PennState

HRP-591 - Protocol for
Human Subject Research

Protocol Title:

Provide the full title of the study as listed in item 1 on the "Basic Information" page in CATS IRB (http://irb.psu.edu).

A SINGLE-CENTER, DOUBLE-ARM, PROSPECTIVE CLINICAL TRIAL TO COMPARE VISUAL PERFORMANCE OF NON-DIFFRACTIVE EXTENDED DEPTH OF FOCUS AND NEUTRAL ASPHERIC MONOFOCAL INTRAOCULAR LENSES

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Version Date: 7/16/2021

Provide the date of this submission. This date must be updated each time the submission is provided to the IRB office with revisions. DO NOT revise the version date in the footer of this document.

Clinicaltrials.gov Registration #: NCT04591054

Provide the registration number for this study, if applicable. See "HRP-103- Investigator Manual, When do I have to register my project at ClinicalTrials.gov?" for more information.

Pending

Important Instructions for Using This Protocol Template:

This template is provided to help investigators prepare a protocol that includes the necessary information needed by the IRB to determine whether a study meets all applicable criteria for approval.

1. **GENERAL INSTRUCTIONS:**
   - Prior to completing this protocol, ensure that you are using the most recent version by verifying the protocol template version date in the footer of this document with the current version provided in the CATS IRB Library.
   - Do not change the protocol template version date located in the footer of this document.
   - Some of the items may not be applicable to all types of research. If an item is not applicable, please indicate as such or skip question(s) if indicated in any of the instructional text.
   - **GRAY INSTRUCTIONAL BOXES:**
     - Type your protocol responses below the gray instructional boxes of guidance language. If the section or item is not applicable, indicate not applicable.
     - **Penn State College of Medicine/Penn State Health researchers**: Delete the instructional boxes from the final version of the protocol prior to upload to CATS IRB (http://irb.psu.edu)**.**
     - **Penn State researchers at all other campuses**: Do NOT delete the instructional boxes from the final version of the protocol.
   - Add the completed protocol template to your study in CATS IRB (http://irb.psu.edu) on the "Basic Information" page.
2. **CATS IRB LIBRARY:**
   - Documents referenced in this protocol template (e.g. SOP's, Worksheets, Checklists, and Templates) can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

3. **PROTOCOL REVISIONS:**
   - When making revisions to this protocol as requested by the IRB, please follow the instructions outlined in the Study Submission Guide available in the Help Center in CATS IRB (http://irb.psu.edu) for using track changes.
   - Update the Version Date on page 1 each time revisions are made.

If you need help…	
University Park and other campuses: Office for Research Protections Human Research Protection Program The 330 Building, Suite 205 University Park, PA 16802-7014 Phone: 814-865-1775 Fax: 814-863-8699 Email: irb-orp@psu.edu	**College of Medicine and Penn State Health:** Human Subjects Protection Office 90 Hope Drive, Mail Code A115, P.O. Box 855 Hershey, PA 17033 (Physical Office Location: Academic Support Building Room 1140) Phone: 717-531-5687 Email: irb-hspo@psu.edu

Table of Contents

1.0 Objectives

1.1 Study Objectives

Describe the purpose, specific aims or objectives. State the hypotheses to be tested.

The purpose of this study is to compare the binocular distance, intermediate, and near visual acuity and patient reported outcomes of the Alcon Vivity and Bausch & Lomb enVista IOLs.

We hypothesize that the Alcon Vivity and Bausch & Lomb enVista IOLs will have similar distance, intermediate, and near visual acuity.

(If the null hypothesis is rejected, then the visual performance of the IOLs may be different).

1.2 Primary Study Endpoints

State the primary endpoints to be measured in the study.

Clinical trials typically have a primary objective or endpoint. Additional objectives and endpoints are secondary. The endpoints (or outcomes), determined for each study subject, are the quantitative measurements required by the objectives. Measuring the selected endpoints is the goal of a trial (examples: response rate and survival).

Primary endpoints will include:

Mean logMAR best-distance corrected visual acuity at intermediate (66 cm) tested in binocular photopic conditions at 3 months.

1.3 Secondary Study Endpoints

State the secondary endpoints to be measured in the study.

Secondary endpoints will include:

- Visual acuity:
  - Mean logMAR uncorrected visual acuity at distance (4 m), intermediate (66 cm), and near (40 cm), tested in monocular and binocular photopic conditions
  - Mean logMAR best-distance corrected visual acuity at distance (4 m) and near (40 cm), testing in monocular and binocular photopic conditions.
  - Proportion of subjects with a binocular distance corrected near visual acuity (DCNVA) of 20/40 (logMAR = 0.3) or better, at 3 months
  - Defocus curve, tested in binocular photopic conditions (4 m)

- Refractive outcomes of comparator products
  - Mean prediction error (MPE)
  - Absolute prediction error (APE)
  - Proportion of subjects within 0.5 and 1.0 D of predicted

2.0 Background

2.1 Scientific Background and Gaps

Describe the scientific background and gaps in current knowledge.

