

STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official Title:

Feasibility Study of a Novel Automated Slit Lamp Camera (Lightfield Medical Ophthalmic Camera Model Vscan001)

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001

Sponsor: Lightfield Medical

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Study Product: Lightfield Medical Model Vscan001

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Study Protocol

1. Introduction

Background

The primary instrument used in eye examinations—the ophthalmic slit lamp—has not changed in over 75 years. The main improvement has been the transition from an incandescent light source to an LED light source. Ophthalmic devices for imaging the back of the eye have been in widespread use for over two decades. Ophthalmic devices to image the front of the eye such as a conventional slit lamp camera, on the other hand, are rarely used because they can only be done by a highly trained physician/optometrist or specialized ophthalmic photographer. Other problems make imaging the front of the eye with a conventional slit lamp camera difficult. Specifically, only a small portion of the exam can be recorded, focus is very difficult, lighting and aperture settings are challenging, and glare artifacts and resolution limits hinder their use.

Lightfield Medical has developed an automated slit lamp using high speed photography and high speed liquid lenses that can capture all of the typical views obtained in a slit lamp exam. The exam can be performed within minutes and uses an LED light source that is no brighter than a conventional slit lamp. High quality images have been obtained on the inventor's own eyes. The device is capable of capturing slit-illuminated eye images from multiple angles and lighting scenarios. Variables such as the optimal number of image views, image resolution, and viewing angles still need to be determined.

Investigational or Study Product

The Lightfield Medical Automated Slit Lamp Camera model Vscan001 is a semi-portable device that looks similar to an ophthalmic slit lamp or other ophthalmic imaging devices such as a the corneal

topographer or ocular coherence tomographer. It consists of a chin and head rest to stabilize the patient's head and a joy-stick mounted base with a similar design to a normal slit lamp. Instead of the usual slit-lamp eyepieces, a high speed 5 megapixel main camera sensor is positioned in front of the patient's eye. A liquid lens capable of focusing every 4 milliseconds is optically coupled to this sensor to control focus in the z-axis of the eye. A wide angle 5 megapixel auxiliary camera is positioned below this main camera to get wide angle views of the eye and to assist with focusing. An LED-based projector is used to move a slit image across the eye in the x-axis. This slit image is focused through a high speed liquid lens which is synced to the camera's liquid lens so a well-focused light slit on the cornea or lens can be imaged. The slit projector is mounted on a rotating base with a pivot point located below the patient's chin (which is, in turn, located directly below the patient's eye) much like a conventional slit lamp arm. A microprocessor controls the slit lamp movement across the eye and other parameters such as slit width and position relative to ocular structures. The operator moves the joystick to obtain initial focus. The operator also manually swings the slit projector arm in an arc to various positions (for instance 0, 22 and 45 degrees off center. (Future models will automate this step.) The unit is coupled to a Windows computer using USB connections. Images will be stored on an encrypted hard drive as both Raw and JPEG images.

The device meets all of the criteria of the FDA PJZ classification for a slit lamp camera and is considered FDA Class 2 exempt. It also meets FDA criteria for non-significant risk classification (see section 5)

Preclinical Data

Successful images have been taken of calibration grids and model eyes. Nomograms have been established to determine the microprocessor instructions to control the slit projector and the liquid lenses to focus both the slit image and the camera.

Clinical Data to Date

Clinical data has been obtained on the inventors' eyes in the development laboratory in the European Union. The images are sharp and mimic those that can be seen during a conventional slit lamp exam. See example data.

Risks/Benefits

The main risk is the light energy delivered to the eye. The LED-based light energy is similar or less than a conventional slit lamp examination. The energy output has been tested by Diestia Laboratories and meets group 1 radiant exposure limits for ultraviolet, visible, and infrared radiation under all light energy conditions, as defined in the ANSI Z80.36-2016 standard Light Hazard Protection for Ophthalmic Instruments. The FDA uses this ANSI standard to determine if a slit lamp camera is Class 2 exempt, and this device would qualify. There are no other source of energy introduced into the human body, and this device would qualify as a non-significant risk device, under FDA guidelines.

