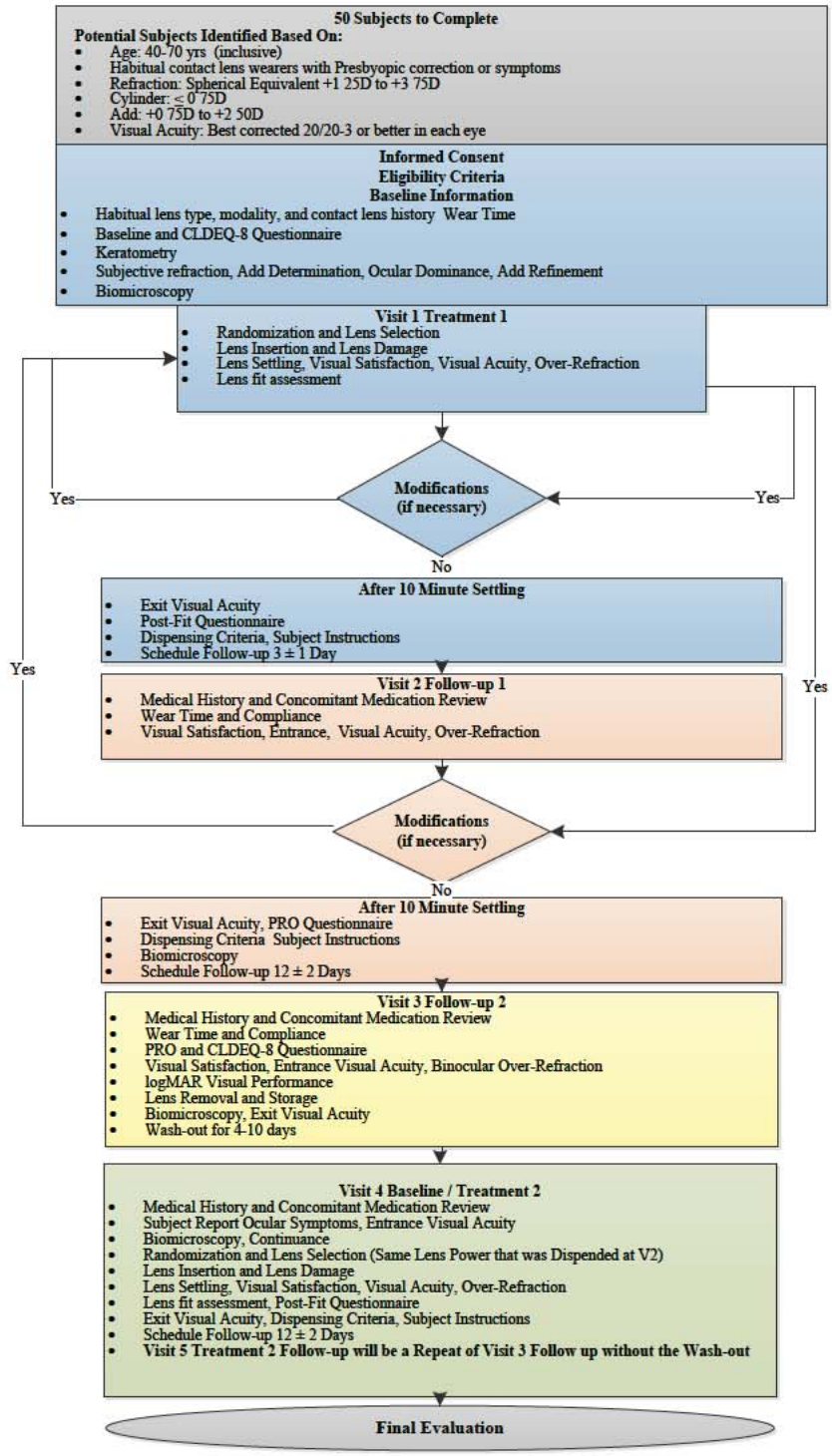
Protocol Title	Clinical Evaluation of Manufacturing Curing Processes for a Reusable Multifocal Optical Design in a Presbyopic Population
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Phase 2
Trial Registration	This study will be registered on ClinicalTrials.gov.
Test Article(s)	Investigational Products: JJVC Investigational Multifocal Contact Lens manufactured in senofilcon A material cured using various processes.
Wear and Replacement Schedules	Wear Schedule: The study lenses will be daily wear reusable, cleaned and stored each night. Replacement Schedule: The study lens that is fit at Visit 1 will be replaced at Visit 2 optimization visit and then worn as daily reusable modality without further planned replacement for 12-14 days. The Test and Control lenses will also be replaced when lost or damaged.
Objectives	This study is an evaluation of the visual performance, subjective response, lens fit and ocular physiological response of the JJV Investigational senofilcon A Multifocal Contact Lenses. The Test lenses will be manufactured using two different manufacturing processes.
Study Endpoints	Primary endpoint: CLUE vision scores. Secondary endpoint: logMAR visual acuity. Other endpoints: lens fit, summary of number of lenses needed to fit (optimize) the subject, CLUE comfort/handling scores, corneal staining, and ocular redness.
Study Design	This is a double-masked, randomized two-way crossover, dispensing clinical trial. A total of approximately 50 eligible hyperopic subjects will be targeted to complete the study. The subjects will be fit in the first study lens based on the randomization scheme and wear the lens for 2-4 days then undergo optimization, if applicable, and wear the optimized pair for an additional 10-14 days. The remaining lens will be fit according to the random scheme following a 4-10-day wash-out period, using the same lens powers, that were dispensed at Visit 2. The primary endpoint will be CLUE vision scores. The secondary endpoint will be the logMAR visual acuity.
Sample Size	A total of approximately 50 subjects will be targeted to complete.
Study Duration	The study will last approximately 2-4 months.

Anticipated Study Population	Healthy male and female volunteers with presbyopia will be invited to participate in the study. Subjects will be adapted soft contact lens wearers in both eyes. Additional information regarding the eligibility of the population can be found in the inclusion/exclusion criteria outlined below.
Eligibility 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. The subject must appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. The subject must be at least 40 years of age and not greater than 70 years of age. 4. The subject's distance spherical equivalent refraction must be in the range of +1.25 D to +3.75 D in each eye. 5. The subject's refractive cylinder must be ≤0.75 D in each eye. 6. The subject's ADD power must be in the range of +0.75 D to +2.50 D. 7. The subject must have best corrected visual acuity of $20/20^{-3}$ or better in each eye. 8. Subjects must own a wearable pair of spectacles if required for their distance vision. 9. The subject must be an adapted soft contact lens wearer in both eyes (i.e. worn lenses a minimum of 2 days per week for at least 8 hours per wear day, for 1 month of more duration). 10. The subject must either already be wearing a presbyopic contact lens correction (e.g., reading spectacles over contact lenses, multifocal or monovision contact lenses, etc.) or if not respond positively to at least one symptom on the "Presbyopic Symptoms Questionnaire". Potential subjects who meet any of the following criteria will be excluded from participating in the study: 1. Currently pregnant or lactating. 2. Any active or ongoing ocular or systemic allergies that may interfere with contact lens wear. 3. Any active or ongoing systemic disease, autoimmune disease, or use of medication, which may interfere with contact lens wear. This may include, but not be limited to, diabetes, hyperthyroidism, Sjögren's syndrome, xerophthalmia, acne rosacea, Stevens-Johnson

	syndrome, and immunosuppressive diseases or any infectious diseases (e.g. hepatitis, tuberculosis). 4. Clinically significant (Grade 3 or 4) corneal edema, corneal vascularization, corneal staining, tarsal abnormalities or bulbar injection, or any other corneal or ocular abnormalities which would contraindicate contact lens wear. 5. Entropion, ectropion, extrusions, chalazia, recurrent styes, dry eye, glaucoma, history of recurrent corneal erosions. 6. Any previous, or planned, ocular or intraocular surgery (e.g. radial keratotomy, PRK, LASIK, lid procedures, dacryocystorhinostomy, cataract surgery, retinal surgery, etc.). 7. A history of amblyopia, strabismus or binocular vision abnormality. 8. Any current ocular infection or inflammation. 9. Any current ocular abnormality that may interfere with contact lens wear. 10. Use of any of the following oral medications within 1 week prior to enrollment: oral retinoid isotretinoin (e.g. Accutane), oral tetracyclines, topical scopolamine, systemic steroids. 11. Use of any ocular medication, with the exception of rewetting drops. 12. History of herpetic keratitis. 13. Participation in any contact lens or lens care product clinical trial within 30 days prior to study enrollment. 14. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician). 15. Any known hypersensitivity or allergic reaction to Optifree®Replenish® multi-purpose care solution, sodium fluorescein or Eye-Cept® rewetting drop solution.
Disallowed Medications/Interventions	Use of any prescription or over-the-counter (OTC) medications that may affect contact lens wear.
Measurements and Procedures	logMAR Visual acuity and Subjective responses for vision using the CLUE questionnaire.
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	Eye-Cept Rewetting drops, lens cases, glass vials, saline, ETDRS light cabinet, logMAR charts, and Near logMAR charts. Optifree®Replenish® Contact Solution.
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
BCC	Binocular Crossed Cylinder
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLDEQ-8	Contact Lens Dry Eye Questionnaire-8
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
HIV	Human Immunodeficiency Virus
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Council for 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, Inc.
LC	Limbus Center
LogMAR	Logarithm of Minimal Angle of Resolution
LSM	Least Square Means
MedDRA©	Medical Dictionary for Regulatory Activities
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

[redacted]

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

Johnson & Johnson Vision has a daily disposable multifocal contact lens, 1-DAY ACUVUE® Moist Multifocal, in the market place. The lens is the only marketed soft multifocal lens to have its optical design optimized for the changes that occur in pupil size with refractive error. There is a desire to evaluate a multifocal contact lens design in a reusable modality. The purpose of this study is to evaluate a multifocal optical design manufactured from senofilcon-A material using two slightly different manufacturing processes to determine if these differences have a significant impact on the on-eye performance of the lens.

1.1. Name and Descriptions of Investigational Products

Test Lens: JJV Investigational senofilcon A Multifocal Contact Lenses. The lenses are manufactured in senofilcon A and use two different manufacturing processes.

1.2. Intended Use of Investigational Products

All lenses are intended to correct spherical refractive error and presbyopia. The lenses are intended to be used as a 2-week, reusable, daily wear lens. The lenses require use of a care system to clean and disinfect the lenses.

1.3. Summary of Findings from Nonclinical Studies

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans. For the most comprehensive nonclinical information regarding JJV investigational senofilcon-A multifocal refer to the latest version of the CR-6317 Investigator Brochure.

1.4. Summary of Known Risks and Benefits to Human Subjects

The Investigational multifocal contact lenses are designed as a continuous asphere providing for the correction of refractive spherical ammetropia and presbyopia. The material is a silicone hydrogel material, senofilcon A.

The intent of the Study lenses are daily wear, reusable lens that the subject wears while awake. These lenses are not intended for extended wear. Anticipated risks and adverse reactions with this lens are similar to other soft daily wear contact lenses used to correct presbyopia. A listing of examples of adverse reactions is found in the Section 13 of this protocol. The investigator should follow normal clinical guidelines regarding examination and care of subjects who participate in this trial. For the most comprehensive clinical information regarding the JJV Investigational senofilcon-A multifocal lens refer to the Investigator Brochure.

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

JJV has evaluated the Test lenses in a previous study [redacted]. The study was a dispensing clinical trial with primary end points of logMAR visual acuity at fit and CLUE vision scores at 1 week. The study was a crossover design with a marketed product serving as the Control. Subjects were fit in the lenses and wore them for 2-4 then attended the first follow-up visit to determine if lens optimization was required. The lenses were than worn for an additional 2 weeks with a 1-week follow-up during that period. There were 32 subjects that completed the study as cohort. The Test lens displayed good visual acuity with the mean distance and intermediate logMAR acuity better than 0.0 and the mean near logMAR acuity better than +0.1 logMAR. This with true of the acuity at the initial fit as well as the 1-week and 2-week visits in the final lens pair. There were two non-ocular adverse events that occurred during the study that were not related to any of the Test lenses.

The Test lenses have also been evaluated in [redacted] which at the writing of this protocol has completed data collection, however does not have a completed clinical study report. During the study there were no serious adverse events reported.

In addition to the above study, JJV had tested similar optical designs that have been manufactured in a similar material however those lenses were worn as daily disposable lenses. The lenses were tested in [redacted], details of which are included below.

[redacted] was a non-dispensing evaluation with a primary endpoint of logMAR visual acuity. There were 22 subjects that completed the trial per protocol. In this study, the lenses provided clinically acceptable visual acuity with the mean bright high contrast binocular logMAR acuity of -0.016, -0.028 and 0.086 for distance, intermediate, and near, respectively. There were no adverse events reported during the study.

[redacted] was a dispensing clinical trial with the primary endpoint of logMAR visual acuity. There were 21 subjects that completed the trial per protocol. The lenses displayed clinically acceptable logMAR visual acuity after approximately 10 days of wear with the mean bright high contrast binocular logMAR acuity of -0.082, -0.042 and 0.054 for distance, intermediate, and near, respectively. There were two adverse events reported during the study; one that was non-ocular and not related to the test articles the other was an ocular adverse event, contact lens induced peripheral ulcer, that was classified as likely related to the study lens. The event resolved with treatment and the subject was discontinued from the study.

[redacted] was a non-dispensing evaluation with a primary endpoint of logMAR visual acuity and contrast sensitivity. The lenses were compared to another investigational lens as well as the marketed 1-Day Acuvue Moist Multifocal contact lens. There were 30 subjects that completed the trial per protocol. In this study, the lenses provided clinically acceptable visual acuity with the mean bright high contrast binocular logMAR acuity of -0.119, -0.099, and 0.025 for distance, intermediate, and near, respectively. There was one non-ocular

adverse event (acute nasopharyngitis) reported in the study. The event was assessed as not related to the study treatment. There were no ocular adverse events reported in this study.

The Test lenses have also been evaluated in [redacted] which as of the writing of this protocol did not have final clinical study reports. For additional details refer to the Investigator Brochure for this study.

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

This study is an evaluation of the visual performance, subjective response, lens fit and ocular physiological response of the JJV Investigational senofilcon A Multifocal Contact Lenses cured with two different processes.

Primary Objective
This study is an evaluation of how the subjective response of two senofilcon A Multifocal Contact Lens using to different manufacturing processes compare to one another.

2.2. Endpoints

The study endpoints will be the subjective CLUE Vision scores and logMAR visual acuity. Additional endpoints will be a summary of lenses needed to fit (optimize) the subject, CLUE comfort/handling scores, the lens fit and ocular physiological responses.

Primary Endpoint
- CLUE vision scores

Secondary Endpoint
- logMAR visual acuity

Other Observations
- Lens fit
- Corneal staining
- Ocular redness (bulbar and limbal)
- Summary of lenses needed to fit (optimize) the subject
- CLUE comfort/handling scores
- PRO individual questions

2.3. Hypotheses

The following primary hypothesis will be tested throughout this investigation.

Primary Hypothesis:

1. After 14 to 20 days of wear, the PRO CLUE vision scores for the Test lens will be non-inferior to the Control lens. A non-inferiority margin of 5 CLUE points will be used. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

If the primary hypothesis is met, the following secondary hypotheses will be tested.

Secondary Hypotheses:

1. After 14 to 20 days of wear, the distance, binocular, high luminance, high contrast visual acuity score for the Test lens will be non-inferior to the Control lens. A non-inferiority margin of -0.05 logMAR will be used.
2. After 14 to 20 days of wear, the intermediate, binocular, high luminance, high contrast visual acuity score for the Test lens will be non-inferior to the Control lens. A non-inferiority margin of -0.05 logMAR will be used.
3. After 14 to 20 days of wear, the near, binocular, high luminance, high contrast visual acuity score for the Test lens will be non-inferior to the Control lens. A non-inferiority margin of -0.05 logMAR will be used.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Healthy male and female subjects who are habitual soft contact lens wearers will be recruited. Subjects will be at least 40 years of age and not older than 70 years of age. They will be hyperopic and have presbyopia**.**

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. The subject must appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. The subject must be at least 40 years of age and not greater than 70 years of age.
4. The subject's distance spherical equivalent refraction must be in the range of +1.25 D to +3.75 D in each eye.
5. The subject's refractive cylinder must be ≤0.75 D in each eye.
6. The subject's ADD power must be in the range of +0.75 D to +2.50 D.
7. The subject must have distance best corrected visual acuity of $20/20^{-3}$ or better in each eye.
8. Subjects must own a wearable pair of spectacles if required for their distance vision.
9. The subject must be an adapted soft contact lens wearer in both eyes (i.e. worn lenses a minimum of 2 days per week for at least 8 hours per wear day, for 1 month of more duration).
10. The subject must either already be wearing a presbyopic contact lens correction (e.g., reading spectacles over contact lenses, multifocal or monovision contact lenses, etc.) or if not respond positively to at least one symptom on the "Presbyopic Symptoms Questionnaire".

3.3. Exclusion Criteria

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

1. Currently pregnant or lactating.
2. Any active or ongoing ocular or systemic allergies that may interfere with contact lens wear.
3. Any active or ongoing systemic disease, autoimmune disease, or use of medication, which may interfere with contact lens wear. This may include, but not be limited to, diabetes, hyperthyroidism, Sjögren's syndrome, xerophthalmia, acne rosacea, Stevens-Johnson syndrome, and immunosuppressive diseases or any infectious diseases (e.g. hepatitis, tuberculosis).
4. Clinically significant (Grade 3 or 4) corneal edema, corneal vascularization, corneal staining, tarsal abnormalities or bulbar injection, or any other corneal or ocular abnormalities which would contraindicate contact lens wear.
5. Entropion, ectropion, extrusions, chalazia, recurrent styes, dry eye, glaucoma, history of recurrent corneal erosions.
6. Any previous, or planned, ocular or intraocular surgery (e.g. radial keratotomy, PRK, LASIK, lid procedures, dacryocystorhinostomy cataract surgery, retinal surgery, etc.).
7. A history of amblyopia, strabismus or binocular vision abnormality.
8. Any current ocular infection or inflammation.
9. Any current ocular abnormality that may interfere with contact lens wear.
10. Use of any of the following oral medications within 1 week prior to enrollment: oral retinoid isotretinoin (e.g. Accutane), oral tetracyclines, topical scopolamine, systemic steroids.
11. Use of any ocular medication, with the exception of rewetting drops.
12. History of herpetic keratitis.
13. Participation in any contact lens or lens care product clinical trial within 30 days prior to study enrollment.
14. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).
15. Any known hypersensitivity or allergic reaction to Optifree®Replenish® multi-purpose care solution, sodium fluorescein or Eye-Cept® rewetting drop solution.

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

The clinical study is a randomized-controlled, double-masked, crossover clinical trial. There are two study treatments. A total of approximately 50 eligible hyperopic subjects will be targeted to complete the study. The first Test article will be dispensed for 3±1 days and an optimization visit will occur. The final lens pair will be dispensed for 12±2 days and the at

the follow-up the final lens measurements will occur. Subjects will complete a 7±3 days washout between each fitting. The second study lens will then be fit based on the power of the lenses dispensed at the optimization visit of the first lens and the above sequence repeated. The second lens will not be optimized.

4.2. Study Design Rationale

The study is intended to compare two study lens types and the initial performance, in terms of the subjective response after a period of lens dispensing. The lenses are dispensed to determine the subjective responses and the comparison is made after a total of 14-20 days of wear.

The crossover study design was chosen to control for variables that may impact the lens performance between subjects. It was determined that a washout was not required as previous studies on similar populations with similar multifocal designs did not show a significant carry over effect on the primary/secondary endpoints measured in the study.

4.3. Enrollment Target and Study Duration

A total of approximately 60 eligible subjects will be enrolled with 50 targeted to complete the study. The study will last approximately 2-4 months.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn in a bilateral and random fashion using a 2×2 crossover design with 2 lens types and 2 periods. Using a computer-generated randomization scheme provided by the study biostatistician, each subject will randomly be assigned to one of two unique sequences (Test/Control or Control/Test). Randomization will be stratified by site.

Permuted block randomization will be used to avoid bias in the assignment of subjects to treatment, and to enhance the validity of statistical comparisons across treatment groups. Each block will contain two different lens trial sequences.

The order of lens wear will be based on the randomization scheme assigned to the study site. The study site will follow the randomization scheme provided and will complete enrollment according to the randomization list and will not pre-select or assign subjects.

5.2. Masking

This is a double-masked study with the subjects and the investigators being masked.

Under normal circumstances, the mask should not be broken until all subjects have completed the study and the database is finalized. Otherwise, the mask should be broken only if specific emergency treatment/course of action would be dictated by knowing the treatment status of the subject. In such cases, the Investigator may, in an emergency, contact the medical monitor. In the event the mask is broken, the Sponsor must be informed as soon as

possible. The date, time, and reason for the unmasking must be documented in the subject record. The Investigator is also advised not to reveal the study treatment assignment to the clinical site or Sponsor personnel.

Subjects who have had their treatment assignment unmasked are expected to return for all remaining scheduled evaluations. Subjects who are discontinued may be replaced.

5.3. Procedures for Maintaining and Breaking the Masking

The test articles mask shall not be broken unless information concerning the lens type is necessary for the urgent medical treatment of a subject. The Sponsor must be notified before the mask is broken.

When dispensing test articles, the following steps should be followed to maintain randomization codes:

1. Investigator or designee (documented on the Delegation Log) will consult the lens fitting schedule/randomization scheme to obtain the test article assignment for that subject prior to dispensing
2. Investigator or designee will record the subject's number on the appropriate line of the randomization scheme if applicable
3. Investigator or designee will pull the appropriate test articles from the study supply. All test articles that are opened, whether dispensed (placed/fit on eye or dispensed outside the clinical site) or not, must be recorded on the Test Article Accountability Log in the "Dispensed" section

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

	Control	Test
Name	JJV Investigational Multifocal Contact Lens 1	JJV Investigational Multifocal Contact Lens 2
Manufacturer	Johnson & Johnson® Vision, Inc.	Johnson & Johnson® Vision, Inc.
[redacted]	[redacted]	[redacted]

[redacted]

Lens Material	senofilcon A	senofilcon A
Nominal Base Curve @ 22°C	8.35 mm	8.35
Nominal Diameter @ 22°C	14.3 mm	14.3
Nominal Distance Powers (D)	+1.00 D to +4.00 D in 0.25 D steps	+1.00 D to +4.00 D in 0.25 D steps
Nominal Cylinder Powers (D) and Axes	None	None
Nominal ADD Powers (D)	Low, Mid, High	Low, Mid, High
Water Content	38%	38%
Center Thickness	0.070 mm (-3.00 D)	0.070 mm (-3.00 D)
Oxygen Permeability (Dk)	122.0	122.0
Wear Schedule in Current Study	Daily Wear Reusable	Daily Wear Reusable
Replacement Frequency	Two Weeks	Two Weeks
Packaging Form (vial, blister, etc.)	Blister	Blister

6.2 Ancillary Supplies/Products

The following solutions will be used in this study:

Table 2: Ancillary Supplies

	Solution	
Solution Name/Description	Eye-Cept® Rewetting Drops	OPTI-FREE® Replenish® Multipurpose Disinfecting Solution
Manufacturer	Optics Laboratory	Alcon Laboratories
Preservative	Non-Preserved	Myristamidopropyl dimethylamine 0.0005% polyquaternium-1 0.001%

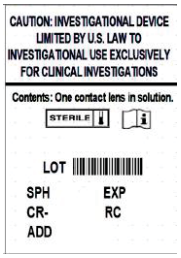
[redacted]

6.3. Administration of Test Articles

Test articles will be dispensed to subject meeting all eligibility requirements, including any dispensing requirements set forth in this clinical protocol. Subjects will be dispensed an adequate supply of test articles to complete the study. Lost or damaged test articles may be replaced at the discretion of the Investigator and/or the Sponsor.