For clinical research studies being conducted at Penn State Health/Penn State College of Medicine, and for other non-PSH locations as applicable, describe the treatment/procedure that is considered standard of care (i.e., indicate how patients would be treated in non-investigational setting); and if applicable, indicate if the study procedure is available to patient without taking part in the study.

Presbyopia correcting intraocular lens (PC-IOL) technology has been available for decades. Lens designs have included refractive (e.g. AMO ReZoom), apodized diffractive (e.g. Alcon Acrysof ReSTOR/PanOptix), accommodating (B&L Crystalens), and extended depth-of-focus (e.g. J&J Symfony) technology. Spectacle independence is significantly higher with PC-IOLs when compared with that of monofocal IOLs.[1,2] Despite their clear benefits, PC-IOLs are not without drawbacks. Any IOL that splits light to deliver distinct distance and near foci creates the potential for photic phenomenon, which patients may perceive as glare, haloes, and starbursts.[3,4]

Pseudoaccommodation is defined as an increased depth-of-focus in an emmetropic eye that does not have the ability to change its refractive power. Spherical aberration, which may come from the cornea or IOL, plays an important role in pseudoaccommodation.[5,6] There is a small body of literature that IOLs (e.g. Mini WELL, SIFI, Catalina, Italy) with highly-positive spherical aberration can result in significant pseudoaccommodation and lower unwanted optical phenomena than current multifocal IOLs.[7]

The Alcon Vivity PC-IOL is a hydrophobic acrylic, non-diffractive, extended depth of focus IOL designed for implantation in the capsular bag following cataract extraction. The single-piece IOL has a 6.0 mm diameter and has a hyper-prolate profile that extends the depth of focus to deliver a broader range of sharp vision, with the glare and halo profile approaching that of a monofocal IOL.[8]

The Bausch & Lomb enVista MX60E is a posterior chamber hydrophobic acrylic IOL. The single-piece IOL has a 6.0 mm diameter and has a neural aspheric optical profile. This neutral aspheric profile, combined with the cornea's natural positive spherical aberration, may extend the depth of focus relative to other negative aspheric hydrophobic acrylic monofocal IOLs on the market.

To date, there is no existing literature comparing the visual performance of the two above mentioned lens technologies; namely, one that relies on a non-diffractive, hyper-prolate profile and another that relies on the cornea's natural positive spherical aberration to provide pseudoaccommodation.

2.2 Previous Data

Describe any relevant preliminary data.

The FDA Summary of Safety and Effectiveness on the Alcon Vivity IOL compares visual and patient reported outcomes of the Alcon Vivity IOL and the Alcon Acrysof SN60WF. While the Alcon Acrysof SN60WF and Bausch & Lomb enVista lenses are not identical, they are considered similar. The document reported improved intermediate vision with the Alcon Vivity over the SN60WF, and rates of reported visual disturbances were similar between the two devices.

2.3 Study Rationale

Provide the scientific rationale for the research.

Whereas the Alcon Acrysof SN60WF has a negative aspheric optical profile, the Bausch & Lomb enVista has a neutral aspheric optical profile. Theoretically, the Bausch & Lomb enVista IOL may provide increased intermediate vision compared with the SN60WF.

3.0 Inclusion and Exclusion Criteria

Create a numbered list below in sections 3.1 and 3.2 of criteria subjects must meet to be eligible for study enrollment (e.g., age, gender, diagnosis, etc.).

Vulnerable Populations:

Indicate specifically whether you will include any of the following vulnerable populations in this research. You MAY NOT include members of these populations as subjects in your research unless you indicate this in your inclusion criteria because specific regulations apply to studies that involve vulnerable populations.

The checklists referenced below outline the determinations to be made by the IRB when reviewing research involving these populations. Review the checklists as these will help to inform your responses throughout the remainder of the protocol.

- **Children –**Review "HRP-416- Checklist - Children"
- **Pregnant Women –** Review "HRP-412- Checklist - Pregnant Women"
- **Cognitively Impaired Adults-** Review "HRP-417- Checklist - Cognitively Impaired Adults"
- **Prisoners-** Review "HRP-415- Checklist - Prisoners"
- **Neonates of uncertain viability or non-viable neonates-** Review "HRP-413- Checklist - Non-Viable Neonates" or "HRP-414- Checklist - Neonates of Uncertain Viability"

[Do not type here]

3.1 Inclusion Criteria

Create a numbered list of the inclusion criteria that define who will be included in your final study sample (e.g., age, gender, condition, etc.)

Each of the following criteria must be met for study participation:

1. Male or female, age 18 or older at the time of study enrollment.
2. Visually significant cataract in the study eyes for which phacoemulsification cataract extraction and posterior chamber IOL implantation is indicated.
3. Anticipated to undergo bilateral sequential cataract surgery
4. Projected postoperative CDVA 0.20 logMAR (Snellen 20/32) or better in the study eyes, as determined by an Investigator's medical judgement.
5. Calculated spherical power targeted at emmetropia at distance in the study eyes.
6. Calculated IOL power between +10.0 - +30.0 D, inclusive, in both eyes.
7. Measured against-the-rule astigmatism less than 0.6 D or with-the-rule/oblique astigmatism less than 1.25 D.
8. If wearing rigid gas permeable (RGP) contact lens in the study eye, willingness to discontinue lens wear for ≥ 21 days prior to preoperative biometry.
9. Availability, willingness, and sufficient cognitive awareness to return for study-required visits and comply with examination procedures.
10. Willingness to sign the IRB-approved informed consent form (ICF) for study participation.