The only other risks envisioned would be possible minor soft tissue mechanical injury during the examination if the patient has trouble putting their chin on the chinrest or their forehead up to the forehead rest. Much like a conventional slit lamp, there is also a small chance that the illumination arm could bump into the patient's nose. These types of minor injuries would be expected to be quite rare and similar in frequency to those incurred during a conventional slit lamp exam.

The benefit of the device is that it would automate the slit lamp exam and allow it to be delegated to a technician. The eye exam can be automatically photo-documented for both the patient and the doctor. Ophthalmologists could review the exam on a computer screen in the room with the patient. Patients could see their pathology and would be better educated about their condition. Telemedicine would now be possible in ophthalmology. Underserved populations throughout the world could get eye care without the presence of an ophthalmologist or optometrist. The only requirements would be a minimally trained technician and a USB memory stick or internet connection.

Study Objectives

The study aims to determine the feasibility of performing an automated slit lamp exam in a clinical setting.

Study Design

General Design

Patients will be recruited to be subjects of this automated slit lamp camera feasibility study. Some of the subjects will have ocular pathology and others will not—the goal of the study is only to determine the feasibility of automated photo documentation in a wide range of patients. A goal of at least 50 patients will be studied, with an option to extend the study to 200 patients. Patients can be examined more than once, particularly if they have pathology that changes over time.

The study will take place in two phases: Optimization/Calibration and General Recruitment

The Optimization/Calibration phase will consist of lengthier examinations (lasting 5-20 minutes) as various settings (shutter speed, aperture, sensor gain, illumination angles and slit widths) are optimized before general recruitment starts. Subjects for this phase may be study personnel or clinic employees who volunteer to also be participants in the study. Study personnel or employees will be under no obligation to participate. Subjects in this category will have a special informed consent (see ICD). The ethical considerations of using study personnel or employees as study subjects have been considered, but their inclusion seems more ethical than making volunteer clinic patients sit through these tedious optimization exams. The medical risks of participating as study subjects are extremely low, and are about the same level of medical risk as a regular slit lamp eye examination. There may also be times when the study personnel will need to recalibrate the instrument and FDA regulations only allow use of the device on humans under IRB review. Allowing study personnel to quickly calibrate on each other will be much more advantageous than recruiting a separate patient subject for this purpose. It is estimated that 5-10 subjects will fall into this category.

The General Recruitment phase of the study will include a much larger number of patients who will be recruited through Northwest Eye Clinic and its associated clinic, Minnesota Eye Consultants who both operate under the umbrella of Unifeye Vision Partners. Some patients may be referred from other surrounding clinics. An email to patients of Northwest Eye Clinic will be sent out. (copy attached). A separate email will also be sent out to potential referring doctors who work in other eye care practices. (copy attached)

Primary/Secondary Study Endpoints

This is primarily a feasibility study. The primary endpoint will be the number of patients who can be successfully imaged compared to the number of patients who could not be successfully imaged. There are several photographic and illumination settings that can be adjusted on the device. The various combinations of shutter speed, aperture, sensor gain, and illumination will be used as exploratory endpoints to come up with the optimal settings for a follow-on study.

Subject Selection and Withdrawal

4.1 Inclusion Criteria

Patients over the age of 18 who have the mobility and ability to rest on the chin and forehead rests will be eligible to be studied. Patients will be allowed to have multiple examinations if they have changing pathologies. Most patients will only have one examination.

4.2 Exclusion Criteria

Patients younger than 18, patients physically unable to position at the device, patients with movement disorders and patients with significant photophobia will be excluded from the study.

4.3 Subject Recruitment and Screening

Patients will be recruited primarily out of the Northwest Eye clinic population. Patients with appropriate ocular pathology will be made aware of the study and offered to join the study. Some subjects may be referred in by doctors in other Minneapolis area clinics. No reimbursement will be provided to either subjects or referring providers. Recruitment will be done through an email to potential patients as well as a recruitment letter sent out to nearby doctors in other clinics.

4.4 Early Withdrawal of Subjects

Patients will be allowed to withdraw from the study at any time.