6.4. Packaging and Labeling

The test articles will be packaged in blisters, as the primary packaging. The test article will be over-labeled to mask the subject to the identity of the lens. The test articles will be in investigational cartons sealed with a tamper evident seal, commercial cartons, or in plastic bags as the secondary packaging form. The sample study label is shown below:



6.5. Storage Conditions

Test articles will be maintained at ambient temperatures at the clinical site. Test articles must be kept under secure conditions.

6.6. Collection and Storage of Samples

When possible, any lens or test article associated with an Adverse Events and/or a Product Quality Complaint must be retained and stored in a glass vial with moderate solution pending directions from the sponsor for potential return to JJV.

6.7. Accountability of Test Articles

JJV will provide the Investigator with sufficient quantities of study article and supplies to complete the investigation. The Investigator is asked to retain all lens shipment documentation for the test article accountability records.

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. This includes:

1. What was dispensed for the subject for trial fitting, to wear out of the office, or issued for the subject to replace appropriately between visits
2. What was returned to the Investigator unused
3. The number and reason for unplanned replacements

The Investigator will collect all unused test articles from the subjects at the end of the subject's participation. Subject returned unused test articles must be separated from the clinical study inventory of un-dispensed test articles and must be labeled with the subject number and date of return. Following final reconciliation of test articles by the monitor, the Investigator or monitor will return all unused test articles to the Sponsor.
If there is a discrepancy between the shipment documents and the contents, contact the study monitor immediately.

Reference [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, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2	Visit 4 Baseline Treatment 2 Fitting	Visit 5 Treatment 2 Follow-up 1
Time Point	Day 0	Day 3±1 from V1	Day 12±2 from V2 Complete 7±3 days washout before V4	Day 7±3 from V3 Day 0	Day 12±2 from V4
Estimated Visit Duration	2.5 hours	1.0 hour	1.5 hour	1.0 hour	1.5 hour
Statement of Informed Consent	x				
Demographics	x				
Medical History/Concomitant Medications	x				
Adverse Events and Concomitant Medications Review		x	x	x	x
Compliance		x	x		x
Habitual Contact Lens Information	x				
Contact Lens History	x				
Wear Time and Comfortable Wear Time with lenses	x	x	x		x
Screening Inclusion/Exclusion Criteria	x				
Subject Reported Ocular Symptoms	x	x	x	x	x
Baseline	x				

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2	Visit 4 Baseline Treatment 2 Fitting	Visit 5 Treatment 2 Follow-up 1
Time Point	Day 0	Day 3±1 from V1	Day 12±2 from V2 Complete 7±3 days washout before V4	Day 7±3 from V3 Day 0	Day 12±2 from V4
Estimated Visit Duration	2.5 hours	1.0 hour	1.5 hour	1.0 hour	1.5 hour
Questionnaire					
CLDEQ-8 Questionnaire	x		x		x
Distance and Near Entrance Visual Acuity	x	x	x	x	x
Lens Removal	x	x	x	x	x
Keratometry	x				
Subjective Refraction and Distance Visual Acuity	x				
Near ADD Determination	x				
Ocular Dominance	x				
ADD Refinement	x				
Near Visual Acuity	x				
Biomicroscopy	x	x	x	x	x
Baseline Inclusion/ Exclusion Criteria	x				
Continuance				x	
Lens Selection	x	x(If modified)		x	
Lens Insertion	x	x		x	
10 Minute Settling	x	x		x	
Visual Satisfaction / Subjective	x	x	x	x	x

[redacted]

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2	Visit 4 Baseline Treatment 2 Fitting	Visit 5 Treatment 2 Follow-up 1
Time Point	Day 0	Day 3±1 from V1	Day 12±2 from V2 Complete 7±3 days washout before V4	Day 7±3 from V3 Day 0	Day 12±2 from V4
Estimated Visit Duration	2.5 hours	1.0 hour	1.5 hour	1.0 hour	1.5 hour
Acceptance					
Study Lens Distance and Near Visual Acuity	x	x	x	x	x
Distance Over Refraction and Visual Acuity	x	x		x	
Subjective Lens Fit Assessment	x	x	x	x	x
Binocular Over Refraction			x		x
Visual Performance			x		x
Modifications	x	x			
Post-Fit PRO Questionnaire	x	x		x	
PRO Questionnaire	x		x		x
Distance and Near Exit Visual Acuity	x	x	x	x	
Dispensing Criteria	x	x		x	
Instructions	x	x	x	x	
Schedule Follow-up	x	x	x	x	
Final Evaluation					x

[redacted]

7.2. Detailed Study Procedures

VISIT 1

Subjects must report to the visit wearing their habitual contact lenses to accurately assess baseline PRO (CLUE) performance. If the subject is not wearing their lenses they must be rescheduled.

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 age, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	
1.4	Habitual Lenses	Questions regarding the subject's habitual lens type and parameters.	
1.5	Contact Lens History	Record the subject's correction type (i.e. monovision, multifocal, sphere with readers, etc.).	
1.6	Wear time and Comfortable Wear time with Habitual lenses	Record the subjects wear time and comfortable wear time with their habitual contact lenses.	
1.7	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.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.8	Baseline PRO and CLDEQ-8 Questionnaires	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of their habitual lenses using the PRO questions.	
1.9	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]

[redacted]

1.10	Entrance Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the subject's habitual contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
1.11	Lens Removal	Have the subject remove their habitual lenses and store in an approved storage solution.	
1.12	Keratometry	Keratometry will be performed OD and OS and the steep and flat dioptric power and corresponding meridians recorded.	[redacted]
1.13	Subjective Refraction and Distance Visual Acuity	An optimal, binocular balanced distance sphero-cylindrical refraction will be performed. Record the refraction and distance visual acuity to the nearest letter. *Note: Best distance visual acuity with sphero-cylindrical refraction must be at least 20/20^{-3} in each eye for the subject to be eligible in the study.*	[redacted]
1.14	Near ADD Determination	The near reading addition will be determined using the binocular crossed cylinder technique (BCC) at 40 cm followed by optimization in a trial frame in step 1.16 below.	[redacted]
1.15	Ocular Dominance	Determine the distance ocular dominance with the best distance correction in place using a +1.00-blur test. If the results are equivocal use the sighting dominance test to determine the dominant eye used for the study.	Appendix F
1.16	ADD Refinement	Place the BCC result in the trial frame and refine the near prescription with trial lenses (or flippers) under binocular conditions.	[redacted]
1.17	Near Visual Acuity	Using the ETDRS 2000 Series Chart 1 or 2 near card placed at 40 cm. Record the near visual acuity OD, OS and OU at 40 cm.	
1.18	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. For the conjunctival redness [redacted] 0.5 unit increments will be used in the grading. Corneal Staining Assessment [redacted] will be graded in 1.0 increments. If any of these slit lamp findings are Grade 3 or higher, the subject will be discontinued. If	[redacted]

[redacted]

		discontinued a final examination must be completed. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	
1.19	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. If so, proceed to lens fitting. If not, complete the final evaluation and discharge the subject.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.20	Randomization	Record the randomization ID.	
1.21	Lens Selection	Select the lens pair and power based on the randomization scheme, spherical equivalent refraction and fitting guide for each eye. Record the Test lens parameters (power and lot number).	Appendix G (Fitting Guide)
1.22	Lens Insertion	Subjects will insert the lenses themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in labeled vial with sterile saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor. Complete the Quality Product Complaint form.	
1.23	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes.	
1.24	Determine Visual Satisfaction	Determine if the subject's vision is acceptable with the lenses. Allow the subject to look down a hallway or out of a window for distance vision assessments, and for them to read a book, magazine or similar for near vision.	
1.25	Study Lens Distance and Near Visual Acuity	Measure the distance and near visual acuity OD, OS and OU. Record the results. **Note:** Use the ETDRS 2000 Series Chart 1 or 2 near card placed at 40 cm to measure the Near visual acuity	[redacted]
1.26	Distance Over-	Perform a distance over-refraction OD and OS	

[redacted]

	Refraction and Distance Visual Acuity	using loose lenses outside of the phoropter under ambient room illumination. The distance over-refraction may also be refined under binocular conditions. Record the results. The results of the distance over-refraction may also be checked for the impact on near vision under monocular and/or binocular conditions.	
1.27	Subjective Lens Fit Assessment	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). • The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). *If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.*	[redacted]
1.28	Modifications	If the subject reports unsatisfactory vision or is unable to obtain 20/30 distance visual acuity OU with the lenses, then a modification must be attempted. If the subject reports satisfactory vision with the lenses a modification is not required, however at the Investigator's discretion and based upon their findings on the measured visual acuity and/or over- refraction the investigator may make a modification. Up to two attempts at modification are permitted if necessary, in order to achieve an acceptable distance and near binocular performance for the subject, and to enable them to wear that particular lens type. Follow the fitting guide allowing for at least 10 minutes of settling time between each lens modification attempted. If modifications are required steps 1.21-1.27 will be repeated for each modification.	Appendix G (Fitting Guides)
1.29	PRO Post-Fit	The subject will evaluate the vision	

[redacted]

	Questionnaire	characteristics, comfort characteristics, handling characteristics, and visual symptoms of the study lenses using the PRO questionnaire.	
1.30	Distance and Near Exit Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU. **Note: The distance visual acuity must be at least 20/30 OU for the lenses to be dispensed.**	[redacted]
1.31	Dispensing Criteria	The lenses will be dispensed for 2-4 days. • Distance Snellen acuity equal to or better than 20/30 OU • Subject must indicate that the vision is acceptable. • Subject must indicate that the comfort of the lenses is acceptable. • Lenses must have an acceptable general lens fit.	
1.32	Patient Instructions	Instruct the Subject the following: • The lenses will be worn on a daily wear basis. • OPTI-FREE® Replenish® solution will be used in a rub regime to disinfect and store the lenses each night in the lens case provided. • If determined necessary by the Investigator sterile non-preserved rewetting drops may be dispensed to be used as needed for dryness. • Subjects will be instructed to wear lenses for a minimum of 6 hours a day, every day during the study. • Subjects will be instructed to wear their glasses when not wearing the study lenses**.** • A patient instruction booklet will be provided. ***Note:*** *In the event a lens is lost or damaged,*	

[redacted]

		the subject will return to the investigator site for replacement. As much as reasonably possible, a damaged lens should be returned to the investigational site and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with sterile saline and returned to the Sponsor.	
1.33	Schedule Follow-up	The subject will be scheduled to return for their follow-up appointment in 3±1 day. ***Note:*** *To count the follow-up visit as a day of wear the Subject must have worn the study lenses for 6 hours prior to the visit.*	

VISIT 2

The subjects must present to Visit 2 wearing the study lenses. To be counted as a day of wear the lenses need to have been worn for at least six (6) hours prior to the visit.

Visit 2: Treatment 1 Follow-up 1			
Step	Procedure	Details	[redacted]
2.1	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
2.2	Wear Time	Record the hours the subject has worn the study lenses and the comfortable wear time on the day of follow-up.	
2.3	Compliance	Record the subject's compliance with wearing the study lenses. ***Note:*** *Subjects must have worn lenses for at least 6 hours per day* *To be counted as a day of wear at this visit the Subject must have worn the study lenses for 6 hours prior to the visit.*	
2.4	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
2.5	Subjective Acceptance	Record whether the subjects distance and near vision with the lenses is acceptable.	
2.6	Distance and Near Entrance Visual Acuity	Measure the distance and near visual acuity OD, OS and OU. Record the results.	[redacted]

[redacted]

		Note: Use the ETDRS 2000 Series Chart 1 or 2 near card placed at 40 cm to measure the Near visual acuity	
2.7	Distance Over-Refraction and Distance Visual Acuity	Perform a distance over-refraction OD and OS using loose lenses outside of the phoropter under ambient room illumination. The distance over-refraction may also be refined under binocular conditions. Record the results and distance visual acuity OD and OS. The results of the distance over-refraction may also be checked for the impact on near vision under monocular and/or binocular conditions.	
2.8	Determination of Lens Optimization	If the subject reports unsatisfactory vision or is unable to obtain 20/30 distance visual acuity OU with the lenses, then a modification must be attempted. If the subject reports satisfactory vision with the lenses a modification is not required, however at the Investigator's discretion and based upon their findings on the measured visual acuity and/or over- refraction the investigator may make a modification. Up to two attempts at modification are permitted if necessary, in order to achieve an acceptable distance and near binocular performance for the subject, and to enable them to wear that particular lens type. Follow the fitting guide and steps 1.21-1.27 in Visit 1 Fitting allowing for at least 10 minutes of settling time between each lens modification.	Appendix G (Fitting Guide)
2.9	Lens Fit Assessment:	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). • The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). *If either lens is deemed unacceptable, the*	[redacted]

[redacted]

		subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.	
2.10	Lens Removal	The study lenses will be removed and discarded.	
2.11	Biomicroscopy	Perform biomicroscopy OD and OS. Slit Lamp Classification Scales will be used to grade the findings. For the conjunctival redness [redacted]) 0.5 unit increments will be used in the grading. Corneal Staining Assessment [redacted]) will be graded in 1.0 increments. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]
2.12	Insertion of Study Lenses	Dispense the subject a new pair of lenses that match the distance and ADD power of the lenses that were removed in Step 2.12 above.	
2.13	PRO Post-Fit Questionnaire	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of the study lenses using the PRO questionnaire.	
2.14	Distance and Near Exit Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU. **Note: The distance visual acuity must be at least 20/30 OU for the lenses to be dispensed.**	[redacted]
2.15	Dispensing Criteria	The lenses will be dispensed for 12±2 day. • Distance Snellen acuity equal to or better than 20/30 OU • Subject must indicate that the vision is acceptable. • Subject must indicate that the comfort of the lenses is acceptable. • Lenses must have an acceptable general lens fit.	
2.16	Patient Instructions	Instruct the Subject the following:	

[redacted]

		• The lenses will be worn on a daily wear basis. • OPTI-FREE® Replenish® solution will be used in a rub regime to disinfect and store the lenses each night in the lens case provided. • If determined necessary by the Investigator sterile non-preserved rewetting drops may be dispensed to be used as needed for dryness. • Subjects will be instructed to wear lenses for a minimum of 6 hours a day, every day during the study. • Subjects will be instructed to wear their glasses when not wearing the study lenses. • Subjects will be instructed to bring their habitual contacts or spectacles to the next visit. ***Note:*** *In the event a lens is lost or damaged, the subject will return to the investigator site for replacement. As much as reasonably possible, a damaged lens should be returned to the investigational site and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with sterile saline and returned to the Sponsor.*	
2.17	Schedule Follow-up	The subject will be scheduled to return for their follow-up appointment in 12±2 days. ***Note:*** *To count the follow-up visit as a day of wear the Subject must have worn the study lenses for 6 hours prior to the visit.*	

VISIT 3

The subjects must present to Visit 3 wearing the study lenses. To be counted as a day of wear the lenses need to have been worn for at least six (6) hours prior to the visit.

Visit 3: Treatment 1 Follow-up 2			
Step	Procedure	Details	[redacted]
3.1	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
3.2	Wear Time	Record the hours the subject has worn the study lenses and the comfortable wear time on the day of follow-up.	
3.3	Compliance	Record the subject's compliance with wearing the study lenses. ***Note:*** *Subjects must have worn lenses for at least 6 hours per day* *To be counted as a day of wear at this visit the Subject must have worn the study lenses for 6 hours prior to the visit.*	
3.4	PRO and CLDEQ-8 Questionnaires	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of the study lenses using the PRO questionnaire.	
3.5	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire	[redacted]
3.6	Subjective Acceptance	Record whether the subjects distance and near vision with the lenses is acceptable.	
3.7	Distance and Near Entrance Visual Acuity	Measure the distance and near visual acuity OD, OS and OU. Record the results. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
3.8	Visual Performance Distance (3M) Intermediate (64 cm) Near (40 cm)	Visual performance will be recorded OD, OS, and OU for the following: **Distance, Bright Illuminance** *High and Low Contrast ETDRS Charts* 3M- HC#1, HC#2, HC#3 and LC#1, LC#2, LC#3 **Near, Bright Illuminance**	[redacted]

[redacted]

		Reduced Guillon-Poling Charts Intermediate *(*64 cm) High Contrast and Low Contrast Near (40 cm) High Contrast and Low Contrast **Distance, Dim Illuminance (with ***Distance*** goggles)** *High Contrast ETDRS Charts* 3M-HC#4, HC#5, HC#6 **Near, Dim Illuminance (with ***Near*** goggles)** *Reduced Guillon-Poling charts* High Contrast Intermediate (64 cm) and Near (40 cm). **Note:** • **The room illuminance must be between 7.3 and 7.9 EV (394-597 lux).** • **Distance, HC-1 Chart luminance Acceptable Range 10.5-10.7 EV (181-208 cd/m^2).** • **Guillon-Poling, Near Chart Luminance Acceptable Range 10.8-11.1 EV (223-274 cd/m^2).** • **Do not use the Mesopic filter for Dim luminance (Dim luminance will be simulated by using the goggles)**	
3.9	Binocular Distance Over-refraction and Distance Visual Acuity	Perform a binocular over-refraction and record the OD and OS results and distance visual acuity. Note: No lens changes are allowed based on the over-refraction.	Appendix D
3.10	Lens Fit Assessment:	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). • The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up).	[redacted]

[redacted]

		If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.	
3.11	Lens Removal	Have the subject remove the study lenses and store in saline in a labeled glass vial. **Note:** Lenses do not need to be stored in a refrigerator.	
3.12	Biomicroscopy	Perform biomicroscopy OD and OS. Slit Lamp Classification Scales will be used to grade the findings. For the conjunctival redness [redacted] 0.5 unit increments will be used in the grading. Corneal Staining Assessment [redacted] will be graded in 1.0 increments. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]
3.13	Distance and Near Exit Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the subject's habitual correction in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
3.14	Schedule Follow-up	The subject will be scheduled to return for their next appointment in 7±3 days. ***Note:*** *Subject may wear their habitual spectacles or contact lenses during the washout period.*	

[redacted]

VISIT 4

The subjects may present to Visit 4 wearing their habitual spectacles or contact lenses.

Visit 4: Baseline Treatment 2			
Step	Procedure	Details	[redacted]
4.1	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
4.2	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
4.3	Distance and Near Entrance Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the subject's habitual correction in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
4.4	Lens Removal (if applicable)	Have the subject remove their habitual lenses and store in an approved storage solution.	
4.5	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. For the conjunctival redness[redacted] 0.5 unit increments will be used in the grading. Corneal Staining Assessment[redacted]) will be graded in 1.0 increments. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]
4.6	Continuance	Determine whether the subject is eligible to continue in the study based on the examination findings.	

Visit 4: Treatment 2 Lens Fitting			
Step	Procedure	Details	[redacted]
4.7	Lens Selection	Select the lens pair based on the randomization scheme and select the power that was dispensed at Visit 2 for each eye. Record the Test lens parameters (power and lot number).	
4.8	Lens Insertion	Subjects will insert the lenses themselves. If	

[redacted]

		the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in labeled vial with sterile saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor. Complete the Quality Product Complaint form.	
4.9	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes.	
4.10	Distance and Near Entrance Visual Acuity	Measure the distance and near visual acuity OD, OS and OU. Record the results. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
4.11	Determine Visual Satisfaction	Determine if the subject's vision is acceptable with the lenses. Allow the subject to look down a hallway or out of a window for distance vision assessments, and for them to read a book, magazine or similar for near vision. ***Note:*** If the subject's vision is unacceptable the subject will be discontinued. Complete the final evaluation.	
4.12	Distance Over-Refraction and Distance Visual Acuity	Perform a distance over-refraction OD and OS using loose lenses outside of the phoropter under ambient room illumination. The distance over-refraction may also be refined under binocular conditions. Record the results. The results of the distance over-refraction may also be checked for the impact on near vision under monocular and/or binocular conditions.	
4.13	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement; • edge lift; • excessive movement in primary and up gaze; or • insufficient movement in all three of the following conditions: primary gaze,	[redacted]

[redacted]

		up gaze, and Josephson push up. *If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.*	
4.14	PRO Post-Fit Questionnaire	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of the study lenses using the PRO questionnaire.	
4.15	Distance and Near Exit Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU. **Note: The distance visual acuity must be at least 20/30 OU for the lenses to be dispensed.**	[redacted]
4.16	Dispensing Criteria	The lenses will be dispensed for 12±2 days. • Distance Snellen acuity equal to or better than 20/30 OU • Subject must indicate that the vision is acceptable. • Subject must indicate that the comfort of the lenses is acceptable. • Lenses must have an acceptable general lens fit.	
4.17	Patient Instructions	Instruct the Subject the following: • The lenses will be worn on a daily wear basis. • OPTI-FREE® Replenish® solution will be used in a rub regime to disinfect and store the lenses each night in the lens case provided. • If determined necessary by the Investigator sterile non-preserved rewetting drops may be dispensed to be used as needed for dryness. • Subjects will be instructed to wear lenses	

[redacted]

		for a minimum of 6 hours a day, every day during the study. • Subjects will be instructed to wear their glasses when not wearing the study lenses. • Subjects will be instructed to bring their habitual contacts or spectacles to the next visit. ***Note:*** *In the event a lens is lost or damaged, the subject will return to the investigator site for replacement. As much as reasonably possible, a damaged lens should be returned to the investigational site and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with sterile saline and returned to the Sponsor.*	
4.18	Schedule Follow-up	The subject will be scheduled to return for their follow-up appointment in 12±2 day. ***Note:*** *To count the follow-up visit as a day of wear the Subject must have worn the study lenses for 6 hours prior to the visit.*	

VISIT 5

The subjects must present to Visit 5 wearing the study lenses. To be counted as a day of wear the lenses need to have been worn for at least six (6) hours prior to the visit.

Visit 5: Treatment 2 Follow-up 1			
Step	Procedure	Details	[redacted]
5.1	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
5.2	Wear Time	Record the hours the subject has worn the study lenses and the comfortable wear time on the day of follow-up.	
5.3	Compliance	Record the subject's compliance with wearing the study lenses. ***Note:*** *Subjects must have worn lenses for at least 6 hours per day* *To be counted as a day of wear at this visit the Subject must have worn the study lenses for 6*	

[redacted]

		hours prior to the visit.	
5.4	PRO and CLDEQ-8 Questionnaires	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of the study lenses using the PRO questionnaire.	
5.5	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire	[redacted]
5.6	Subjective Acceptance	Record whether the subjects distance and near vision with the lenses is acceptable.	
5.7	Distance and Near Entrance Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
5.8	Visual Performance Distance (3M) Intermediate (64 cm) Near (40 cm)	Visual performance will be recorded OD, OS, and OU for the following: **Distance, Bright Illuminance** *High and Low Contrast ETDRS Charts* 3M- HC#1, HC#2, HC#3 and LC#1, LC#2, LC#3 **Near, Bright Illuminance** *Reduced Guillon-Poling Charts* Intermediate *(*64 cm) High Contrast and Low Contrast Near (40 cm) High Contrast and Low Contrast **Distance, Dim Illuminance (with ***Distance*** goggles)** *High Contrast ETDRS Charts* 3M-HC#4, HC#5, HC#6 **Near, Dim Illuminance (with ***Near*** goggles)** *Reduced Guillon-Poling charts* High Contrast Intermediate (64 cm) and Near (40 cm). **Note:** • **The room illuminance must be between 7.3 and 7.9 EV (394-597 lux).** • **Distance, HC-1 Chart luminance Acceptable Range 10.5-10.7 EV (181-208 cd/m^2).** • **Guillon-Poling, Near Chart**	[redacted]

[redacted]

		Luminance Acceptable Range 10.8-11.1 EV (223-274 cd/m^2). • **Do not use the Mesopic filter for Dim luminance (Dim luminance will be simulated by using the goggles)**	
5.9	Binocular Distance Over-refraction and Distance Visual Acuity	Perform a binocular over-refraction and record the OD and OS results and distance visual acuity. Note: No lens changes are allowed based on the over-refraction.	Appendix D
5.10	Lens Fit Assessment:	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). *If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.*	[redacted]
5.11	Lens Removal	Have the subject remove the study lenses and store in saline in a labeled glass vial. **Note:** Lenses do not need to be stored in a refrigerator.	
5.12	Biomicroscopy	Perform biomicroscopy OD and OS. Slit Lamp Classification Scales will be used to grade the findings. For the conjunctival redness [redacted] 0.5 unit increments will be used in the grading. Corneal Staining Assessment [redacted] will be graded in 1.0 increments. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]

[redacted]

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	Distance Subjective Sphero-cylindrical Refraction and Distance Exit Visual Acuity	An optimal, binocular balanced distance sphero-cylindrical refraction will be performed. Record the refraction and distance visual acuity to the nearest letter.	[redacted]
F.2	Subject Disposition	Indicate if the subject completed the study successfully. If subject discontinued from the study indicate the reason.	