5. Investigational Product

5.1 Description

The Vscan001 device is a semiportable device that looks similar to an ophthalmic slit lamp and other ophthalmic imaging devices such as a corneal topographer or ocular coherence tomographer. It consists of a chin and head rest to stabilize the patient's head and then a joy-stick mounted base with a design similar to a normal slit lamp. Instead of the usual slit-lamp optics, a high speed 5 megapixel main camera sensor is positioned in front of the patient's eye. A liquid lens capable of focusing every 4 milliseconds is optically coupled to this sensor to control focus in the z-axis of the eye. A wide angle 5 megapixel auxiliary camera is positioned below this main camera to get wide angle views of the eye and to assist with focusing. A projector is used to move a slit image across the eye in the x-axis. This is coupled to a high speed liquid lens that is synced to the camera's liquid lens so that slit image can be focused on various eye structures and the image of the slit itself will be in focus on the main camera's sensor. The slit projector is mounted on a rotating base, much like a conventional slit lamp arm. A microprocessor controls the slit lamp movement across the eye, and it also controls other parameters such as slit width and position relative to ocular structures. The operator will need to move the joystick

to obtain initial focus. The operator will also need to manually swing the slit projector arm to various positions. (Future models will automate the rotation of the slit projector arm.) The unit will be coupled to a laptop computer using USB and HDMI connections. During image acquisition, the projected light slit will move across the the eye and the cameras will take a series of images at different depths. Wide angle views will also be obtained in various gaze directions. A library of images will be obtained for each patients. Images will be stored on an encrypted hard drive as both Raw and JPEG images.

The device is considered non-significant risk per the FDA guidelines outlined in 21 CFR 812.3(m):

What is a Significant Risk Device Study?

Under 21 CFR 812.3(m), an SR device means an investigational device that:

Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject—NO

Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject—NO

Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject—NO

or,

Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject—NO

B. What is a Nonsignificant Risk Device Study?

An NSR device study is one that does not meet the definition for an SR device study—SATISFIED

The device also qualifies as a Class 2 exempt device. The FDA has a PJZ classification for slit lamp cameras that establishes whether a device qualifies as 510(k) exempt and this device meets all of the established criteria:

FDA Title 21, Chapter 1, Subchapter H, Section 886.1120

(a) Identification. An ophthalmic camera is an AC-powered device intended to take photographs of the eye and the surrounding area.—SATISFIED

(b) Classification. Class II (special controls). The device, when it is a photorefractor or a general-use ophthalmic camera, is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to the limitations in § 886.9.

PJZ cameras are prescription devices indicated only for the capture and storage of images of the eye and surrounding area in the general population. PJZ cameras cannot be indicated for any specific population (e.g., pediatrics, AMD patients, etc.), cannot contain any type of “diagnostic” or “aid in diagnosis” claims in the indication for use, and cannot reference any specific disease. PJZ cameras do not exceed group 1 radiant exposure limits for ultraviolet, visible, and infrared radiation under all light energy conditions, as defined in the ANSI Z80.36-2016 standard Light Hazard Protection for Ophthalmic Instruments.—SATISFIED, SEE ANSI CERTIFICATION

PJZ cameras are designed for true color or monochrome imaging in visible spectrum of light and consists of an incoherent light source, image forming lens, aperture, and a sensitive photodetector array (e.g., a CCD array) in the image plane. PJZ excludes cameras that make use of advanced imaging technology (e.g., confocal imaging, adaptive optics, two photon imaging, stroboscopic or scanning illumination). PJZ excludes cameras that feature any special imaging modalities, such as multispectral imaging, fluorescence, autofluorescence, fluorescein angiography, indocyanine green (ICG) angiography, etc. PJZ exclude cameras that designed to contact cornea or any other ocular structure for imaging.—ALL COMPONENTS SATISFIED

The device meets all of the criteria of the FDA PJZ classification for a slit lamp camera and is considered FDA Class 2 exempt.

The study will also comply with the labeling and record-keeping regulations in FDA Title 21, Chapter 1, Subchapter H, Section 812.2(b):

An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:

- (i) Labels the device in accordance with § 812.5;
- (ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
- (iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by an IRB under § 56.109(c).
- (iv) Complies with the requirements of § 812.46 with respect to monitoring investigations;
- (v) Maintains the records required under § 812.140(b) (4) and (5) and makes the reports required under § 812.150(b) (1) through (3) and (5) through (10);
- (vi) Ensures that participating investigators maintain the records required by § 812.140(a)(3)(i) and make the reports required under § 812.150(a) (1), (2), (5), and (7); and
- (vii) Complies with the prohibitions in § 812.7 against promotion and other practices.