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	

[redacted]

Unscheduled Visit			
U.2	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit.	
U.3	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
U.4	Entrance VA	Record the entrance distance and near visual acuity (OD, OS and OU) to the nearest letter. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
U.5	Subjective Sphero-cylindrical Refraction	An optimal, binocular balanced distance sphero-cylindrical refraction will be performed. Record the refraction and distance visual acuity to the nearest letter.	[redacted]
U.6	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. For the conjunctival redness [redacted] 0.5 unit increments will be used in the grading. Corneal Staining Assessment [redacted] will be graded in 1.0 increments. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]
U.7	Lens Dispensing	Additional study lenses may be dispensed when required.	
U.8	Lens Fit Assessment:	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze,	[redacted]

[redacted]

Unscheduled Visit			
		upgaze, and push-up). *If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.*	
U.9	Exit Visual Acuity	Record the subject's exit distance and near visual acuity (OD, OS and OU) to the nearest letter. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]

7.4. Laboratory Procedures

Not Applicable

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent
- they are eligible
- completed all study visits

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 lost to follow-up
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant)
- Subject develops significant or serious adverse events causing discontinuation of study lens wear
- Subjects who have experienced a Corneal Infiltrative Event (CIE)
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment)
- Subject missed two consecutive study visits
- Subject not compliant with study lens wear schedule

[redacted]

- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit

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
- Record the spherocylindrical refraction with best corrected distance visual acuity
- Collect used test article(s) (worn or brought to the visit) from the subject and discard them, unless otherwise stated in Section 6.7
- Collect all unused test article(s) from the subject

An additional subject may be enrolled if a subject discontinues from the study prematurely.

In cases where a subject is lost to follow-up, every possible effort must be made to contact the subject and determine the reason for discontinuation/withdrawal. The measures taken to follow up must be documented including two written attempts and a certified letter (or equivalent) as the final attempt.

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed medications and therapies are medications or therapies that contraindicate contact lens wear. See the Exclusion criteria for specific details.

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 in order 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

If more than 2 subjects in the investigational soft contact lens group develop serious expected (e.g., definite or probable MK) or unexpected device related adverse events, the study will be suspended. Upon review and consultation with IRB, DMC, and JJV safety review committee, the study may be terminated. This potential stopping rule is established based on our trial involving approximately 200 subjects wearing the investigational soft contact lens for up to 3 years with an assumed MK rate that is below 0.2% per patient-year. The rate of 0.2% per

patient year is the established rate for extended wear lenses in adults, which was requested by the FDA as a criterion for evaluating a contact lens for pediatric use in an FDA response to a pre-IDE submission. To be conservative, 200 independent patient years were used in the calculation. The probability of observing 2 cases or more incidents of MK is 0.061, and 3 cases or more incidents of MK is 0.007 (given an MK rate of 0.2% per patient year).

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.

JJV 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 JJV, it is determined that it would be unwise to continue at the clinical site.

JJV (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

A Product Quality Complaint (PQC) refers to any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of test articles after they have been released for clinical trial use.

Potential complaints may come from a variety of sources including but not limited to subjects, clinical research associates (CRA), clinical operations managers (COM), medical monitors, and site personnel, etc. The following are not considered product quality complaints:

- Subject satisfaction inquiries reported via "Subjective Questionnaires" and "Patient Reported Outcomes (PRO)"
- Clinical test articles that are stored improperly or damaged after receipt at the investigational site
- Lens replacements that occur due to drops/fall-outs

- Damage deemed by clinicians or clinical staff to be caused by handling by the user, and not indicative of a quality deficiency (i.e. tears, rips, etc.), only in situations where there is no deficiency alleged by the subject

Within 24 hours of site personnel becoming aware that a PQC has occurred, the PQC must be recorded in the EDC system, which will trigger an automatic email notification to the appropriate COM/CRA and Clinical QA representative. In cases where the EDC system in use is not configured to send automatic notifications or when an EDC system is not used, the COM/CRA is responsible for notifying Clinical QA upon discovery that a PQC has occurred.

Upon receipt of the EDC notification, the COM/CRA will contact the study site to collect additional information which will include:

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness)
- Who received the complaint
- Study number
- Clinical site information (contact name, site ID, telephone number)
- Lot number(s)
- Unique Subject Identifier(s)
- Indication of who first observed complaint (site personnel or subject)
- OD/OS indication, along with whether the lens was inserted
- Any related AE number if applicable
- Detailed complaint description (scheduled/unscheduled visit, wear time, symptoms, resolution of symptoms, etc.)
- Eye Care Provider objective (slit lamp) findings if applicable
- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return (Refer to Form Control [redacted] for test article return instructions)

Once a complaint is received, it will be assessed by the COM, CRA, or trained site personnel to determine if it is an Adverse Event/Serious Adverse Event (AE/SAE). If the complaint results in an AE/SAE, the COM/CRA, or trained site personnel will follow Section 13 of this protocol. If the AE/SAE was potentially the result of a product quality related deficiency, these procedures also applies and will be executed in parallel.

In some cases, a PQC form may be generated in EDC by the site in error. In this event, the PQC forms will be marked "Intentionally Left Blank" or "ILB". Justification for ILB must be documented.

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
- 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 Conjunctivalization

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:

- Contact Lens Induced Peripheral Ulcer (CLPU)
- 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)
- Contact Lens Papillary Conjunctivitis (CLPC)
- 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 contact lens or solution related studies for safety concerns, but due to general concerns relating to pregnancy and contact lens 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

All data summaries and statistical analyses will be performed using the Statistical Analysis System (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.

Summaries will be presented by study lens type and will be performed separately by completion status (Safety Population or Per-Protocol Population). All analyses will be conducted on per-protocol population (see Section 14.3).

14.2. Sample Size Justification

Historical study [redacted] tested hyperopes in presbyopic population. The data from [redacted] was used to estimate the sample size of the study. The rationale is the Test lens in [redacted] has the same optical and mechanical designs, but a different curing method compared with both test article in this trial.

Using the POWER procedure in SAS 9.4, the table below shows the power to test the primary hypothesis with overall type I error 0.05 and 50 subjects.

Primary Hypothesis:	Criteria	True Difference (Test-Control)	Power
CLUE Vision	Test-Control>=-5	0	0.48
		2	0.72
		4	0.89

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.

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.

[redacted]

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

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

Primary efficacy analysis:
Overall quality of vision scores will be analyzed using a linear mixed model adjusting for baseline values as fixed covariates. The model will include the experimental design factors: sequence of lens wear, period, lens type, time point and interaction between lens and time point as fixed effects. The covariance between residual errors from the same subject across lens wearing periods/time point will be selected based on the finite-sample corrected Akaike's Information Criterion.[6] Covariance structures considered may include: Homogenous compound symmetry (CS) and Unstructured covariance structure (UN). The structure that returns the lowest Akaike Information Criteria Corrected (AICC) will be selected as the structure that best fit the data.

Comparisons between the Test lens and Control lens at 2-week follow-up will be carried out using 95% confidence intervals constructed of least-square means (LSM) differences (Test minus Control) from the linear mixed model. The non-inferiority of the Test lens relative to the Control will be concluded if the lower confidence limit of LSM difference is above the non-inferiority margin -5. The superiority will be established if the lower confidence limit is above 0.

In all models, the Kenward and Roger method[7] will be used for the calculation of the denominator of degrees of freedom.

14.6. Secondary Analysis

Secondary efficacy analysis:
Binocular, high luminance, high contrast visual performance on logMAR scale will be analyzed using a linear mixed model to test for the difference between the study lens systems. Each model will include the experimental design factors: sequence of lens wear, lens wearing period, lens type, distance and the interaction between lens type and distance as fixed effects. Other baseline characteristics known of importance such as age, gender, and/or add power will be included as fixed covariates when appropriate. Site and subject nested in site will be included as random effects when appropriate. The covariance between residual errors from the same subject at the same distance across lens wearing periods will be selected based on the finite-sample corrected Akaike's Information Criterion.[6] Covariance structures considered may include: Homogenous compound symmetry (CS) and Unstructured covariance structure (UN). The structure that returns the lowest Akaike Information Criteria Corrected (AICC) will be selected as the structure that best fit the data.

Comparisons between the Test lens and Control lens will be carried out using 95% confidence intervals constructed of least-square means (LSM) differences (Test minus Control) from the linear mixed models. The non-inferiority of the Test lens relative to the Control will be concluded if the upper confidence limit of LSM difference is below the non-inferiority margin 0.05 logMAR. The superiority will be established if the upper confidence limit is below 0.

14.7. Other Exploratory Analyses

Not Applicable

14.8. Interim Analysis

Not Applicable.

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.

Subject dropout is expected to be one of the main reasons of missing data in this clinical trial. Past clinical trials don't provide the evidence that subject dropout is systematic or not-at-random. To evaluate the impact of missing data, sensitivity analysis will be conducted using multiple imputation methods if the proportion of subject dropout is greater than the 15%. The SAS/STAT procedures PROC MI and PROC MIANALYZE will be utilized with a parametric regression method used to make at least 5 imputations.

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 JJV database manager and sent to JJV for analysis.

External Date Sources for this study include:
Not Applicable

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
- test article receipt/dispensing/return records
- date of study completion
- reason for early discontinuation of test article 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 considered to be 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, JJV 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 JJV. The Investigator may use this information for the purposes of the study only. It is understood by the Investigator that JJV will use information developed in this clinical study in connection with the development of the investigational product and therefore may disclose it as required to other clinical investigators and to regulatory agencies. In order 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 JJV 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 the purpose of monitoring and auditing by JJV 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.

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) in the United States[5] 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, with the exception of 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.

18.5. Privacy of Personal Data

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 JJV.

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 JJV management representative prior to study initiation.

JJV 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

JJV 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

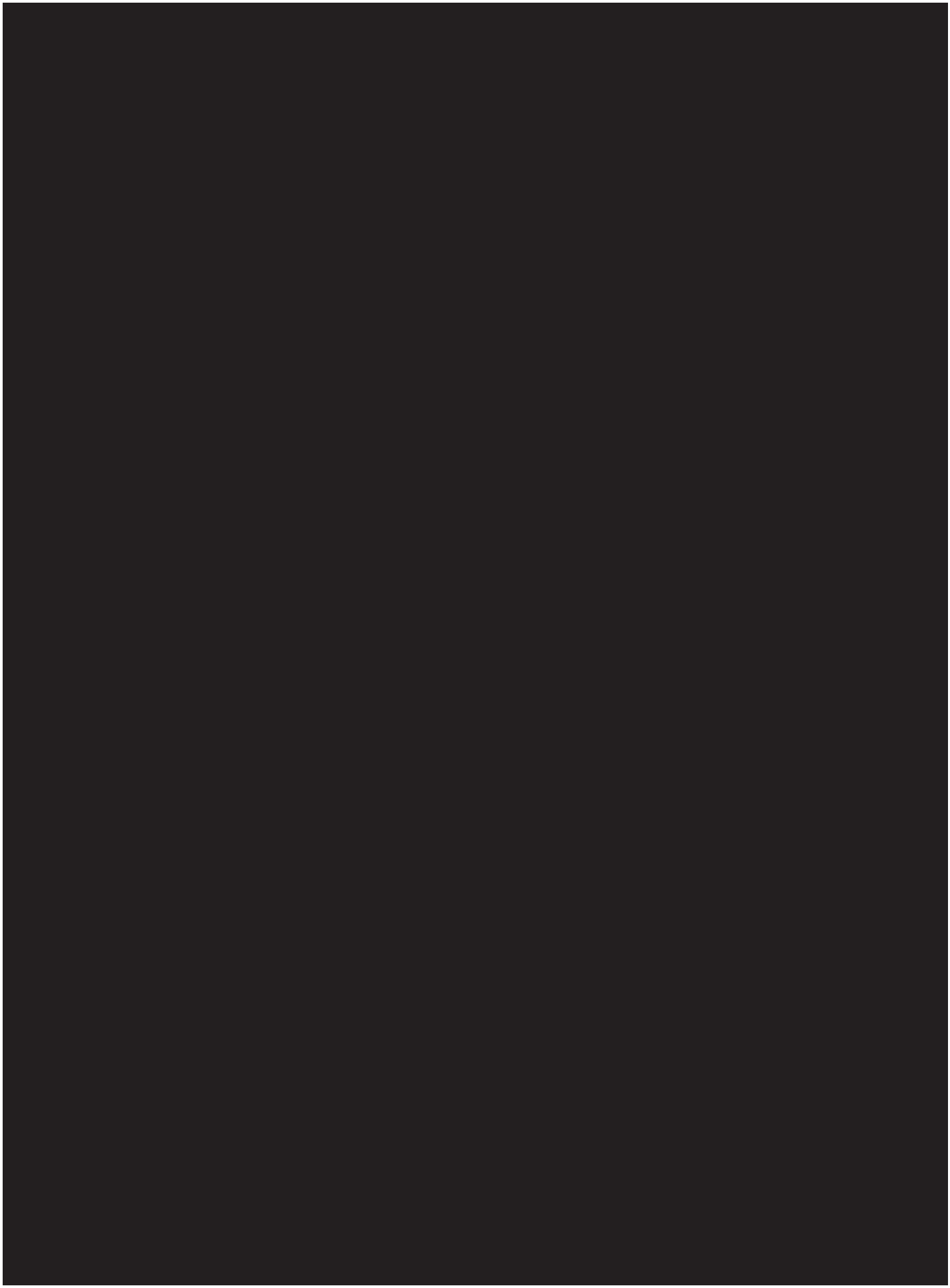
21. PUBLICATION

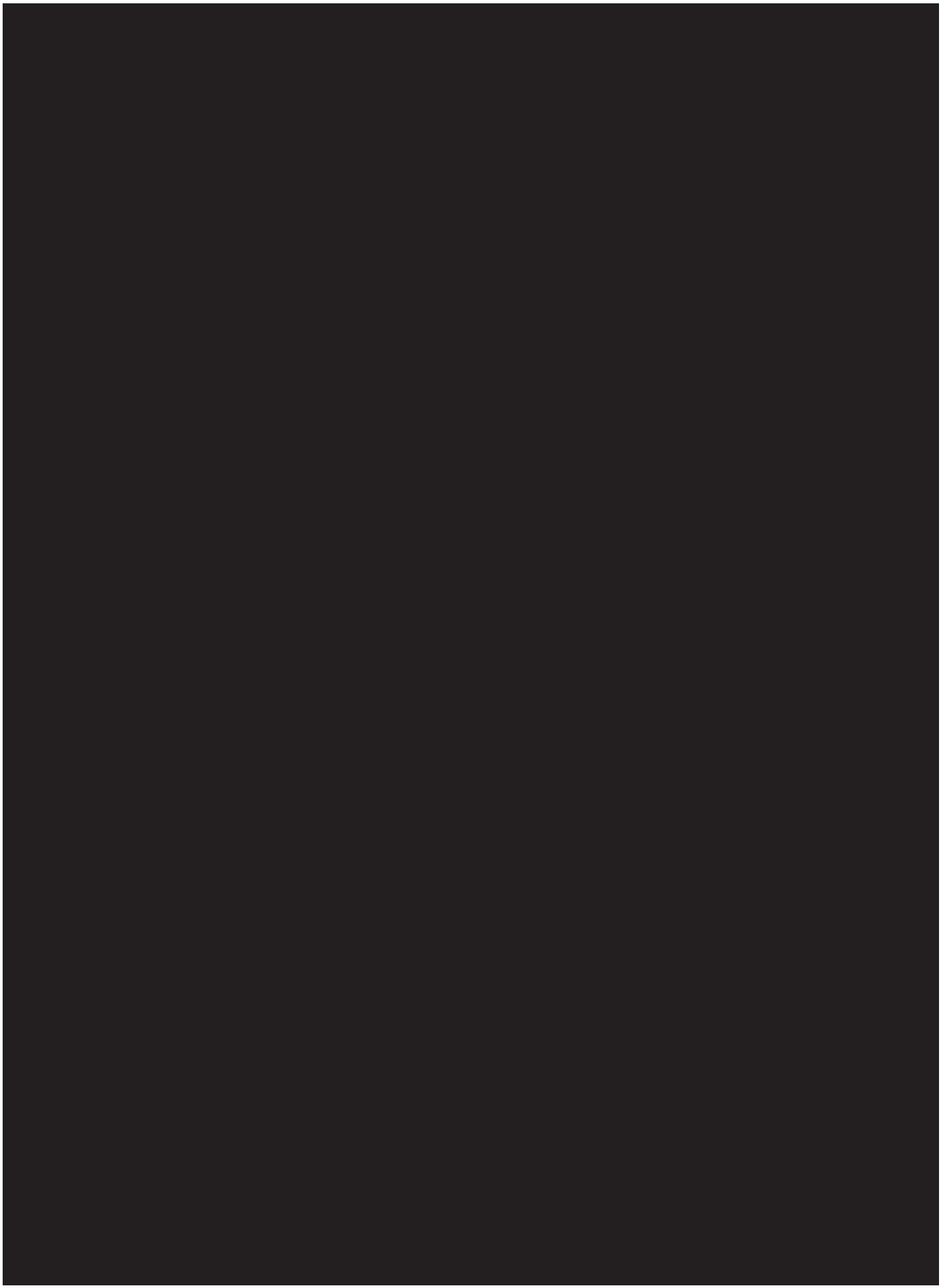
This study will be registered on ClinicalTrials.gov by the Sponsor.

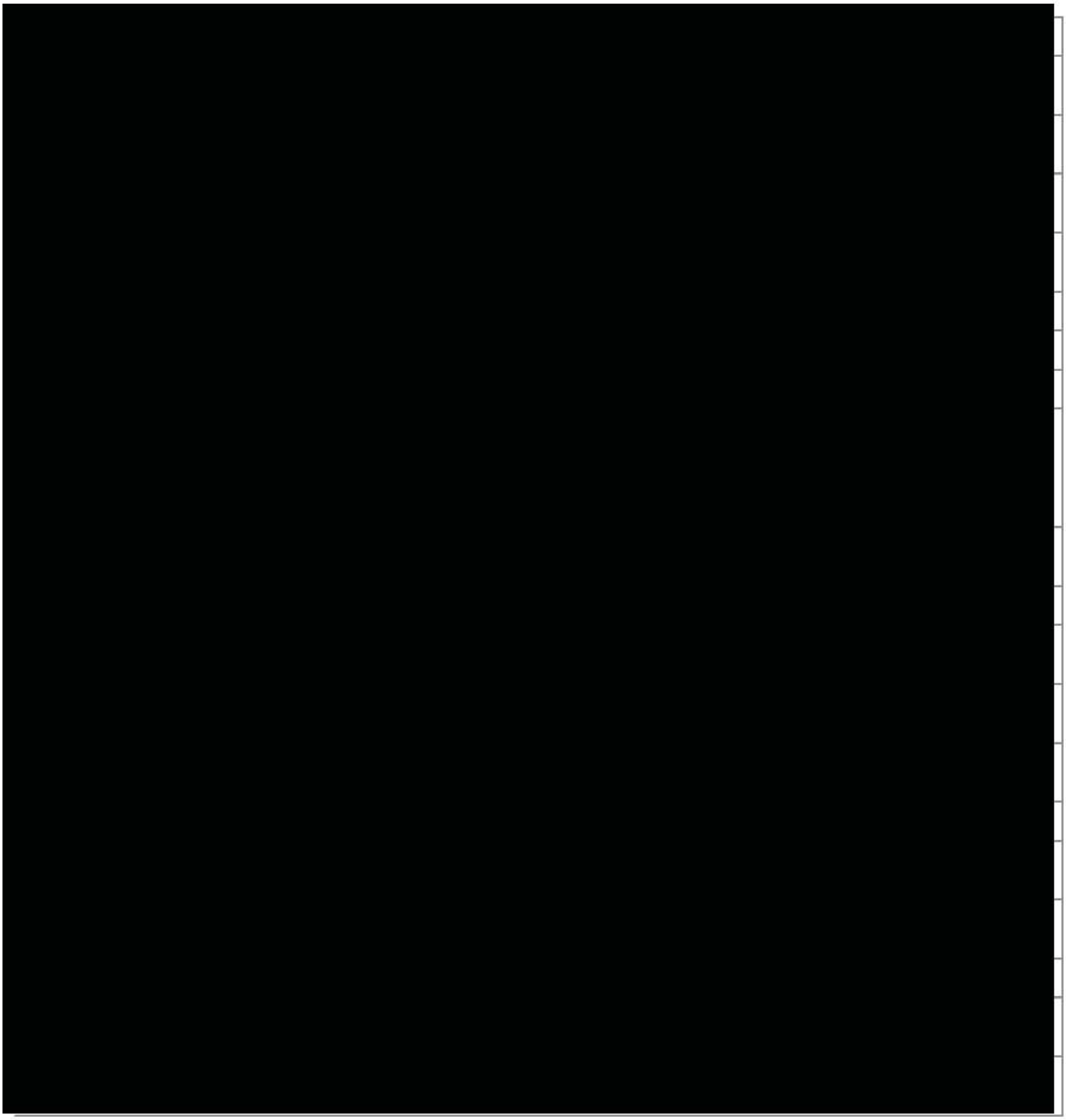
22. REFERENCES

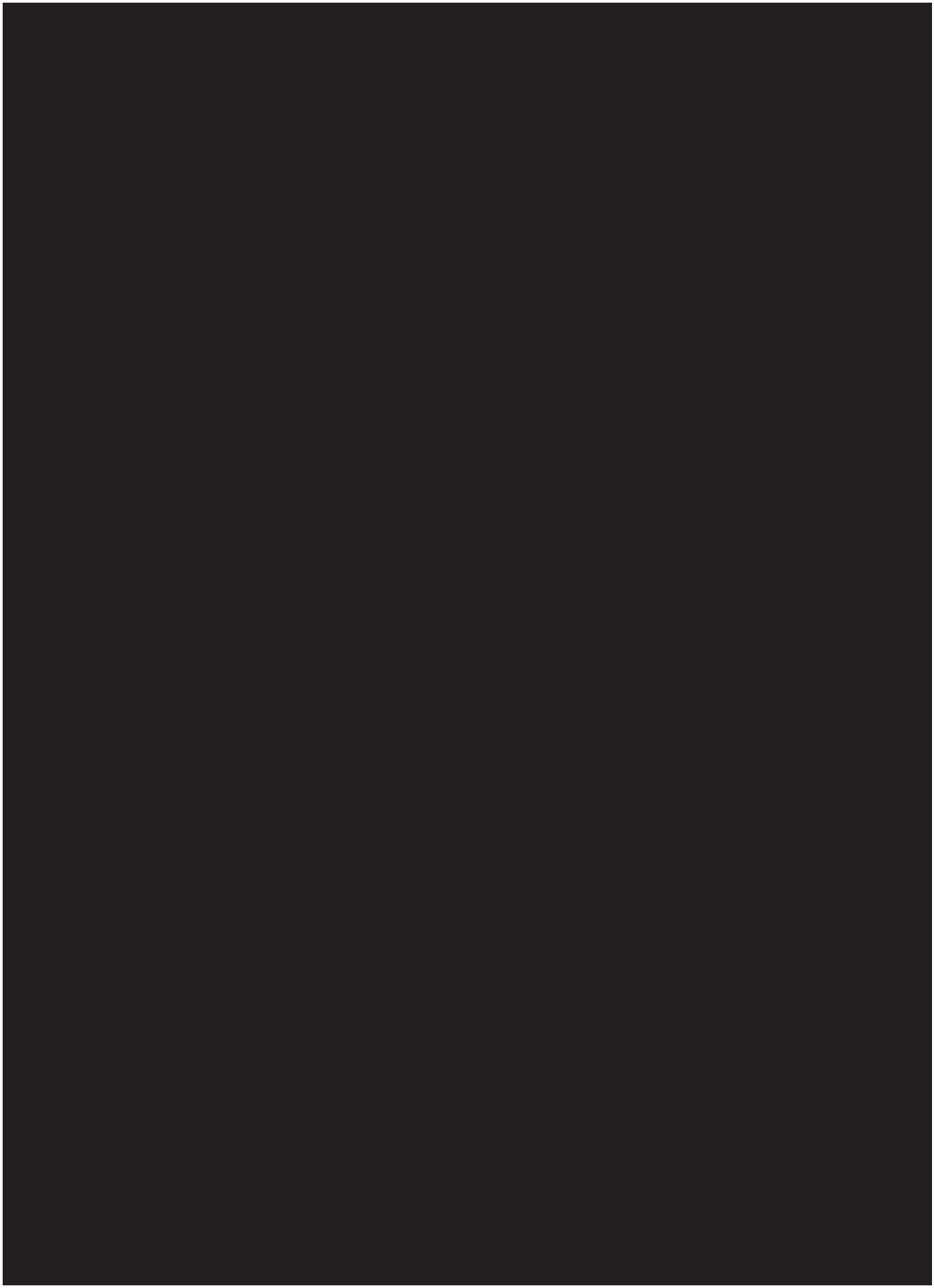
1. ISO 14155:2011: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice. Available at: https://www.iso.org/standard/45557.html
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). Available at: http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
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. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
5. Health Information Portability and Accountability Act (HIPAA). Available at: https://www.hhs.gov/hipaa/for-professionals/privacy/index.html
6. Keselman HJ, Algina J, Kowalchuk RK, Wolfinger RD. A Comparison of Two Approaches for Selecting Covariance Structures in the Analysis of Repeated Measures. *Communications in Statistics—Simulation and Computation.* 1998;27:591-604.
7. Kenward MG, Roger JH. Small Sample Inference for Fixed Effects from Restricted Maximum Likelihood. *Biometrics*. 1997;53:983–997.

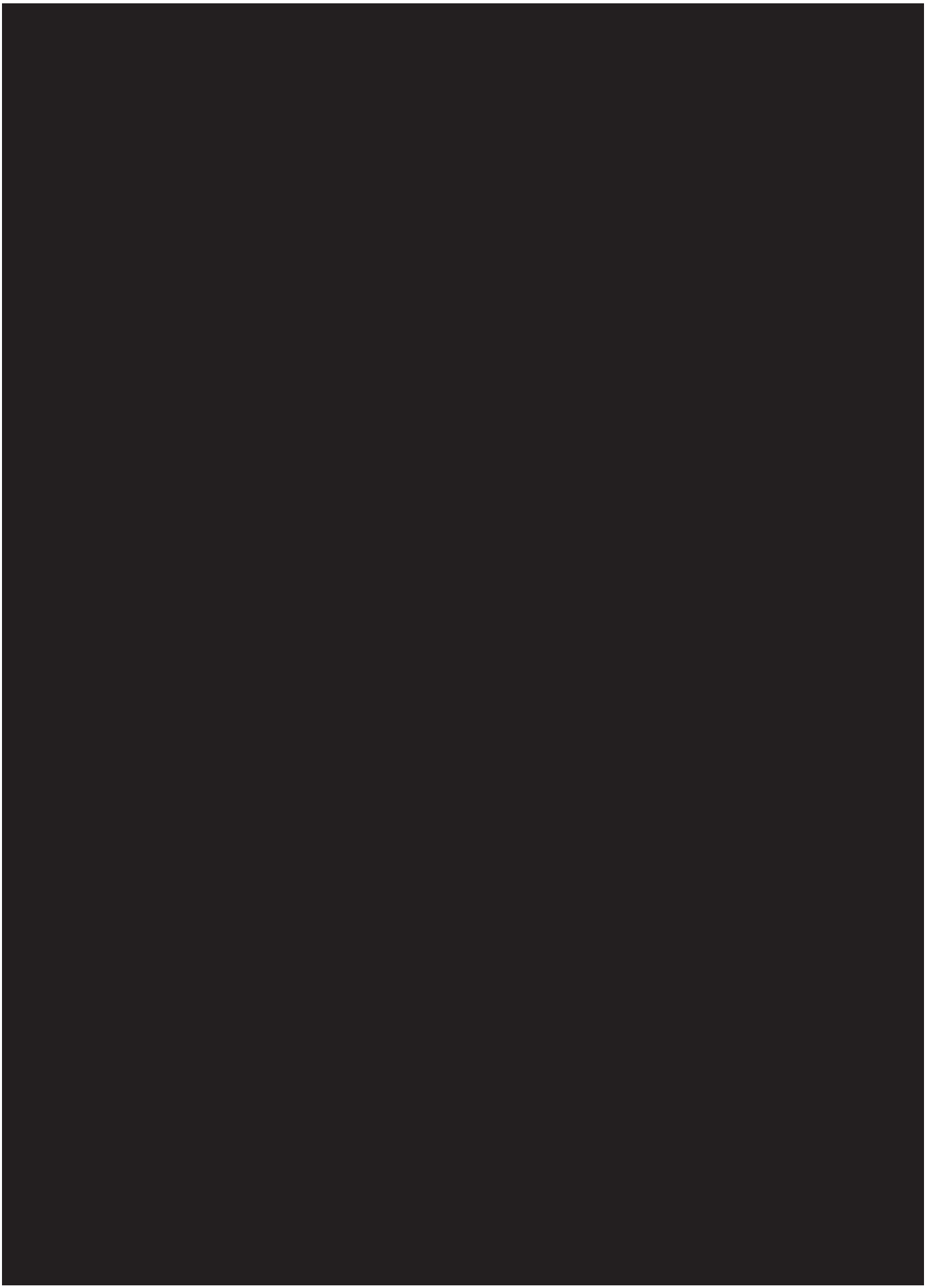
APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