5.2 Treatment Regimen

Not applicable as no treatment is administered.

5.3 Method for Assigning Subjects to Treatment Groups

Not applicable as no treatment is administered.

5.4 Subject Compliance Monitoring

Subjects will be monitored to see if they can complete the examination.

5.5 Prior and Concomitant Therapy

Not applicable as there is no therapeutic component to this study.

5.6 Packaging, Receiving, Storage, Dispensing and Return

Not applicable except as it regards to the delivery and receiving of the device which is documented in the device log.

6. Study Procedures

Patients will be recruited to the study as outlined above. Informed consent will be obtained by explaining the risks and benefits of the study and using the attached informed consent document. Any research staff with a financial conflict of interest (specifically John S. Berestka and Matthew Berestka) will not be involved in obtaining informed consent. Subjects will be screened for the study by using the inclusion criteria and exclusion criteria.

Subjects who meet the screening criteria, who volunteer to participate, and sign the informed consent document will be brought to a dedicated room and seated at the instrument. They will be positioned much like they would be for a normal ophthalmic slit lamp exam. The device operator will obtain focus by moving the joystick until the eye is centered and the two focusing lines are in sync. The device will be activated and the automated exam will begin. The device operator will move the illumination arm through five preset positions to capture images from different angles. Subjects will be allowed to abort the exam just by sitting back and pulling their head back from the device. Images will be captured to an encrypted hard drive. No treatment effect will be derived from the device, as it is merely taking photographs.

Patients will typically only have one examination and that will be the extent of their study involvement. A small number of patients with changing pathology may come back for additional examinations.

Subjects will be evaluated by whether or not they were able to be examined using the Vscan001 medical device.

An exploratory endpoint will be the quality of the photographic images. Various combinations of aperture, shutter speed, sensor gain, slit characteristics and view angles will be subjectively evaluated by the study team, but these endpoints will not be evaluated statistically. These exploratory endpoints will be used to design future studies with the best photographic quality.

No diagnostic or medical decisions will be made or attempted with this technology as it is merely a photo-documentary technology.

7. Statistical Plan

7.1 Sample Size Determination

This study's endpoint will be a simple count of subjects able to be examined and those unable to be examined. The comparison of these to numbers will be expressed as simple percentage of those subjects able to be examined compared to the total number of subjects in the General Recruitment (non-calibration) phase. The sample size is an arbitrary choice as no statistical analysis will be performed. We will enroll between 50 and 200 patients.

7.2 Statistical Methods

A simple proportion of subjects who could complete the imaging process compared to all enrolled subjects will be computed and expressed as a percentage.

7.3 Subject Population(s) for Analysis

The study population will English-speaking adults over 18 who have at least one eye and meet the inclusionary and exclusionary criteria. The subjects will demographically correlate with the demographic criteria of the Northwest Eye patient base which is largely white, elderly and suburban, but still somewhat ethnically and racially diverse.

8. Safety and Adverse Events

8.1 Definitions

Patients will be monitored for any physical or optical injury to the eye or body.

8.2 Assessment of Safety and Efficacy

Any patient who has sustains an injury by either physical signs or symptoms will be evaluated by an ophthalmologist or primary care physician who is not part of the study. The ophthalmologist or primary care physician's report will be communicated to the principal investigator as soon as it is completed so a determination of adverse event can be made.

8.3 Recording and Reporting of Adverse Events

Adverse events will be communicated to the IRB within 72 hours. Severe adverse events will be communicated to the IRB within 24 hours.

The study will comply with FDA Title 21, Chapter 1, Subchapter H, Section 812.46:

(a) Securing compliance. A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the requirements of this part or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. A sponsor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

(b) Unanticipated adverse device effects. (1) A sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect.

(2) A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects shall terminate all investigations or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than 5 working days—Lightfield Medical is the sponsor and will comply with these regulations.