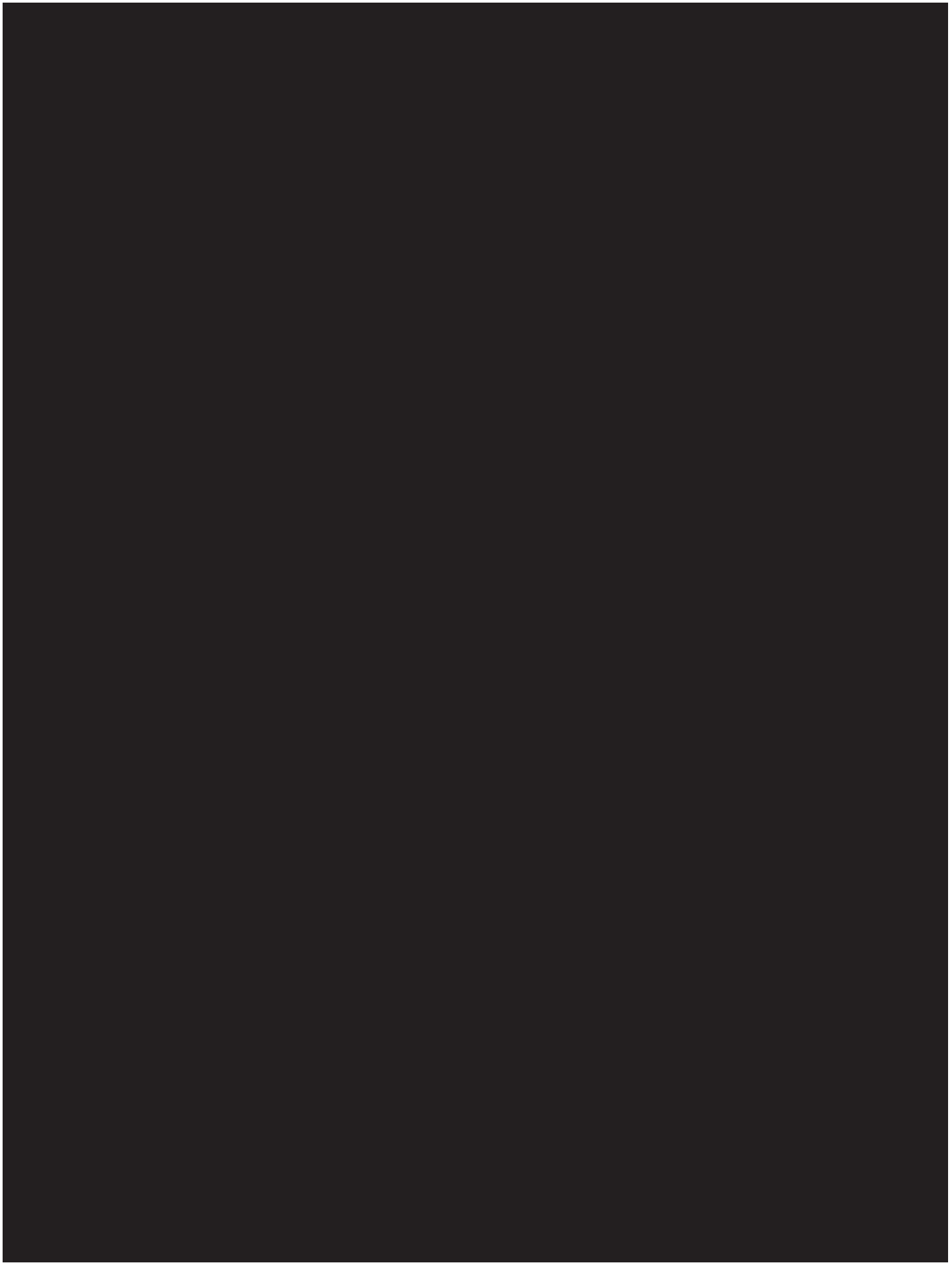


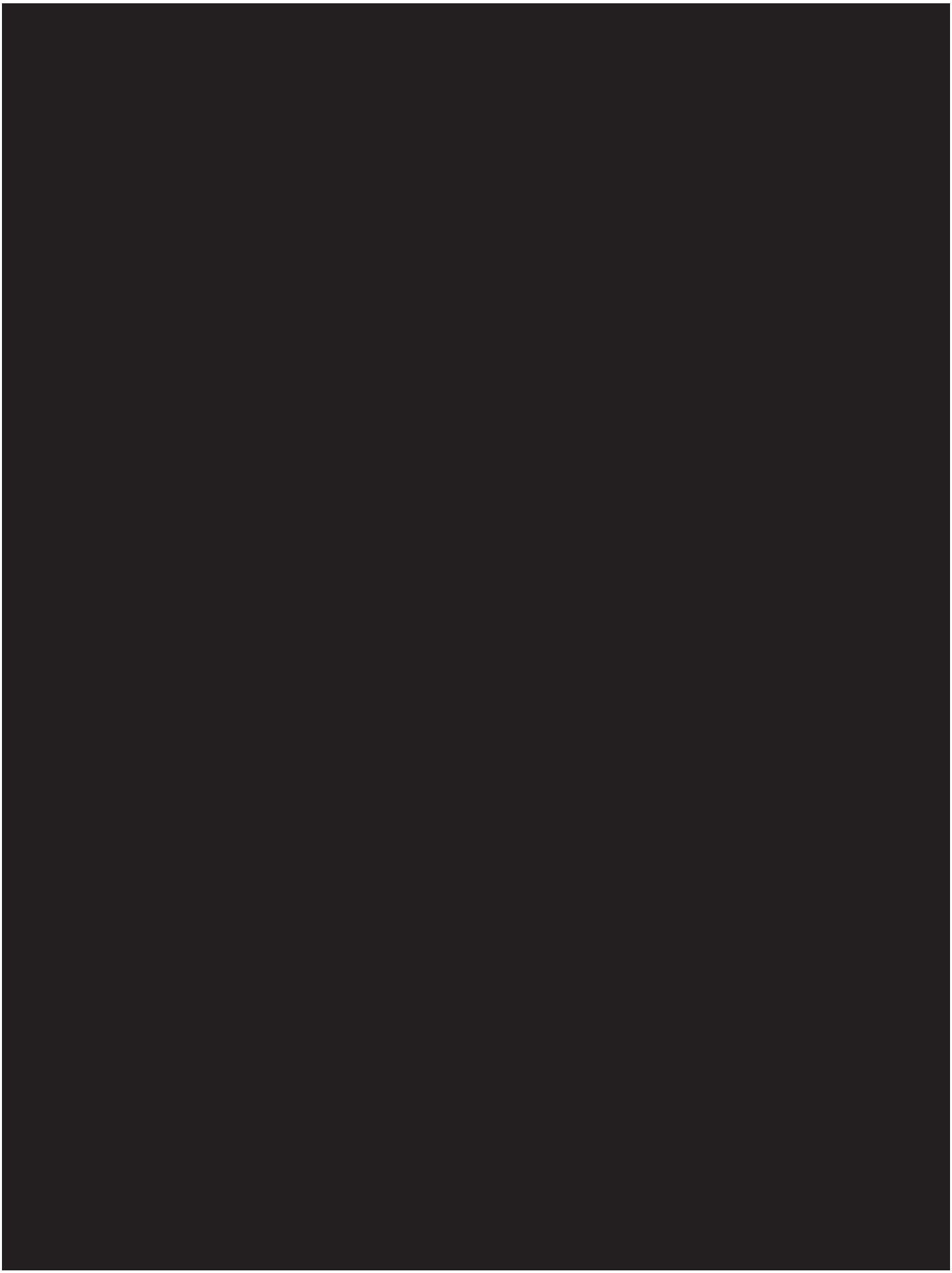


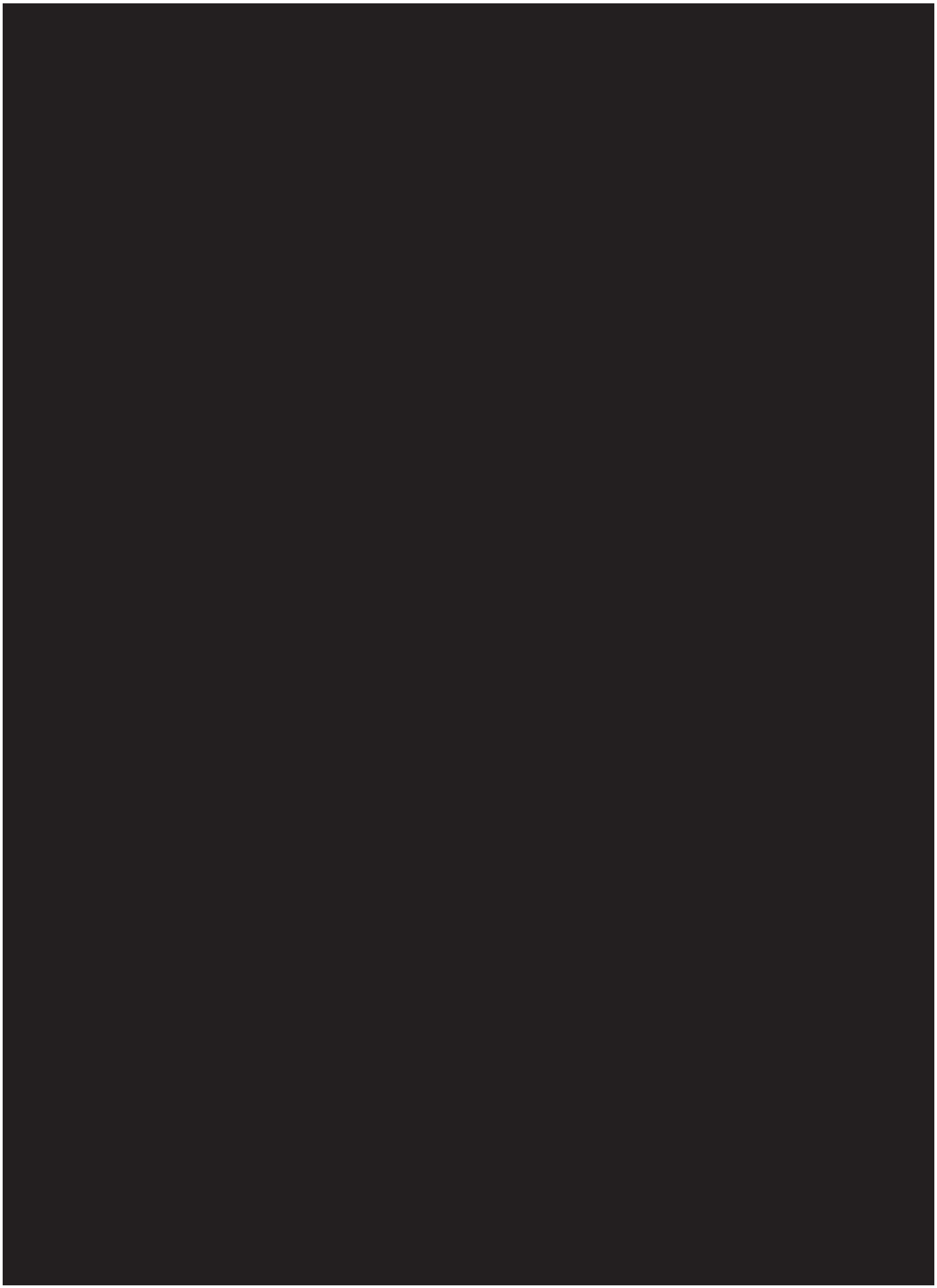


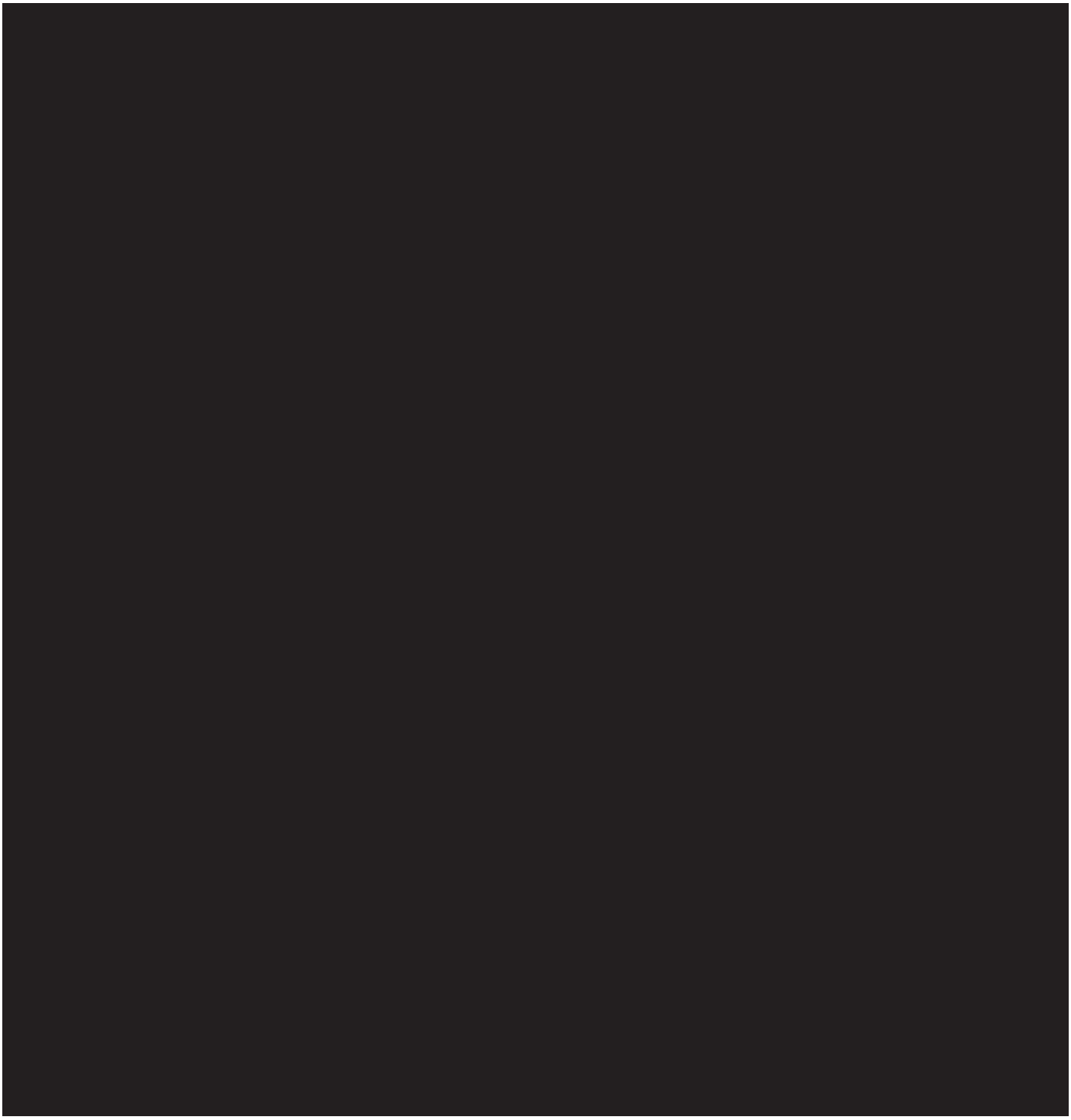


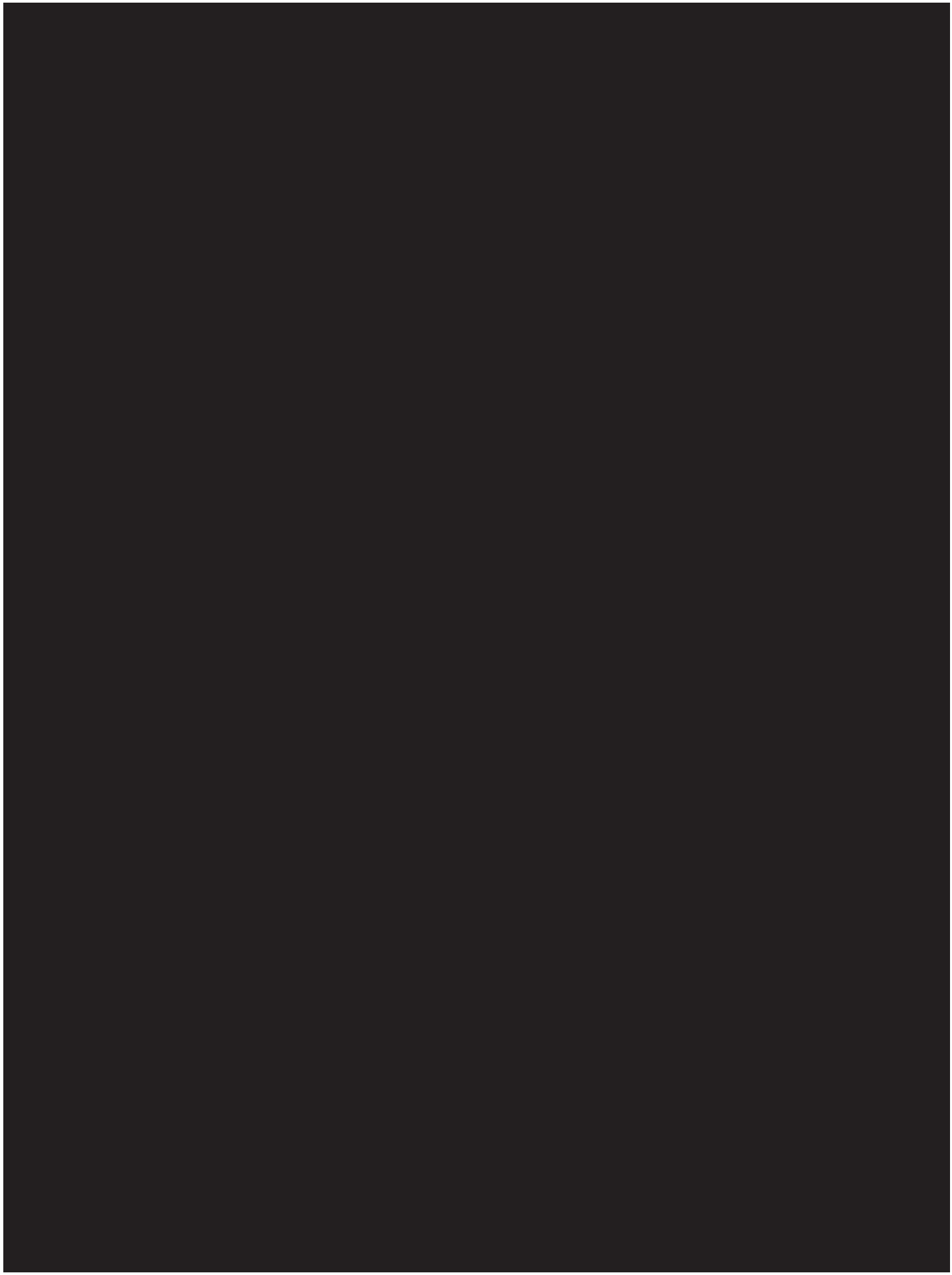


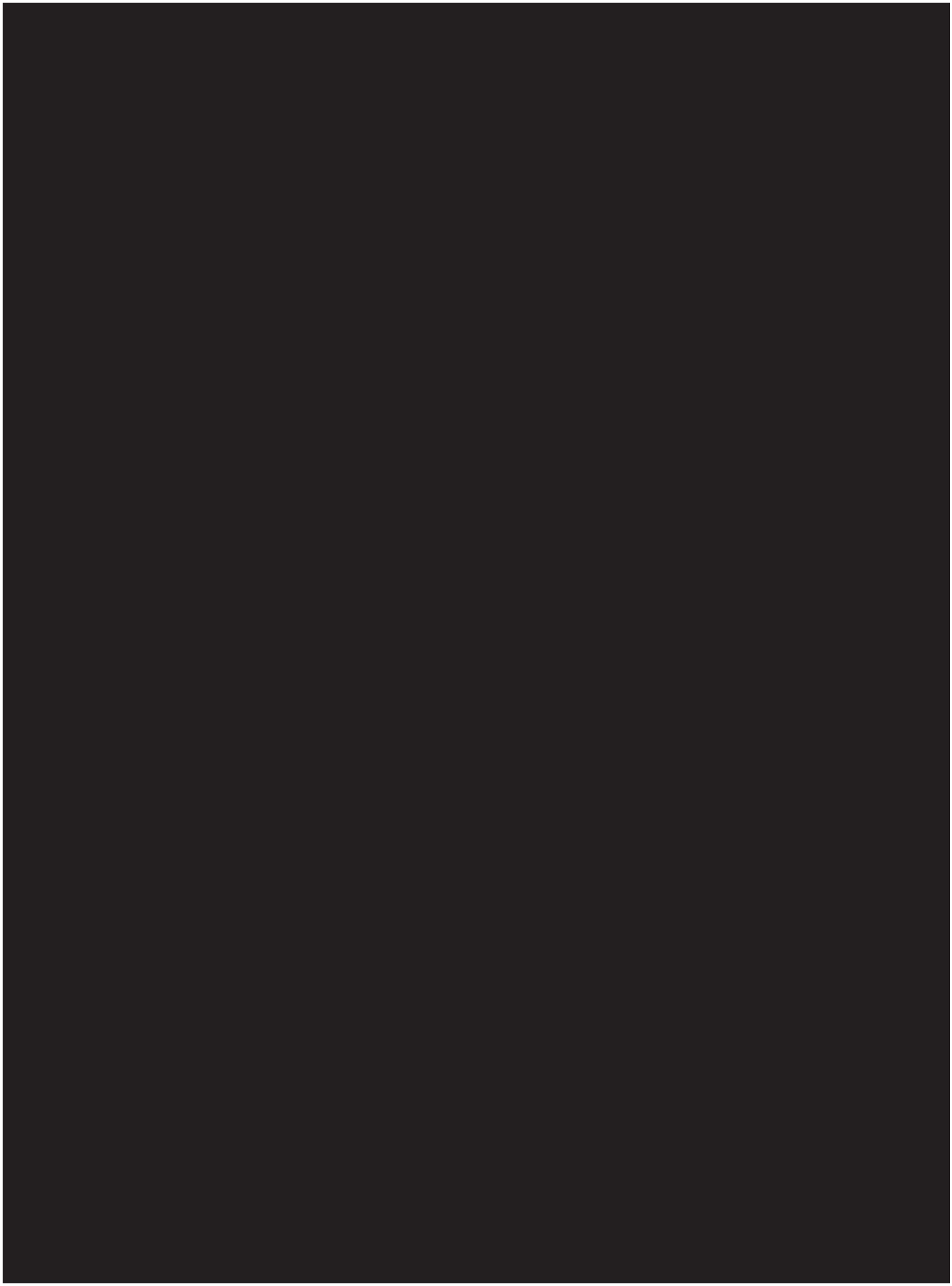


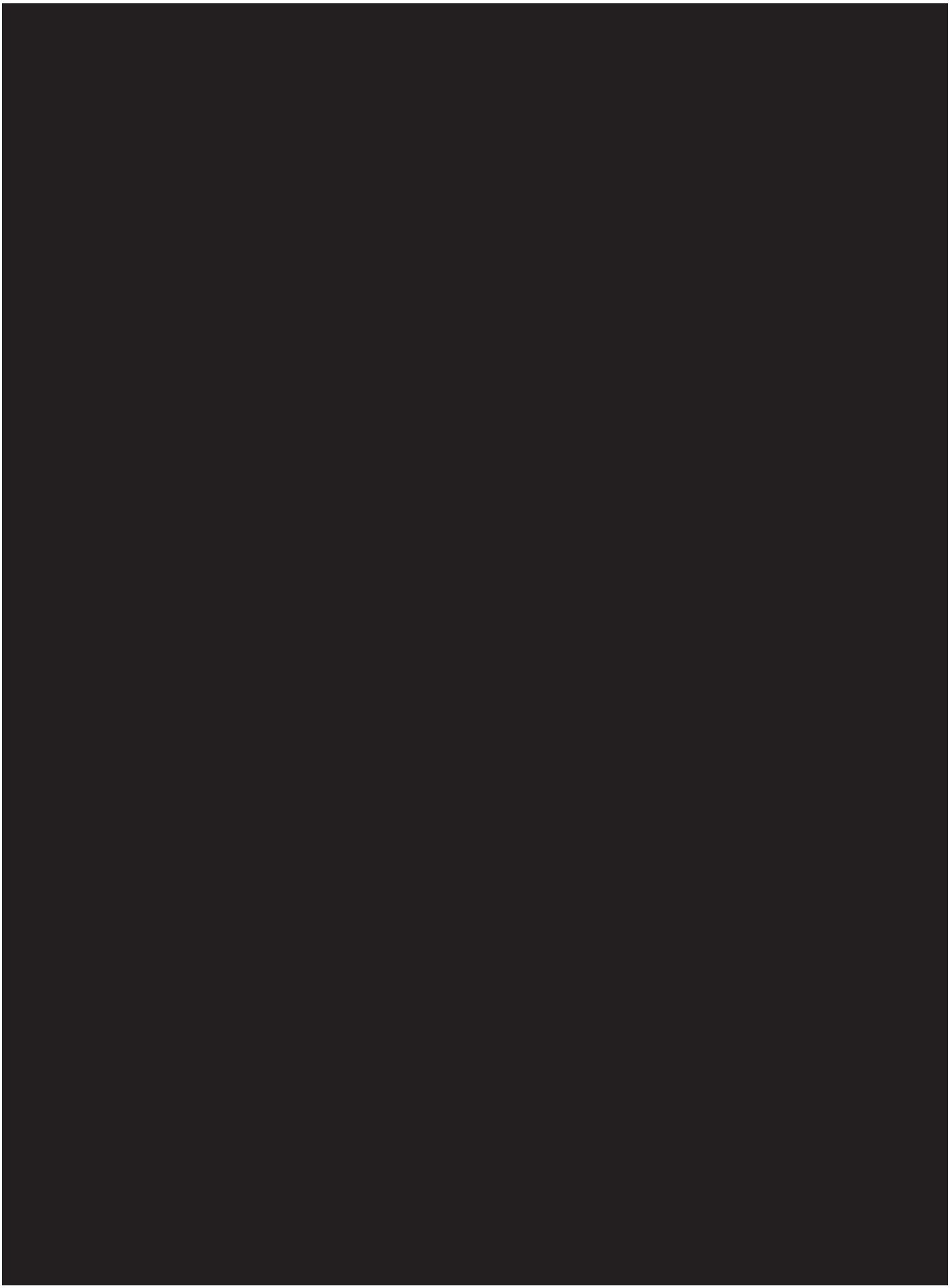


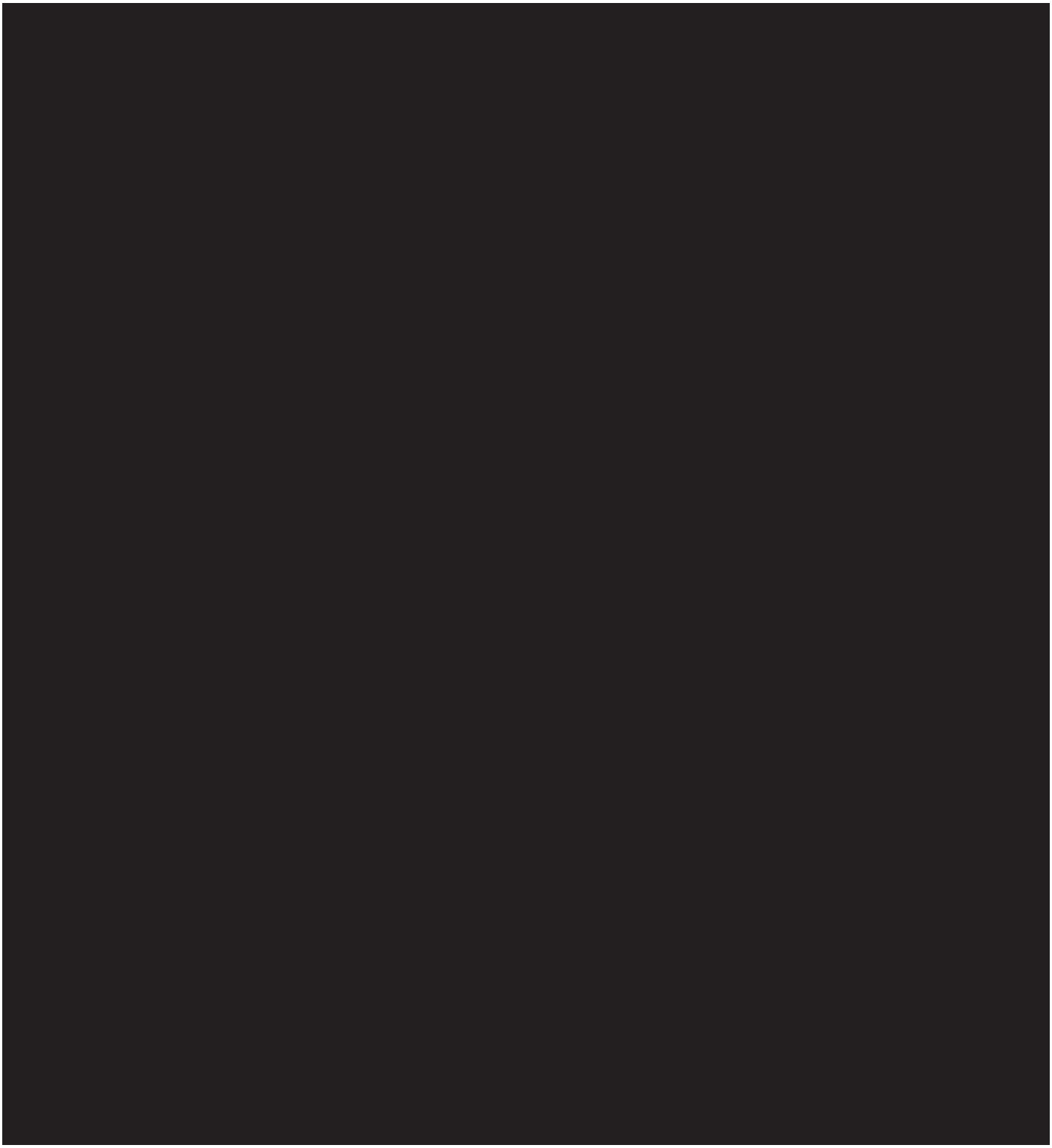


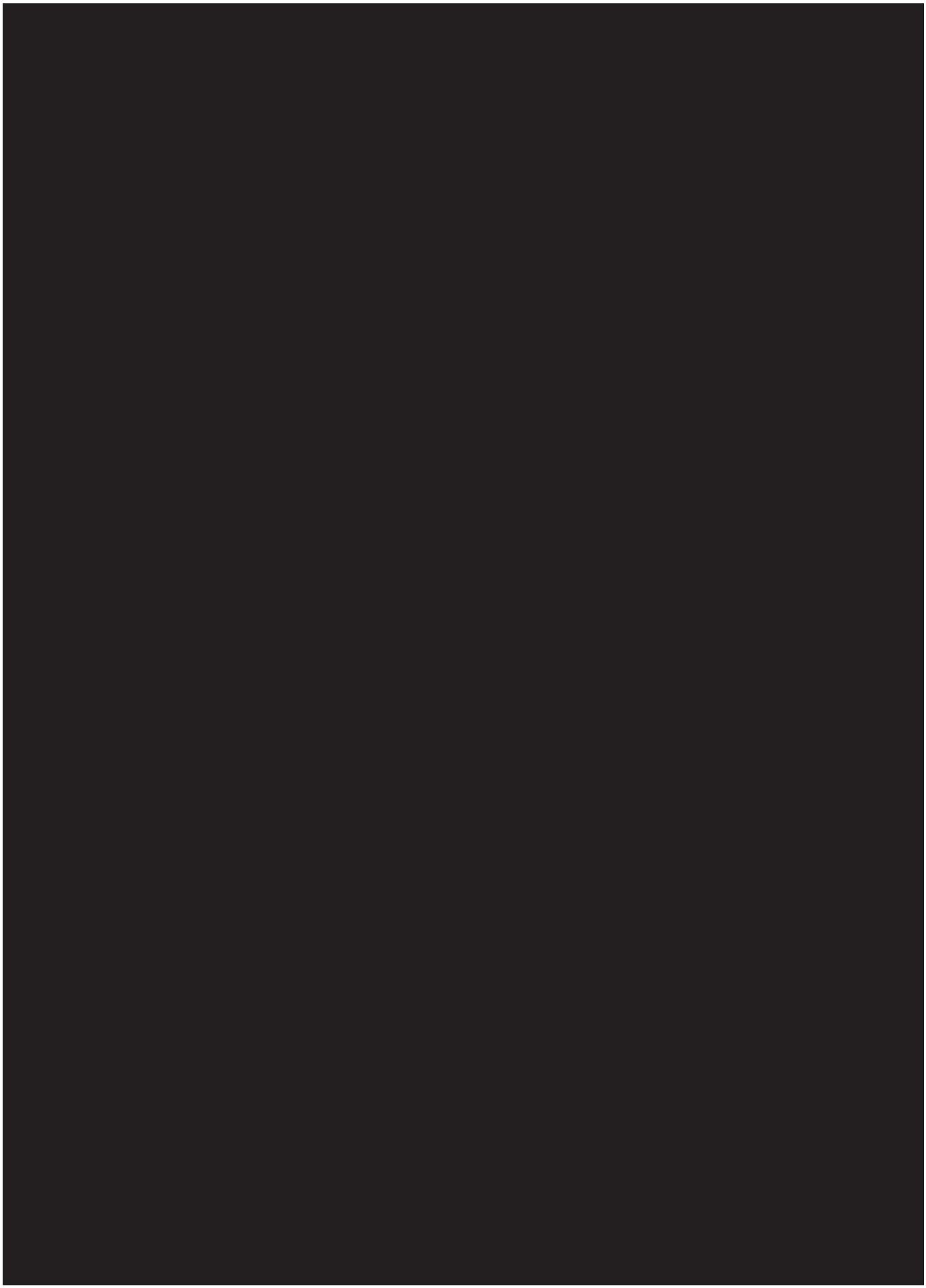


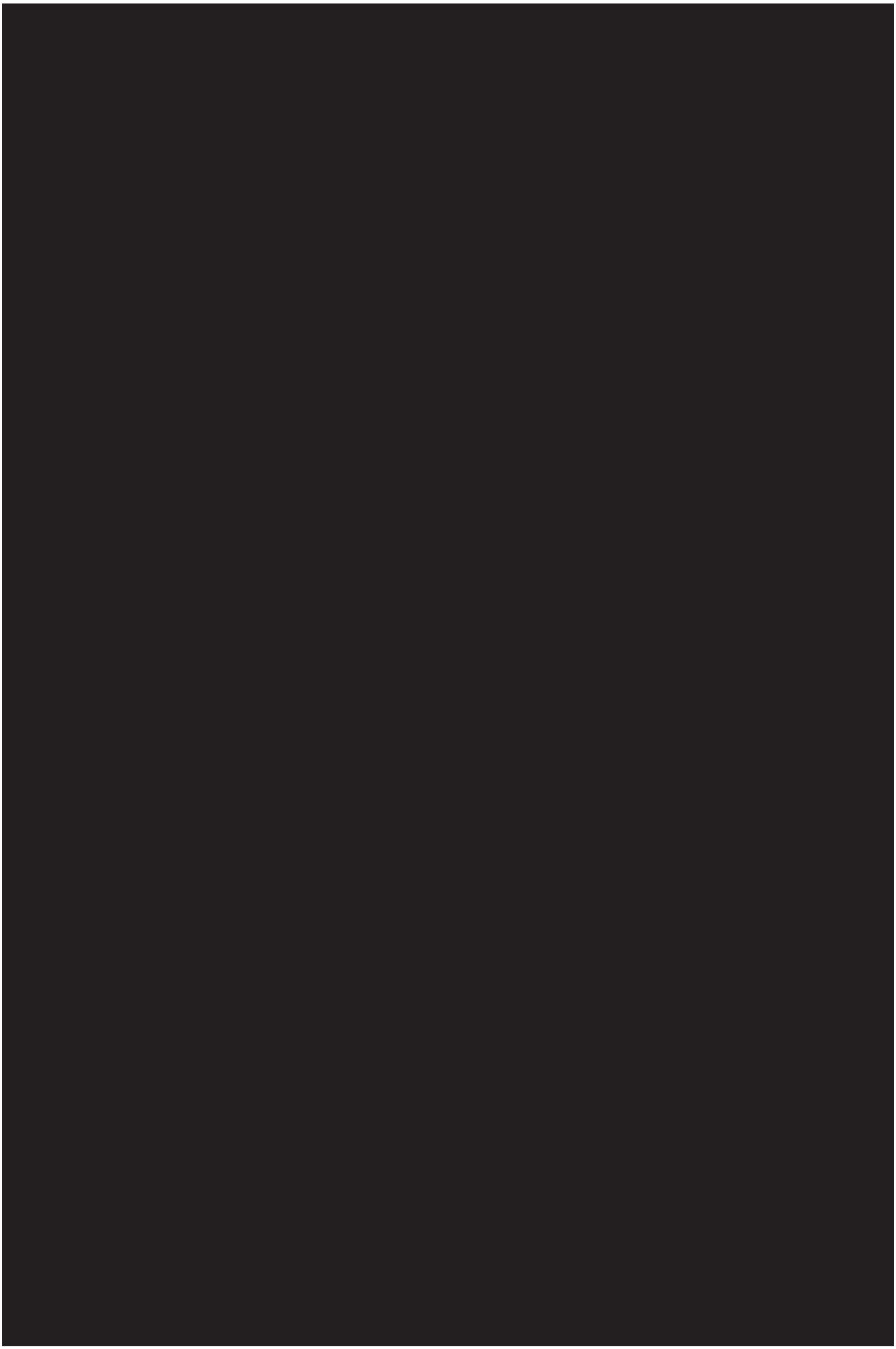


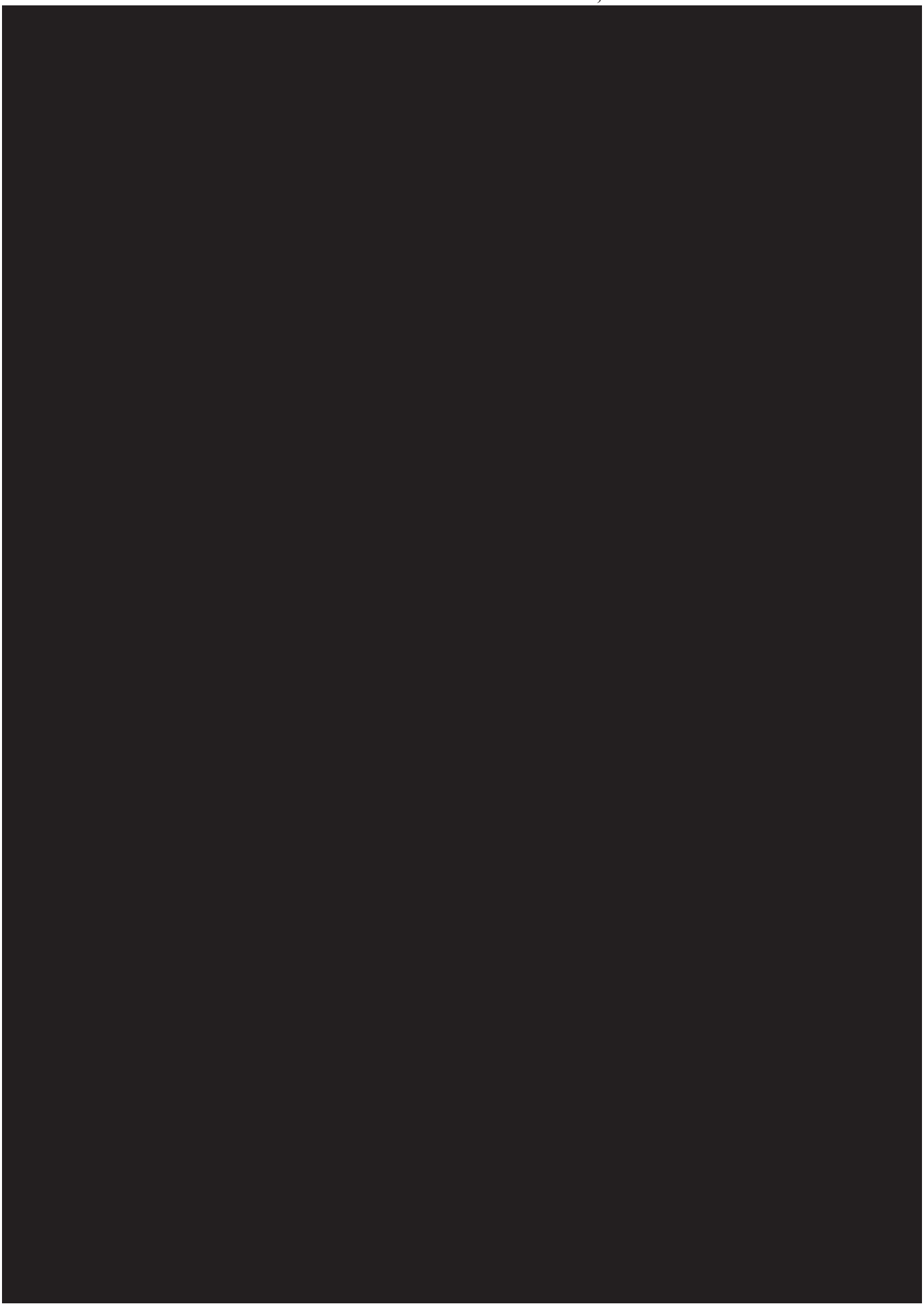


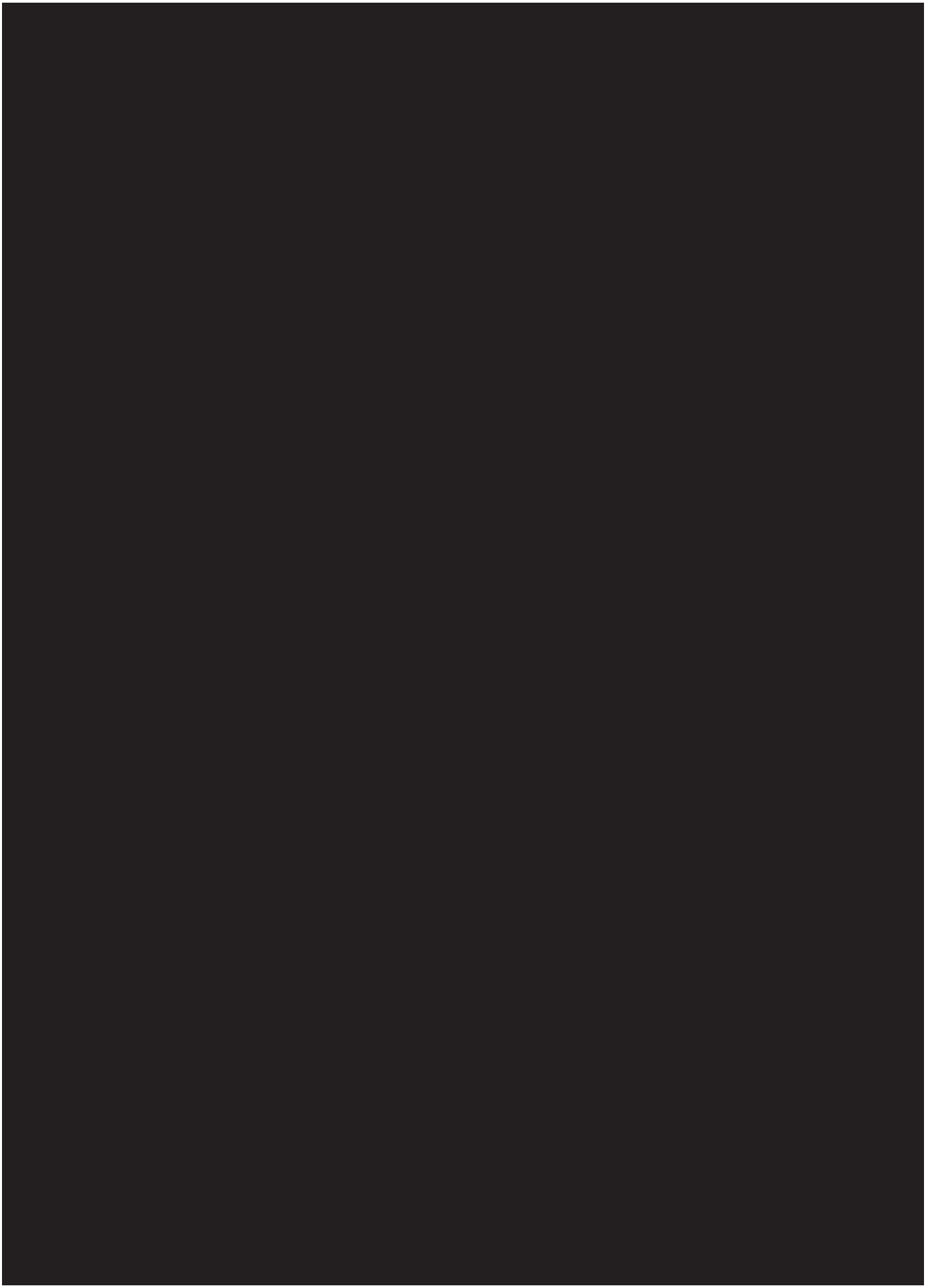


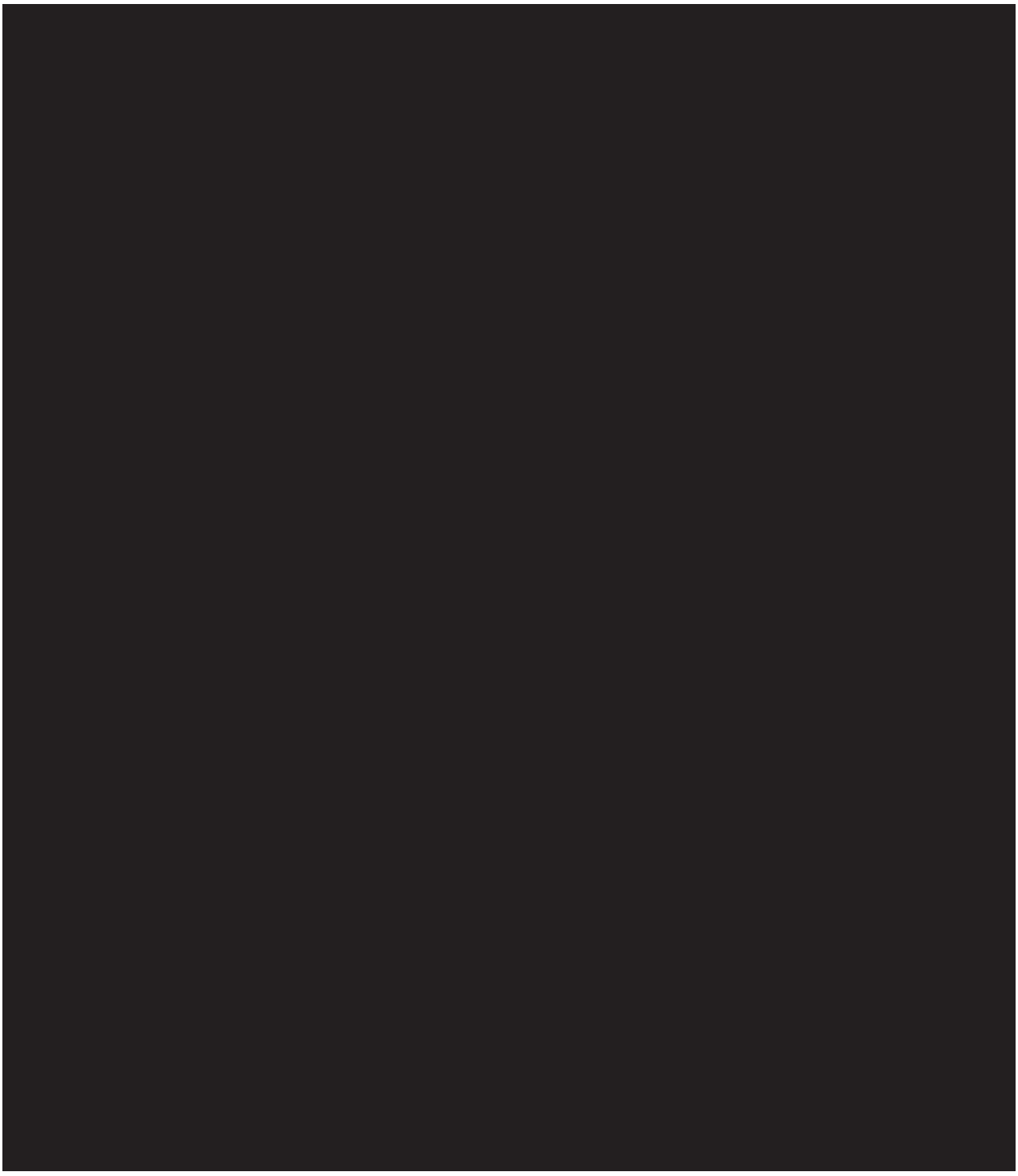












APPENDIX B : PATIENT INSTRUCTION GUIDE

Patient Instruction Guide will be provided separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Not Applicable

APPENDIX D: BINOCULAR OVER REFRACTION

Binocular Over-refraction Technique

1. Place trial frame on subject
2. Add +1.00 D sphere to OS
3. Add + 0.50DS OD and check VA
    - if VA remained unchanged or improved, repeat step 3
    - if VA decreased, add minus until best VA first achieved *note: add minus for 0.5 seconds to avoid reflex accommodation.
4. Record VA
5. Change +1.00 D sphere to OD
6. Repeat steps 3 and 4

APPENDIX E: PRESBYOPIC SYMPTOMS QUESTIONNAIRE

Presbyopic Symptoms Questionnaire

1. Do you notice that you often have to hold things farther away so that you can read them?
2. Do you notice that you often have difficulty focusing on near objects (i.e., experiencing blurry vision when looking at things close-up)?
3. Do you often have headaches or eyestrain, or feel fatigued, when reading or conducting other near activities?
4. Do you often have difficulty reading small or fine prints, such as phone books, medicine bottles or package labels, etc.?
5. Do you often have difficulty reading under dim or low light?

APPENDIX F: OCULAR DOMINANCE

OCULAR DOMNANCE TEST

+1.00 D LENS TEST

Step 1 Place the subjects best sphero-cylindrical distance refraction in a trial frame.

Step 2 Have the subject view a BVA line of letters.

Step 3 With both eyes open alternate a +1.00 D trial lens between the right and left eye and ask the subject to indicate over which eye does the lens cause the line of letters to appear more blurred. The eye that the greatest blur is reported is the distance dominant eye. If the subject indicates that the amount of blur is about the same between the two eyes then record as neither eye dominant.

SIGHTING OCULAR DOMINANCE

Step 1 Ask the subject to extend both arms out and use his/her hands to form a triangle. The subject will be asked to keep both eyes open, and look through the triangle at a small object on the wall (e.g., a light switch or doorknob).

Step 2 Occlude the subject's left eye, then right eye. While alternating the occluder from the subject's eyes, ask the subject when they see the object.

If the subject sees the object when the left eye is covered, the subject is *right eye* dominant.

If the subject sees the object when the right eye is covered, the subject is *left eye* dominant.

If the subject sees the object with both eyes, the opening between the hands may be too large. Therefore, ask the subject to make a smaller opening and repeat the procedure.

APPENDIX G: TEST LENS FITTING GUIDE

Step 1.

Choose the first lens based on the best spherical equivalent refraction and ADD power for both eyes. Select the first lens per table 1 below.

Table 1. Initial Lens Selection

	ADD							
	+0.75	+1.00	+1.25	+1.50	+1.75	+2.00	+2.25	+2.50
Dominant Eye	LOW	LOW	LOW	MID	MID	MID	MID	MID
Non-Dominant Eye	LOW	LOW	LOW	MID	MID	HGH	HGH	HGH

Assess the subject's vision at distance and near after the lens has settled (10 minutes). If the vision is acceptable continue with the fit assessment and dispensing as per the protocol.