See additional procedures for handling adverse events in section 10 or this protocol

8.4 Unblinding Procedures

No randomization will be used.

8.5 Stopping Rules

The study will be stopped if less than 50% of patients are able to be imaged adequately.

8.6 Medical Monitoring

Injury is not expected, but the imaging will take place in a busy ophthalmic practice where there is always an ophthalmologist or optometrist present during open hours. Referral for non-ophthalmic injuries outside of the scope of an eye care provider will be made to a primary care physician.

9. Data Handling and Record Keeping

9.1 Confidentiality

Data will be kept in a locked cabinet in a locked room and on an encrypted hard drive in a password-protected desktop computer.

9.2 Source Documents

The source documents will be electronic raw and jpeg images stored on an encrypted hard drive. The encrypted hard drive will be backed up to an online service.

9.3 Records Retention

All records will be retained until study completion and for an additional 2 years.

10. Study Monitoring, Auditing, and Inspecting

The study will be monitored by the principal investigator, the sponsor and IRB. All study staff will successfully obtain a GCP certification for device studies. Logs of training and staff status will be kept for audits.

The study will comply with FDA Title 21, Chapter 1, Subchapter H, Section 812.140

(a) Investigator records. A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

(1) All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.

(2) Records of receipt, use or disposition of a device that relate to:

(i) The type and quantity of the device, the dates of its receipt, and the batch number or code mark.

(ii) The names of all persons who received, used, or disposed of each device.

(iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

(3) Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

(i) Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

(ii) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

(iii) A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

(4) The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

(5) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

(b) Sponsor records. A sponsor shall maintain the following accurate, complete, and current records relating to an investigation:

(1) All correspondence with another sponsor, a monitor, an investigator, an IRB, or FDA, including required reports.

All of the components above will be recorded and logged.

(2) Records of shipment and disposition. Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.

(3) Signed investigator agreements including the financial disclosure information required to be collected under § 812.43(c)(5) in accordance with part 54 of this chapter.

(4) For each investigation subject to § 812.2(b)(1) of a device other than a significant risk device, the records described in paragraph (b)(5) of this section and the following records, consolidated in one location and available for FDA inspection and copying:

(i) The name and intended use of the device and the objectives of the investigation;

(ii) A brief explanation of why the device is not a significant risk device:

(iii) The name and address of each investigator:

(iv) The name and address of each IRB that has reviewed the investigation:

(v) A statement of the extent to which the good manufacturing practice regulation in part 820 will be followed in manufacturing the device; and

(vi) Any other information required by FDA.

(5) Records concerning adverse device effects (whether anticipated or unanticipated) and complaints and

(6) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

(c) IRB records. An IRB shall maintain records in accordance with part 56 of this chapter.

(d) Retention period. An investigator or sponsor shall maintain the records required by this subpart during the investigation and for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application, a notice of completion of a product development protocol, a humanitarian device exemption application, a premarket notification submission, or a request for De Novo classification.

(e) Records custody. An investigator or sponsor may withdraw from the responsibility to maintain records for the period required in paragraph (d) of this section and transfer custody of the records to any other person who will accept responsibility for them under this part, including the requirements of § 812.145. Notice of a transfer shall be given to FDA not later than 10 working days after transfer occurs.

All of the components above will be recorded and logged.

The study will also prepare reports as applicable and in compliance with FDA Title 21, Chapter 1, Subchapter H, Section 812.150:

(a) Investigator reports. An investigator shall prepare and submit the following complete, accurate, and timely reports:

(1) Unanticipated adverse device effects. An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

(2) Withdrawal of IRB approval. An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

(3) Progress. An investigator shall submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.

(4) Deviations from the investigational plan. An investigator shall notify the sponsor and the reviewing IRB (see § 56.108(a) (3) and (4)) of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB in accordance with § 812.35(a) also is required.

(5) Informed consent. If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

(6) Final report. An investigator shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.