If the vision is not acceptable, ensure that the proper initial lens power was selected by performing a distance over-refraction with +/- 0.25D trial lenses (or flippers) to determine if a change in the initial lens power is required (note: the over-refraction should be performed outside of the phoropter in normal room illumination). Recheck both distance and near vision with the over-refraction in place. If a change in the initial lens power is not required refer to the fitting steps listed below in step 2 (table 2).

Step 2.

Table 2. Lens change if required. *

Distance Complaint								
ADD	+0.75	+1.00	+1.25	+1.50	+1.75	+2.00	+2.25	+2.50
Dominant Eye	N/A	N/A	N/A	LOW	LOW	MID	MID	MID
Non-Dominant Eye	N/A	N/A	N/A	MID	MID	MID +	MID +	MID +

Near Complaint								
ADD	+0.75	+1.00	+1.25	+1.50	+1.75	+2.00	+2.25	+2.50
Dominant Eye	LOW	LOW	LOW	MID	MID	MID	MID	MID
Non-Dominant Eye	LOW+	LOW+	LOW+	MID+	MID+	HGH+	HGH+	HGH+

*Note: a + following the contact lens design indicates to add +0.25 D to the distance contact lens power on the non-dominant eye (see example below).

Example: The subject is a +1.75 ADD and has a near complaint and it is determined a change in lens pairs is needed. Referring to table 2 near complaint section, under the +1.75 ADD it states to keep the dominant eye the same (i.e. MID) and add +0.25D to the non-dominant eye (i.e. MID+).

Subjects spherical equivalent distance refraction

OD: +2.50
OS: +3.00 (OS non-dominant eye)

The new lens chosen should be as follows:

OD: +2.50 MID ADD (i.e. no change)
OS: +3.25 MID ADD

Step 3.
If after the above lens modifications have been attempted and the subject's vision is still not satisfactory, and additional optimizations are allowed by the protocol, lens changes may be attempted, based on the Investigator's clinical experience, to determine if acceptable vision can be achieved.

APPENDIX H: CLINICAL TECHNICAL PROCEDURES (CTP)

- [redacted] LIMBAL & CONJUNCTIVAL (BULBAR) REDNESS
- [redacted] EXPANDED SODIUM FLUORESCEIN CORNEAL STAINING
- [redacted] DETERMINATION OF NEAR ADD
- [redacted] NEAR logMAR VISUAL ACUITY MEASUREMENT PROCEDURE
- [redacted] LENS FITTING CHARACTERISTICS
- [redacted] SUBJECT REPORTED OCULAR SYMPTOMS
- [redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS
- [redacted] BIOMICROSCOPY SCALE
- [redacted] KERATOMETRY
- [redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION
- [redacted] ETDRS DISTANCE VISUAL ACUITY MEASURMENT PROCEDURE
- [redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

[redacted] LIMBAL AND CONJUNCTIVAL (BULBAR) REDNESS

[redacted]

[redacted] **Limbal & Conjunctival (Bulbar) Redness**

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Page 1 of 7

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Attachment A Efron Grading Scale for Limbal Redness (0.5 unit increments)

Attachment B Efron Grading Scale for Limbal Redness (1.0 unit increments)

Attachment C Efron Grading Scale for Bulbar Redness (0.5 unit increments)

Attachment D Efron Grading Scale for Bulbar Redness (1.0 unit increments)

Attachment E

[redacted] EXPANDED SODIUM FLUORESCEIN CORNEAL STAINING

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Expanded Sodium Fluorescein Corneal Staining

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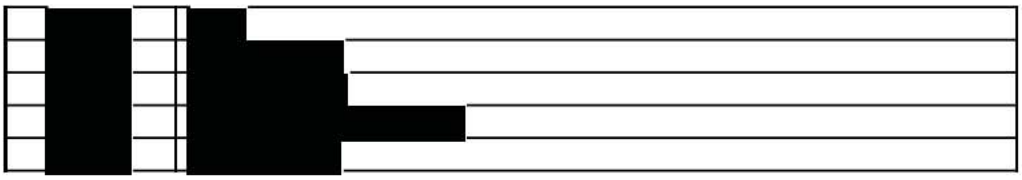

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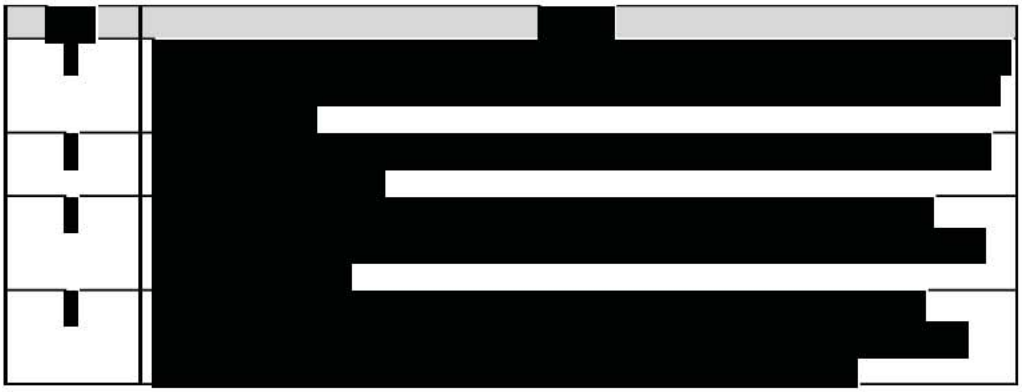

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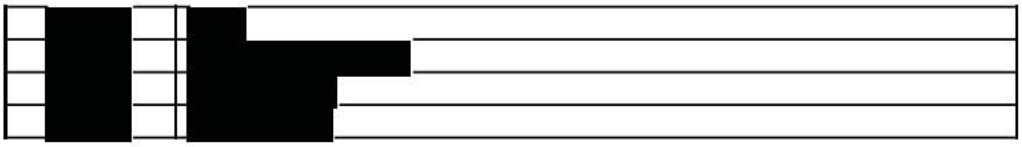

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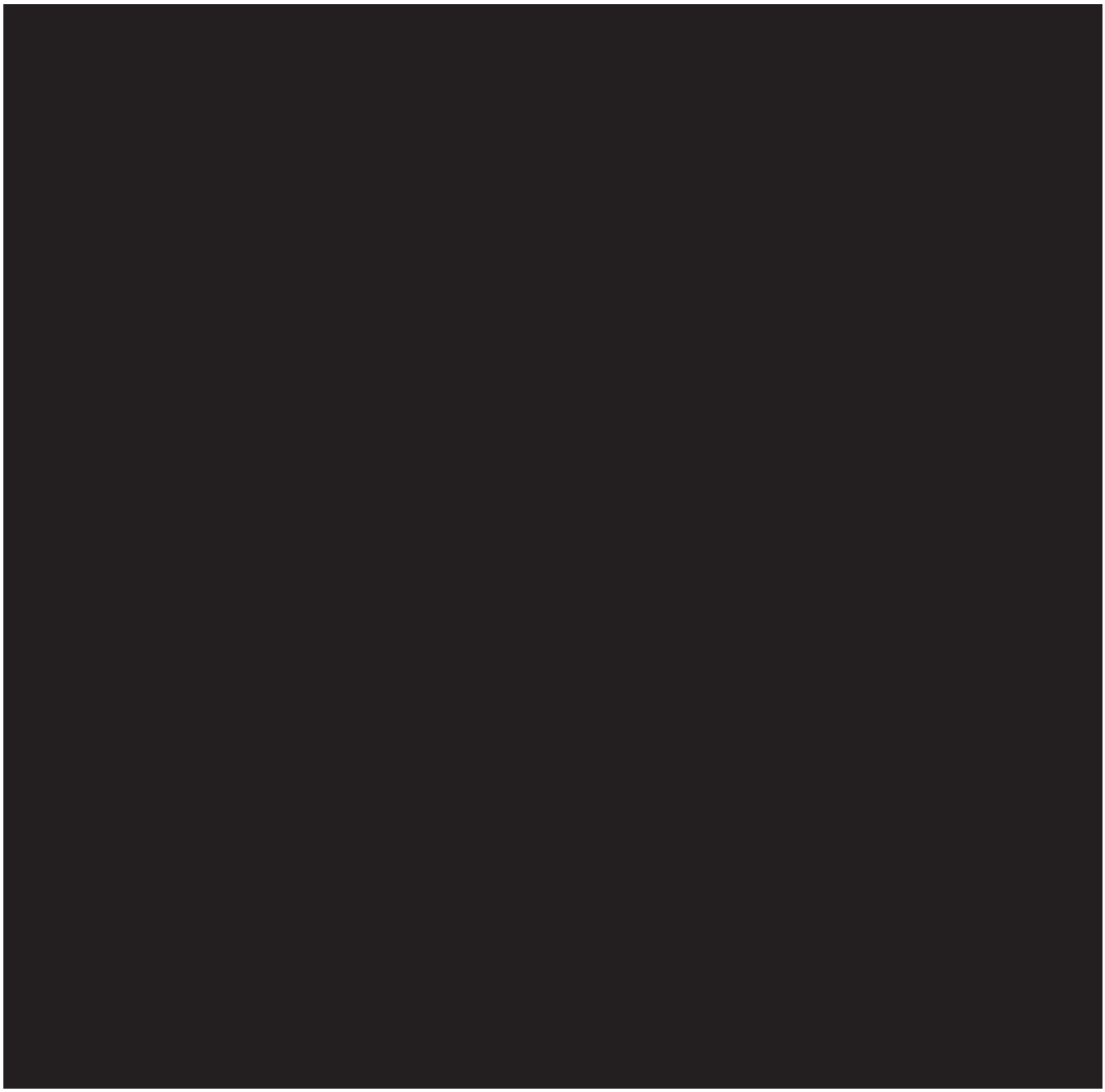

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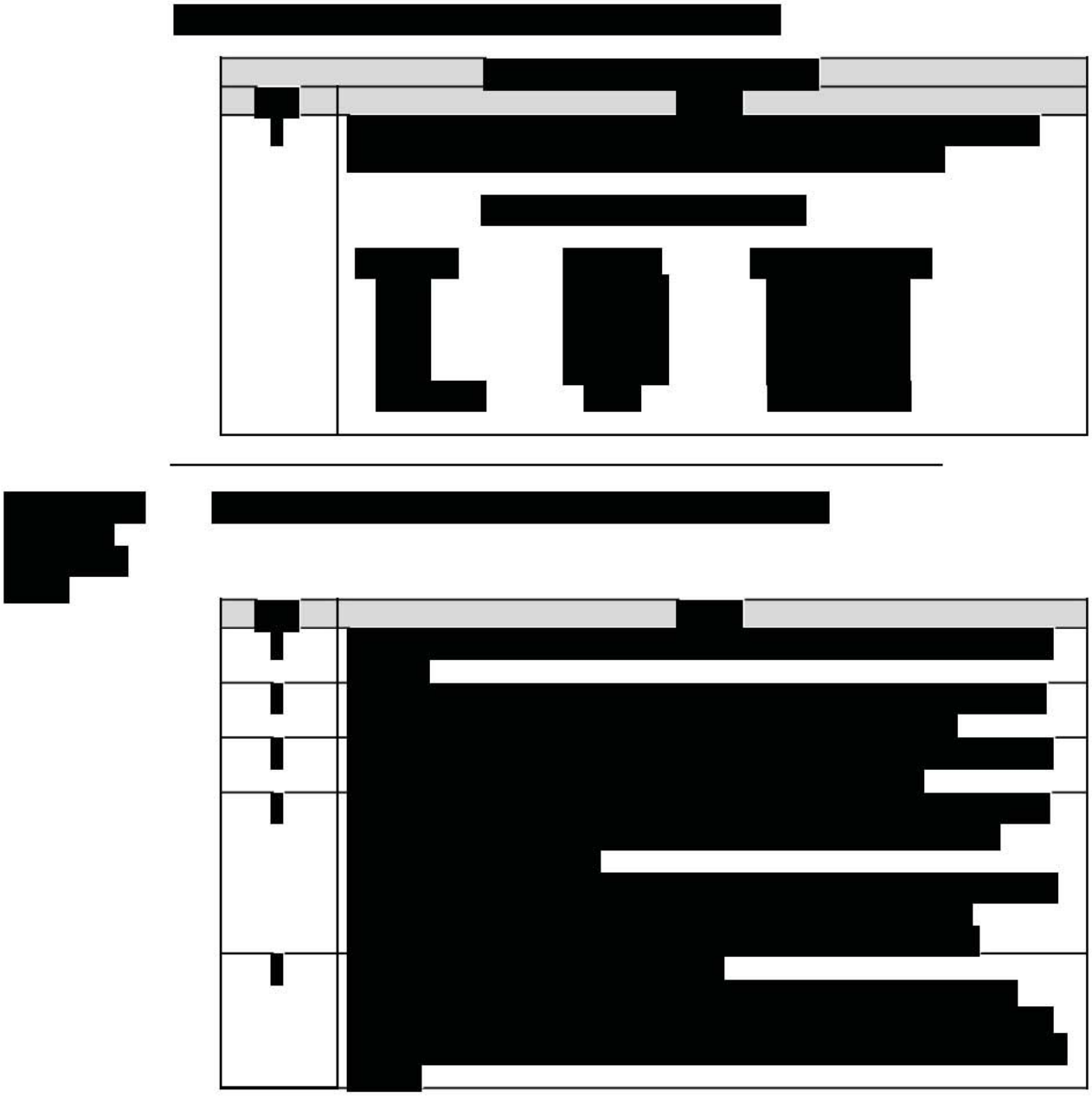