(7) Other. An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

(b) Sponsor reports. A sponsor shall prepare and submit the following complete, accurate, and timely reports:

- (1) Unanticipated adverse device effects. A sponsor who conducts an evaluation of an unanticipated adverse device effect under § 812.46(b) shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.
- (2) Withdrawal of IRB approval. A sponsor shall notify FDA and all reviewing IRB's and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.
- (3) Withdrawal of FDA approval. A sponsor shall notify all reviewing IRB's and participating investigators of any withdrawal of FDA approval of the investigation, and shall do so within 5 working days after receipt of notice of the withdrawal of approval.
- (4) Current investigator list. A sponsor shall submit to FDA, at 6-month intervals, a current list of the names and addresses of all investigators participating in the investigation. The sponsor shall submit the first such list 6 months after FDA approval.
- (5) Progress reports. At regular intervals, and at least yearly, a sponsor shall submit progress reports to all reviewing IRB's. In the case of a significant risk device, a sponsor shall also submit progress reports to FDA. A sponsor of a treatment IDE shall submit semi-annual progress reports to all reviewing IRB's and FDA in accordance with § 812.36(f) and annual reports in accordance with this section.
- (6) Recall and device disposition. A sponsor shall notify FDA and all reviewing IRB's of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.
- (7) Final report. In the case of a significant risk device, the sponsor shall notify FDA within 30 working days of the completion or termination of the investigation and shall submit a final report to FDA and all reviewing the IRB's and participating investigators within 6 months after completion or termination. In the case of a device that is not a significant risk device, the sponsor shall submit a final report to all reviewing IRB's within 6 months after termination or completion.
- (8) Informed consent. A sponsor shall submit to FDA a copy of any report by an investigator under paragraph (a)(5) of this section of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.
- (9) Significant risk device determinations. If an IRB determines that a device is a significant risk device, and the sponsor had proposed that the IRB consider the device not to be a significant risk device, the sponsor shall submit to FDA a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.
- (10) Other. A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

All of the reports above will be provided as indicated.

11. Ethical Considerations

The study is voluntary and prospective patients will be informed that participation in the study will not in any way affect their access to care from Northwest Eye or Minnesota Eye Consultants. The optimization/calibration phase of the study will be performed on study personnel and clinic employees. There would be ethical concerns if study personnel or employees might feel coerced into having some sort of treatment or be exposed to significant risk. In this study, this group of subjects will be voluntarily participating, will sign a special consent, will need be receiving any treatment whatsoever, and will incur no more risk than a conventional slit lamp examination. Consideration of recruiting patients to serve as volunteers in this phase of the study was given, but this did not seem ethical as these calibrations can be lengthy, somewhat tedious and physically fatiguing, especially for the predominately elderly clinic population that subjects will be recruited from.

The sponsor, the principal investigator, and the technical officer/device trainer all have a financial interest in the company that manufactures the device.

To minimize any conflict of interest, the principal investigator, John S. Berestka, MD and the technical officer/device trainer, Matthew L. Berestka, will be not allowed to be involved in the informed consent process. Other staff members (all of whom have no financial or other conflict of interest) will perform the informed consent process.

The study will comply with FDA Title 21, Chapter 1, Subchapter H, Section 812.43:

(a) Selecting investigators. A sponsor shall select investigators qualified by training and experience to investigate the device.

(b) Control of device. A sponsor shall ship investigational devices only to qualified investigators participating in the investigation.

(c) Obtaining agreements. A sponsor shall obtain from each participating investigator a signed agreement that includes:

(1) The investigator's curriculum vitae.

(2) Where applicable, a statement of the investigator's relevant experience, including the dates, location, extent, and type of experience.

(3) If the investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination.

(4) A statement of the investigator's commitment to:

(i) Conduct the investigation in accordance with the agreement, the investigational plan, this part and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA;

(ii) Supervise all testing of the device involving human subjects; and

(iii) Ensure that the requirements for obtaining informed consent are met.

(5) Sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement as required under part 54 of this chapter. The sponsor shall obtain a commitment from the clinical investigator to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study. This information shall not be submitted in an investigational device exemption application, but shall be submitted in any marketing application involving the device.

(d) Selecting monitors. A sponsor shall select monitors qualified by training and experience to monitor the investigational study in accordance with this part and other applicable FDA regulations.

All of the components above will be provided.

STUDY SUMMARY