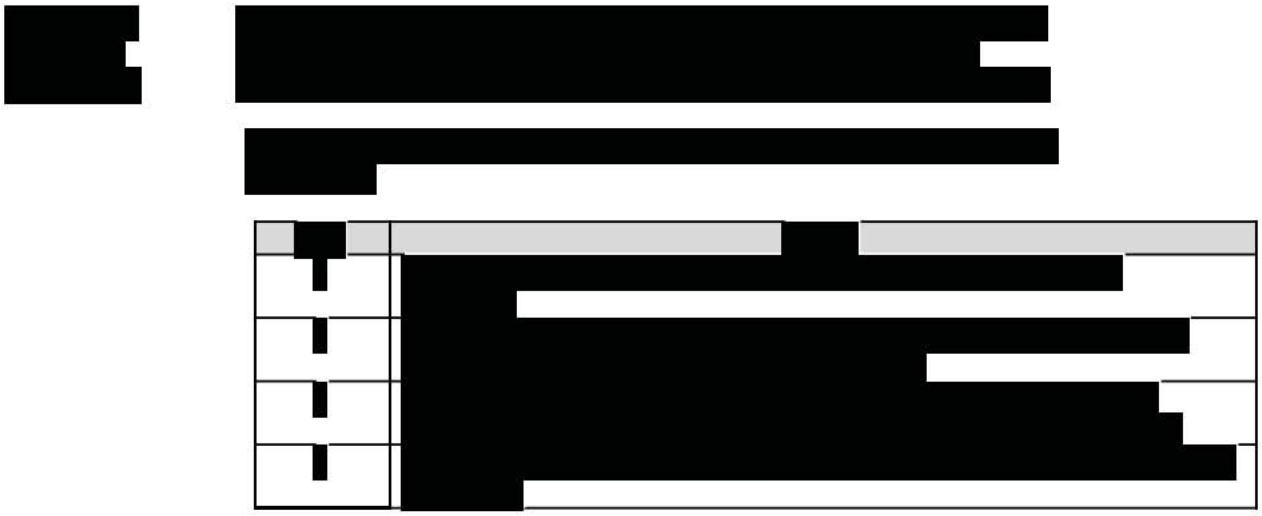

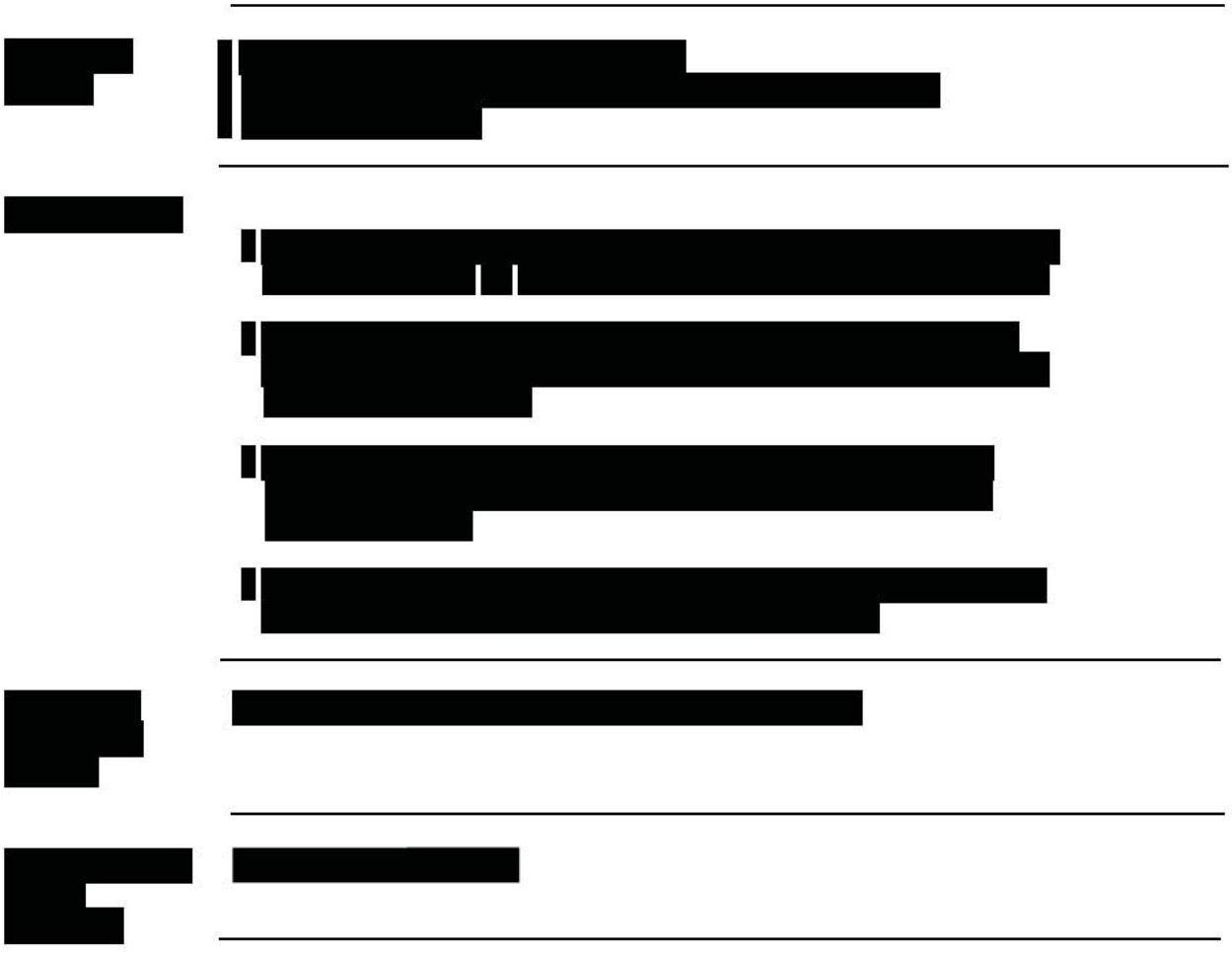

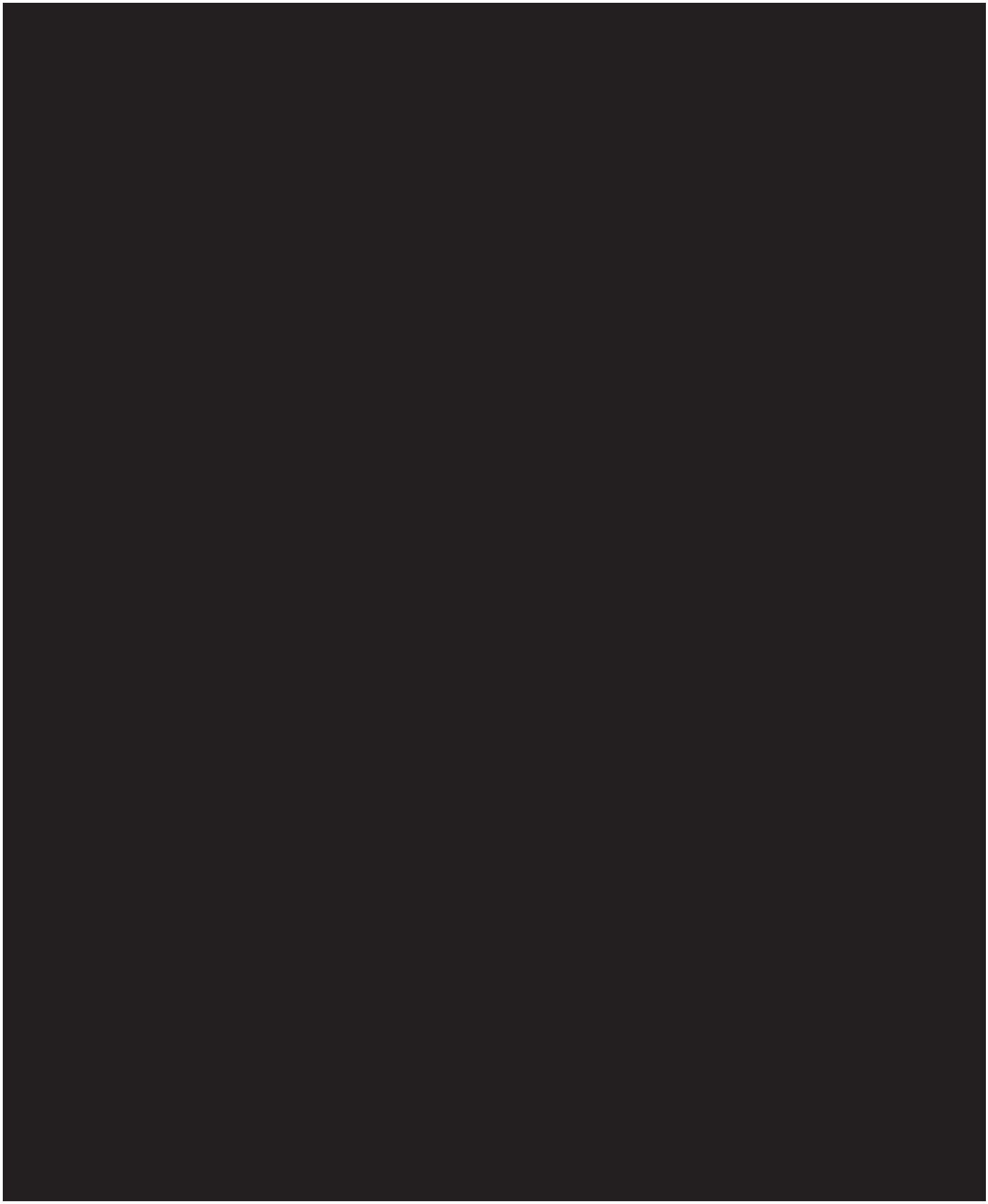

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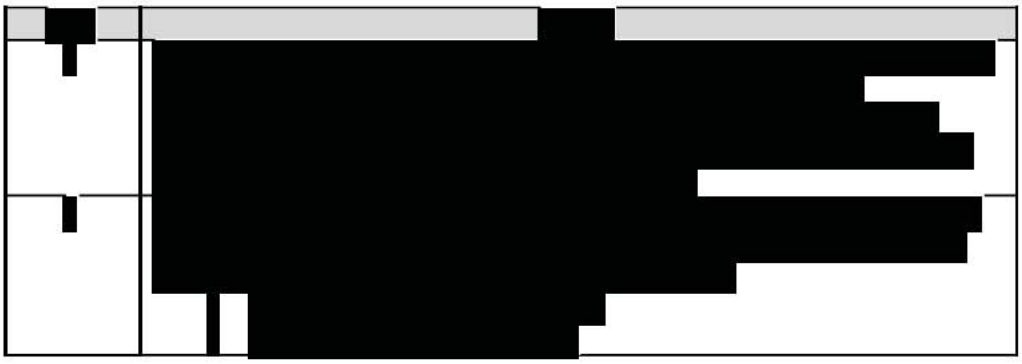

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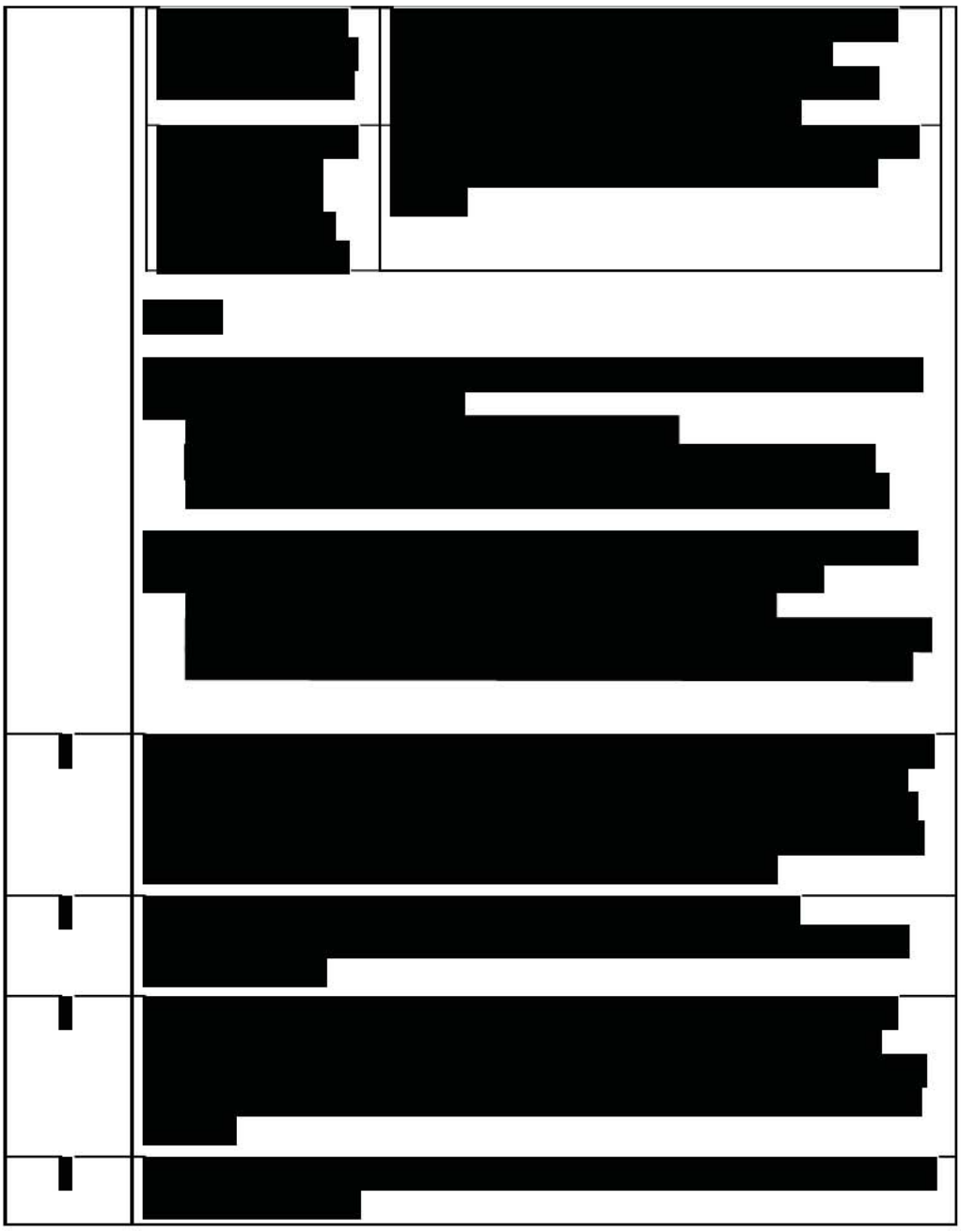

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Lens Fitting Characteristics

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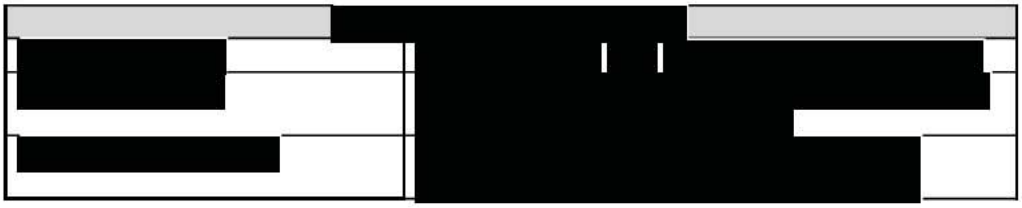

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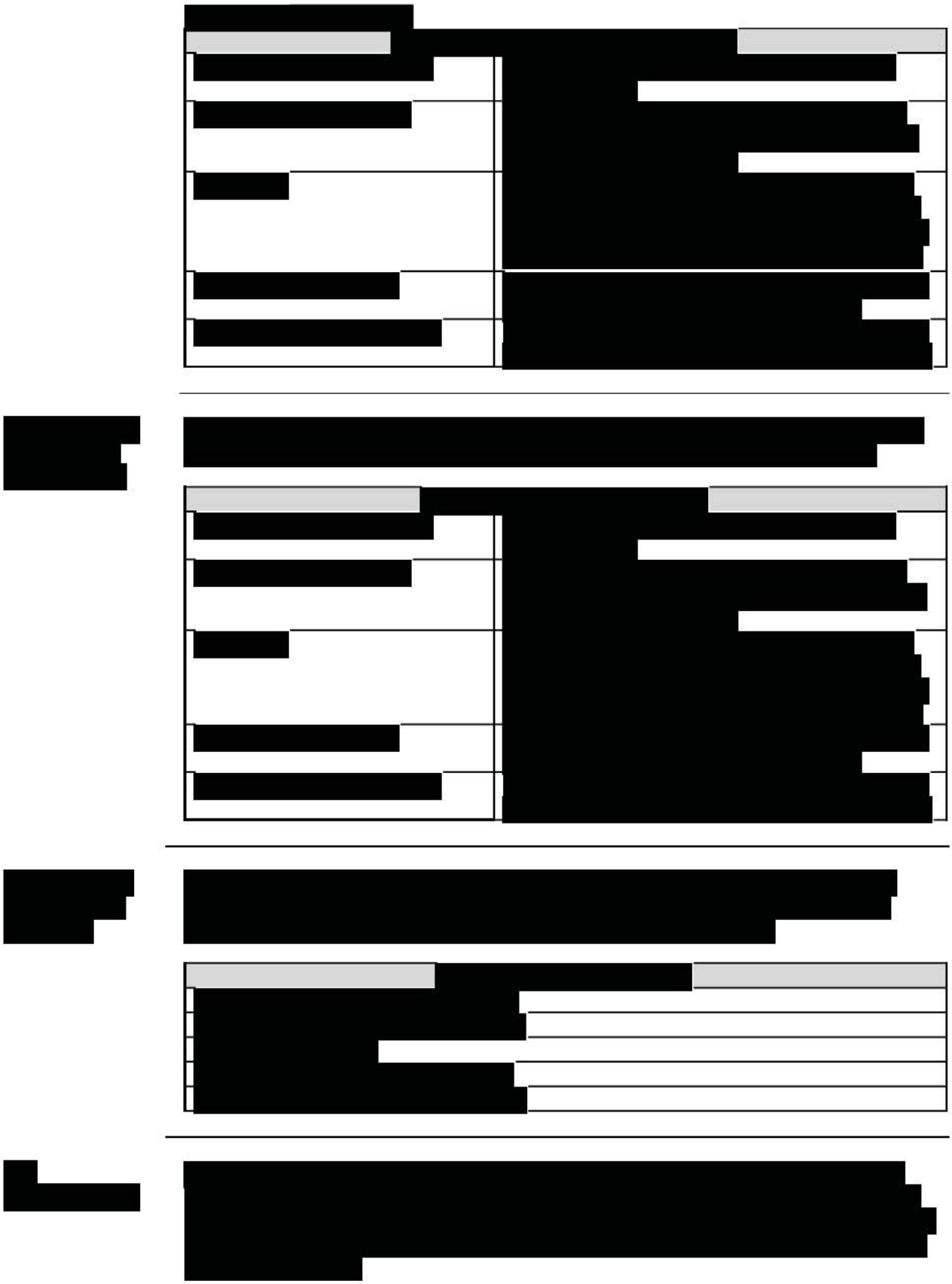

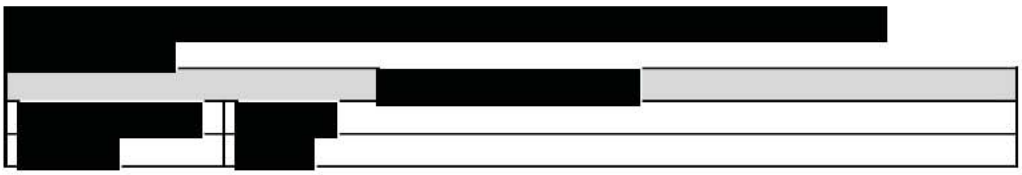

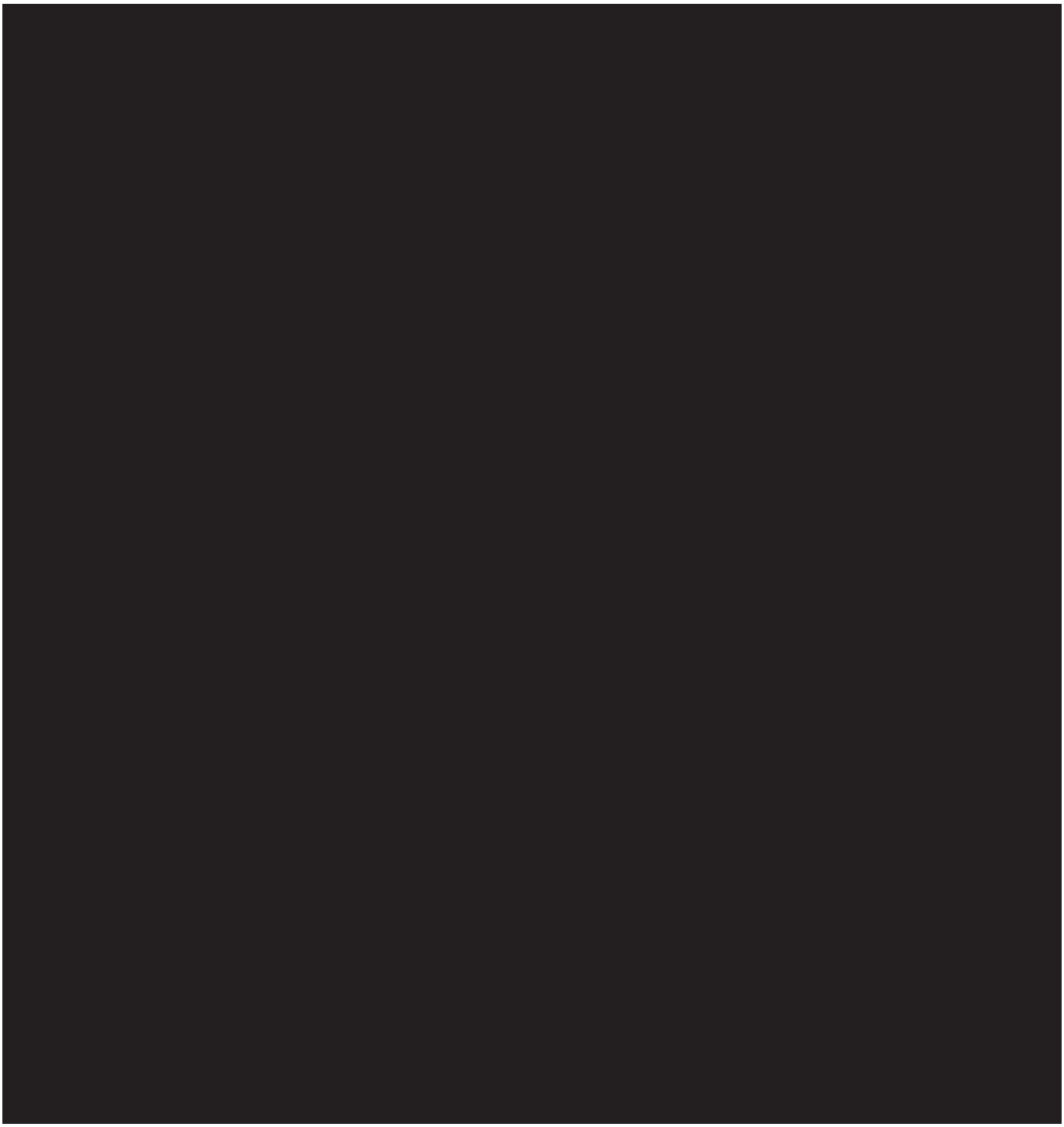

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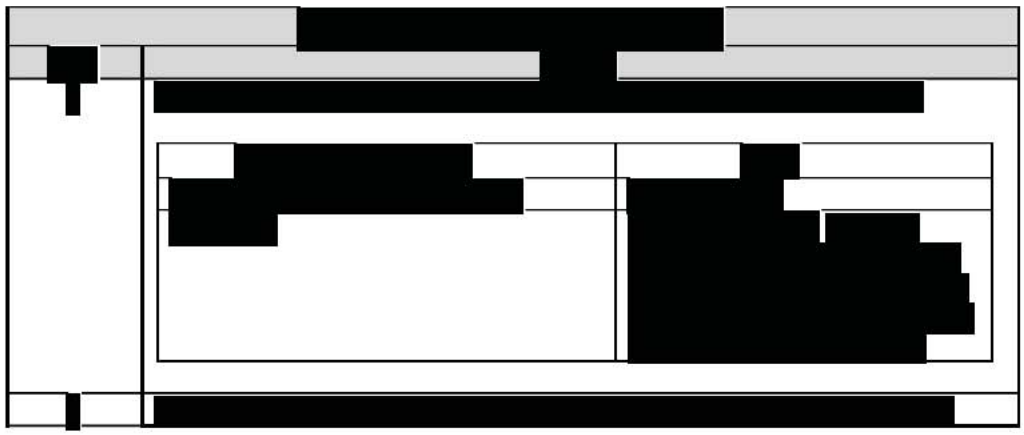

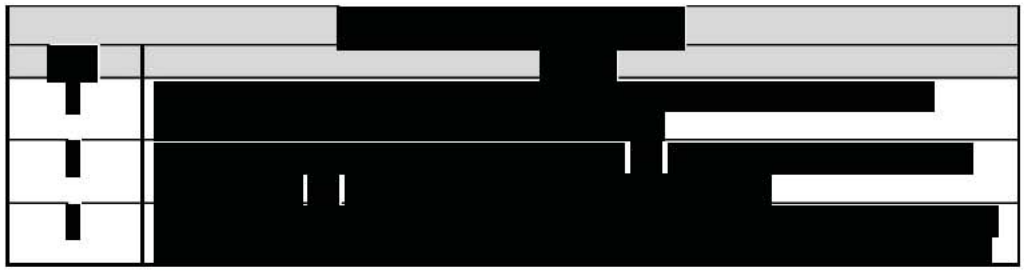

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Biomicroscopy Scale

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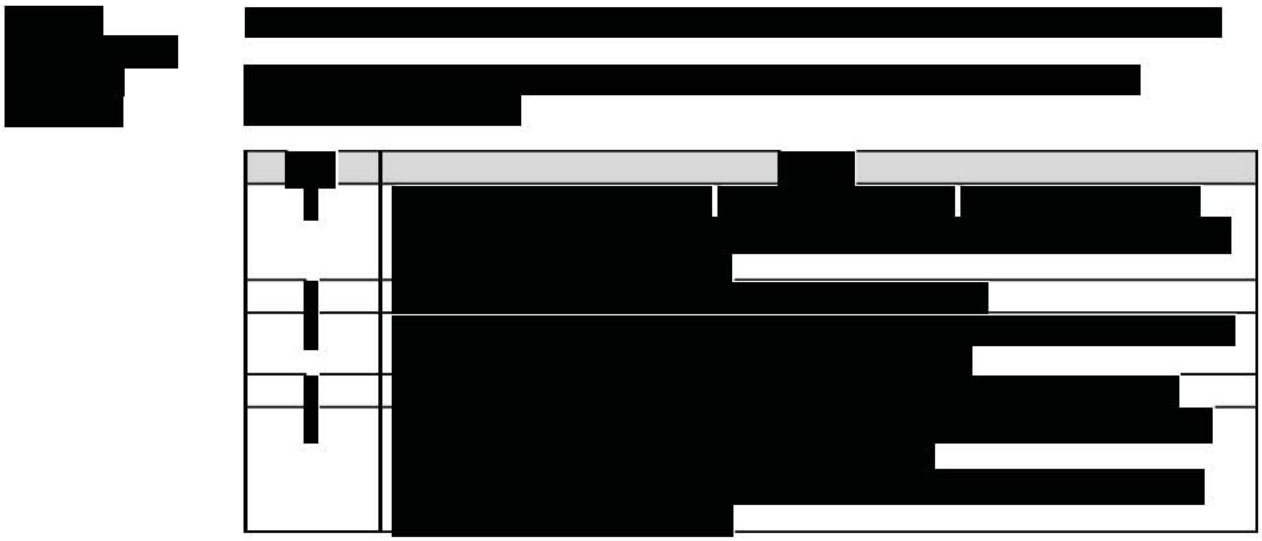

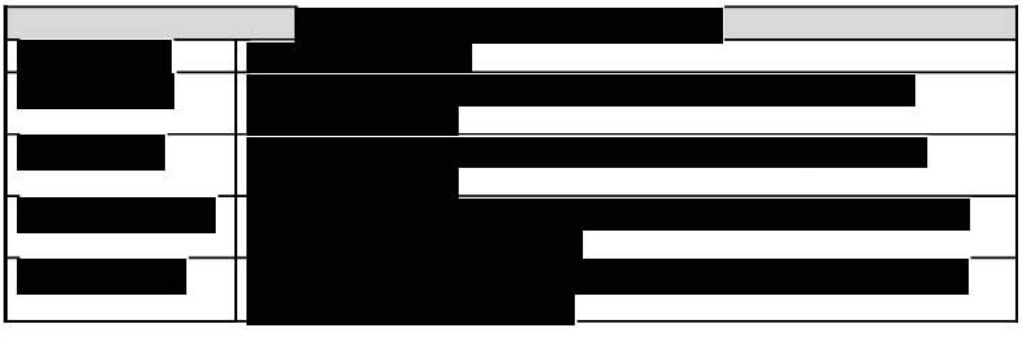

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Keratometry Procedure

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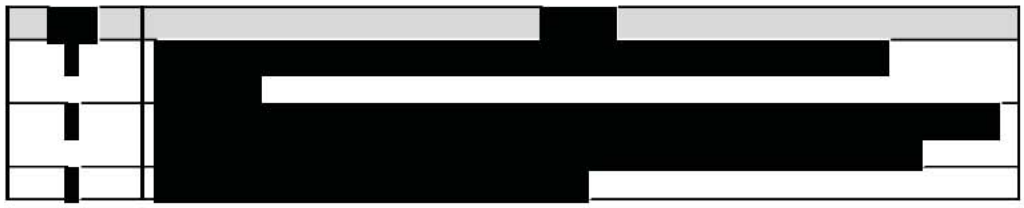

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[redacted] **DISTANCE AND NEAR VISUAL ACUITY EVALUATION**

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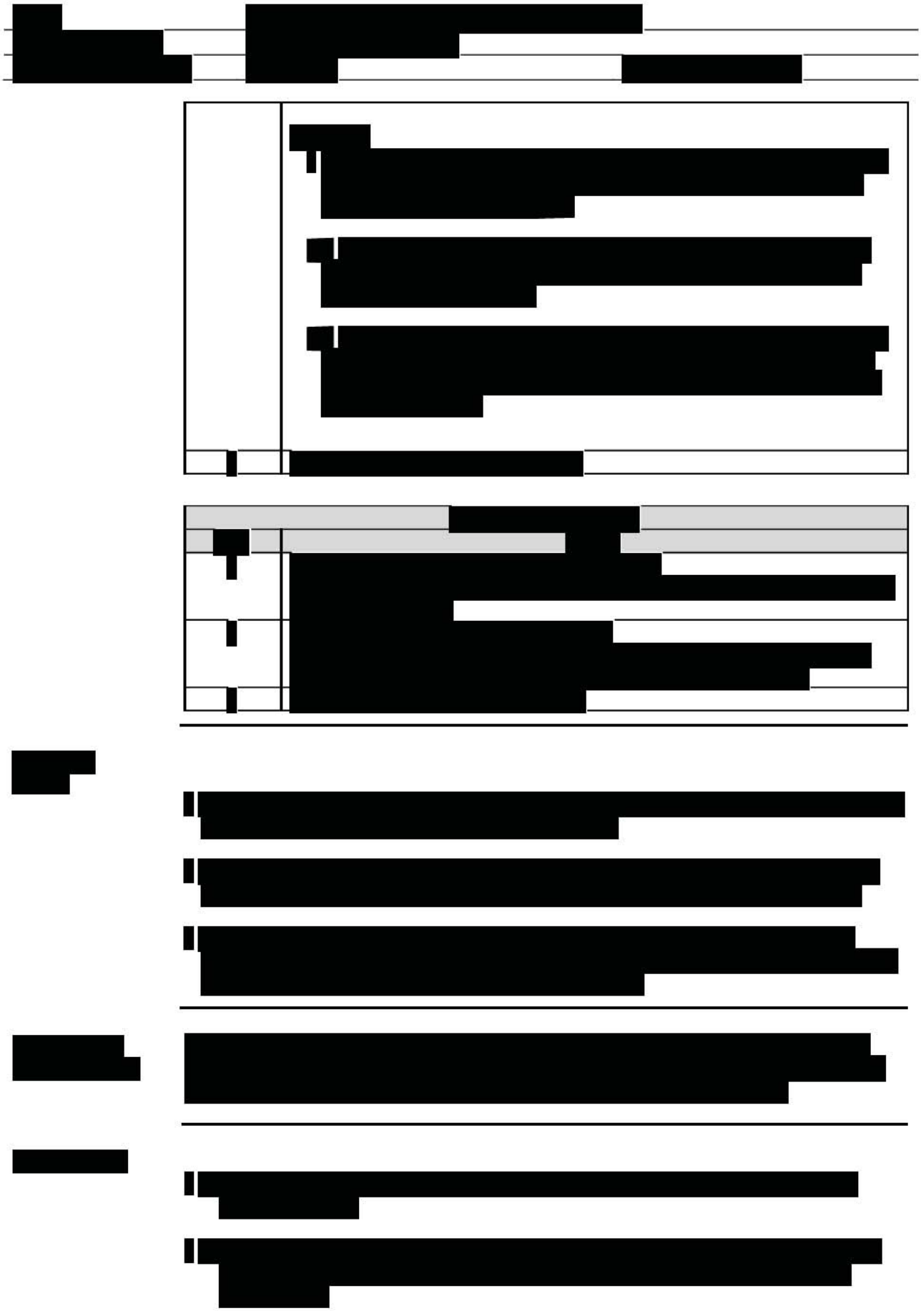

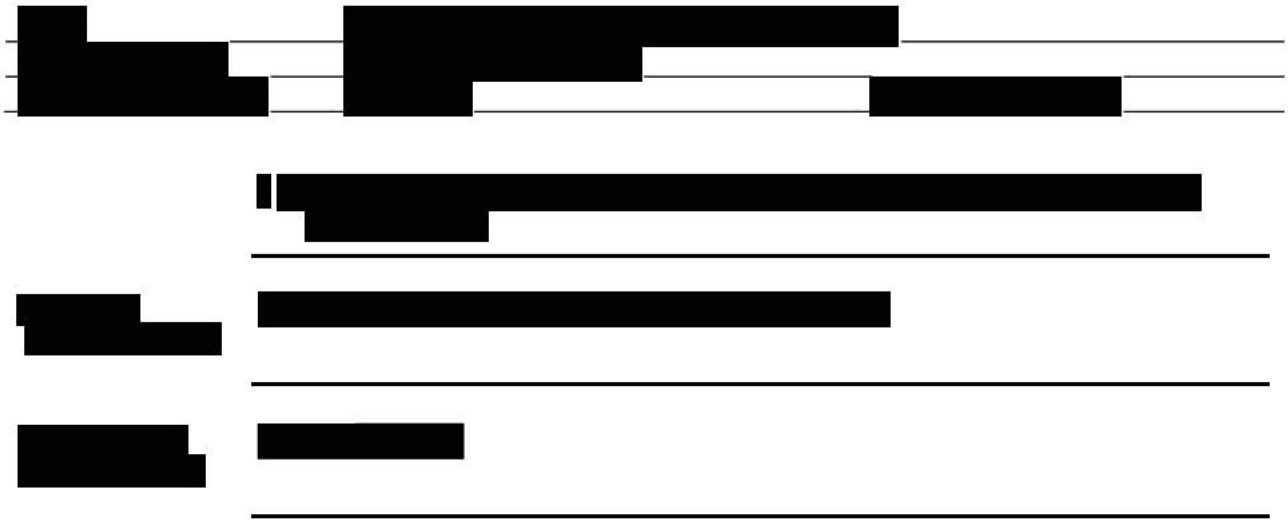

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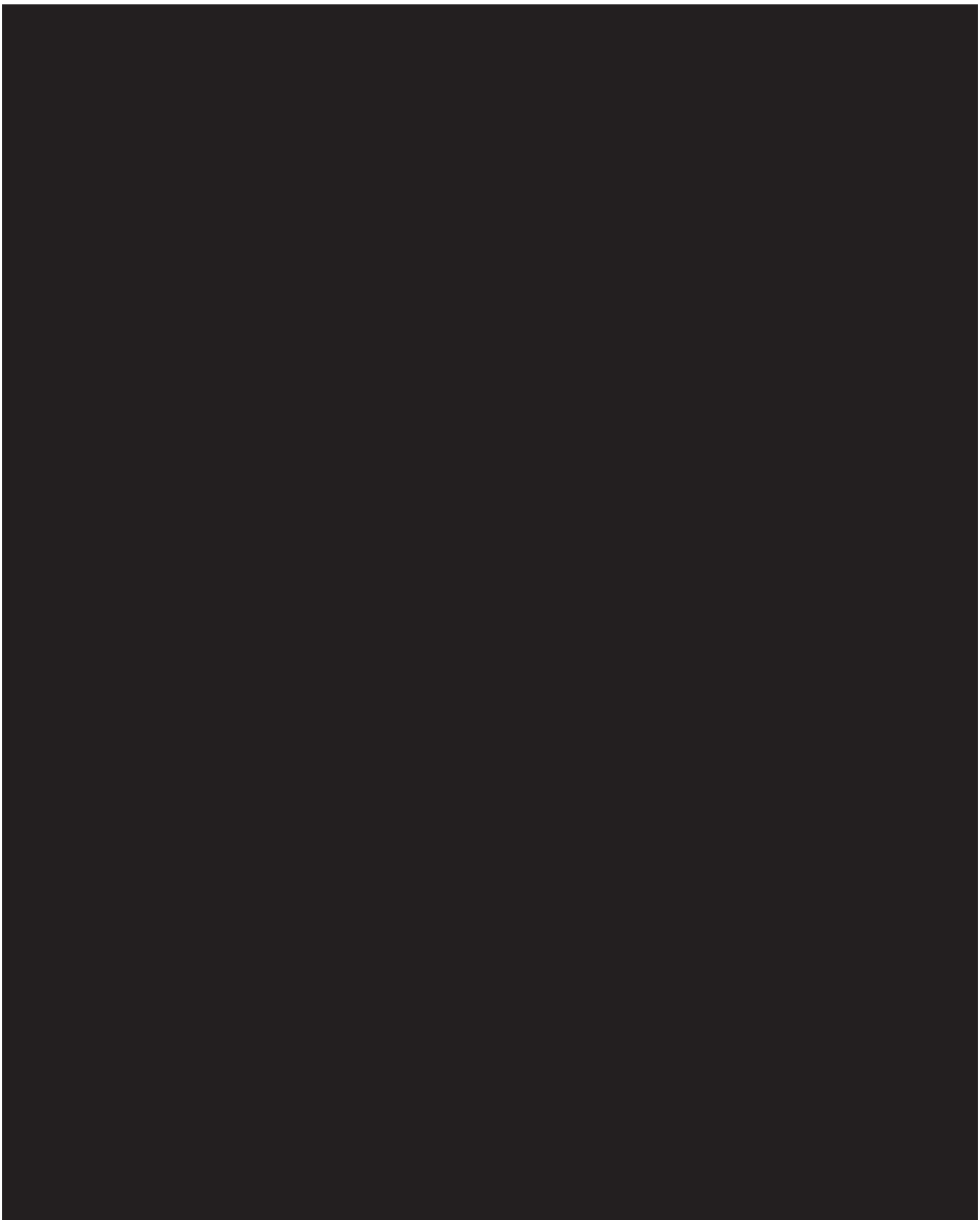

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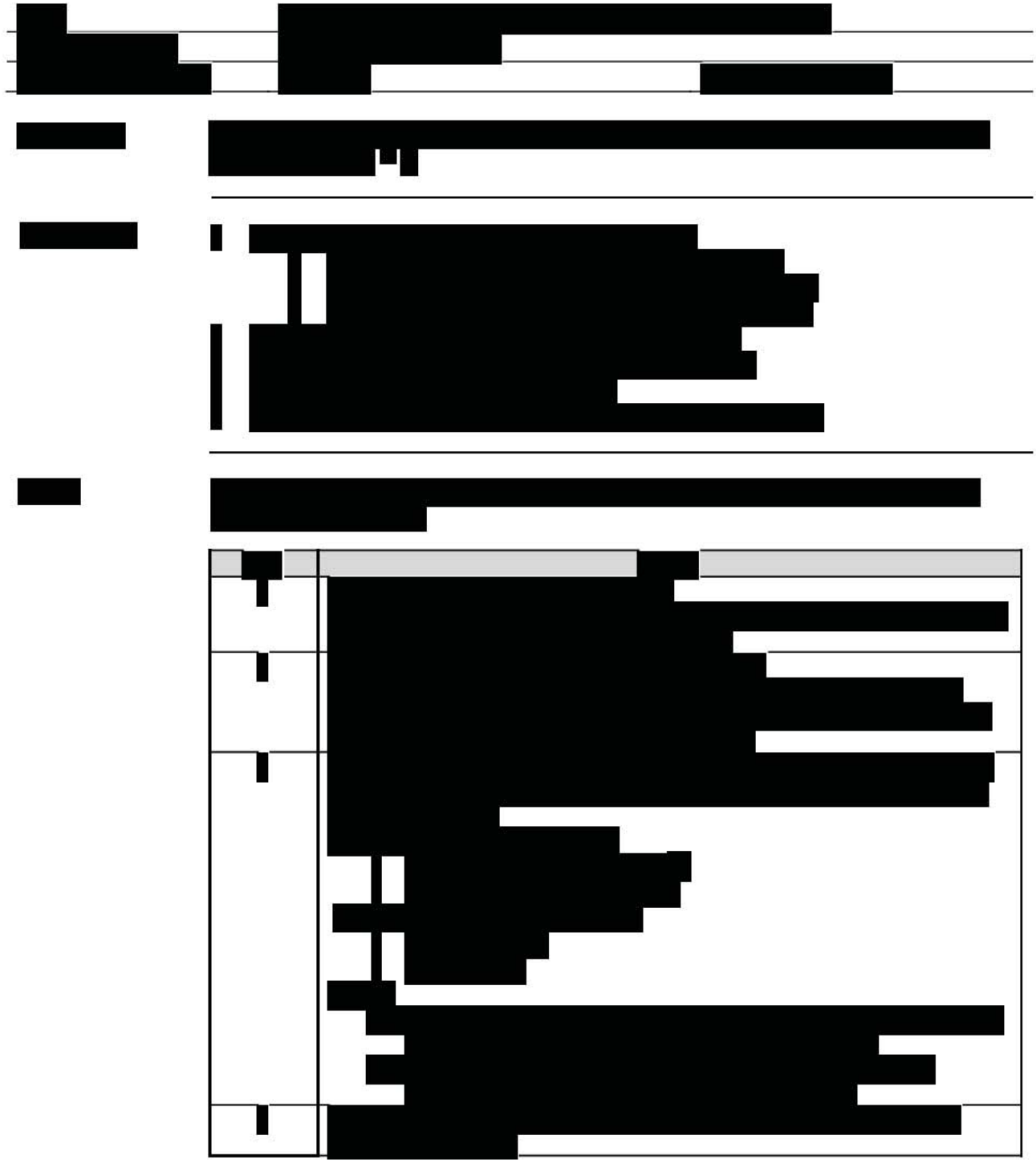

[redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

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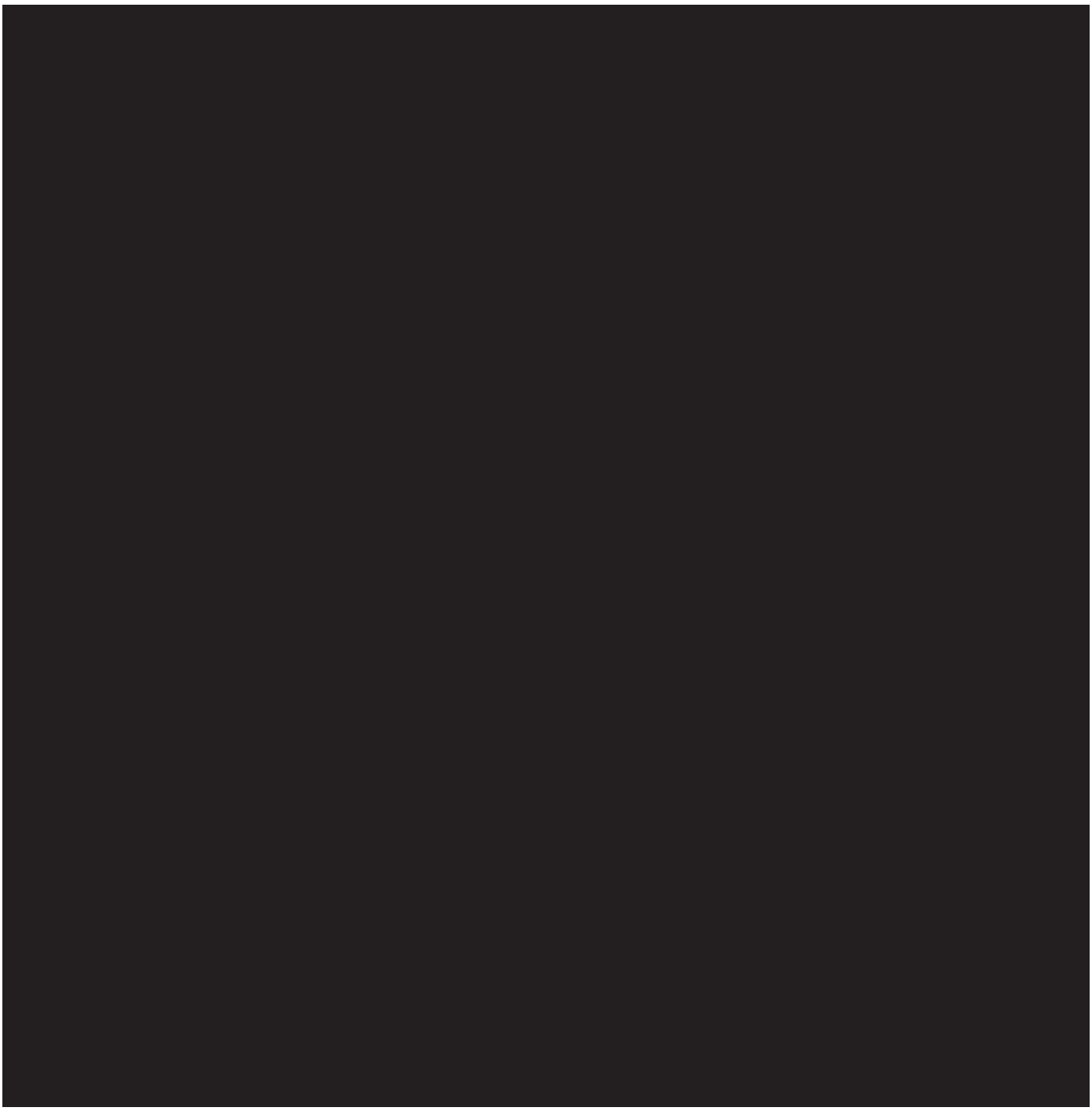

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

CR-6317 Clinical Evaluation of Manufacturing Curing Processes for a Reusable Multifocal Optical Design in a Presbyopic Population

Version and Date: 1.0 06 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),[4] 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

[redacted]