3.2 Exclusion Criteria

Create a numbered list of the exclusion criteria that define who will be excluded in your study.

Patient candidates presenting any of the following characteristics will not be eligible for study participation:

1. Mature cataract in the study eye that is likely to prolong surgical procedure and/or lead to intraoperative complications prior to attempted IOL implantation.
2. Any visually significant intraocular media opacity other than cataract in the study eye (as determined by the investigator). Such opacities might include corneal scar or vitreous hemorrhage.
3. Abnormal corneal findings in the study eye (e.g. keratoconus, pellucid marginal degeneration, irregular astigmatism).
4. Any anterior segment pathology in the study eye that could significantly affect outcomes (e.g. chronic uveitis, iritis, aniridia, clinically significant corneal dystrophies, poor pupil dilation, etc.)
5. Any condition in the study eye that could affect IOL stability (e.g. pseudoexfoliation, zonular dialysis, evident zonular weakness or dehiscence, etc.).
6. History of severe dry eye in the study eye that, in the judgement of the investigator, would impair the ability to obtain reliable study measurements.
7. History of serious corneal disease (e.g. herpes simplex, herpes zoster keratitis, etc.) in the study eye.
8. History of any clinically significant retinal pathology or ocular diagnosis in the study eye that could, in the investigator's best judgement, alter or limit final post-operative visual prognosis (e.g. diabetic retinopathy, ischemic disease, macular degeneration, retinal detachment, optic neuropathy, amblyopia, strabismus, aniridia, epiretinal membrane, etc.).
9. History of cystoid macular edema in either eye.
10. History of uveitis in either eye.
11. History of intraocular or corneal surgery in the study eye besides laser peripheral iridotomy (LPI), selective laser trabeculoplasty (SLT), or argon laser trabeculoplasty (ALT).
12. Uncontrolled glaucoma in the study eye (per Investigator judgement).
13. Current ocular infection in the study eye.
14. Presence of uncontrolled systemic disease that could increase operative risk (e.g. diabetes mellitus, mental illness, dementia, clinically significant atopic disease, etc.).
15. Planned concomitant ocular procedure during cataract surgery inclusive of glaucoma surgery e.g. MIGS or limbal relaxing incisions.
16. Symptoms that might be consistent with active COVID-19 including fever, chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches.
17. If COVID-19 positive, at least two weeks since last symptoms.
18. Unsuitable for study participation for any other reason, as determined by the Investigator's clinical judgement.
19. If you have been in another research study during the past 3 months or are in another research study now.
20. If you typically wear rigid gas permeable (RGP) contact lenses, you must not put them in the eye planned for surgery for at least 30 days before your pre-operative eye anatomy measurements are performed.
21. If you are a female and able to become pregnant, you will be asked to use medically acceptable birth control and to prevent pregnancy.

3.3 Early Withdrawal of Subjects

3.3.1Criteria for removal from study

Insert subject withdrawal criteria (e.g., safety reasons, failure of subject to adhere to protocol requirements, subject consent withdrawal, disease progression, etc.).

Subjects may be terminated from the study due to:

- Failure to meet protocol eligibility criteria prior to the first Operative Visit
- Intraoperative complications preventing IOL implantation
- Investigator decision that termination is medically indicated

- Voluntary withdrawal from the study
- Loss to follow-up (LTF)
- Other administrative reasons (e.g. completion of protocol-required study surgeries, surgical logistics, study or investigator termination, etc.)

3.3.2 Follow-up for withdrawn subjects

Describe when and how to withdraw subjects from the study; the type and timing of the data to be collected for withdrawal of subjects; whether and how subjects are to be replaced; the follow-up for subjects withdrawn from investigational treatment.

Subjects who fail to meet protocol eligibility criteria prior to IOL implantation will not be followed beyond the date they are determined to be ineligible. Subjects who terminate due to the occurrence of an adverse event will be followed until resolution or stabilization of the event.

Terminated subjects who have undergone IOL implantation will not be replaced.

4.0 Recruitment Methods

- Upload recruitment materials for your study in CATS IRB (http://irb.psu.edu). **DO NOT** include the actual recruitment wording in this protocol.
- StudyFinder: If StudyFinder (http://studyfinder.psu.edu) is to be used for recruitment purposes, separate recruitment documents do not need to be uploaded in CATS IRB. The necessary information will be captured from the StudyFinder page in your CATS IRB study.
- Any eligibility screening questions (verbal/phone scripts, email, etc.) used when contacting potential participants must be uploaded to your study in CATS IRB (http://irb.psu.edu).

[Do not type here]

4.1 Identification of subjects

Describe the source of subjects and the methods that will be used to identify potential subjects (e.g., organizational listservs, established recruitment databases, subject pools, medical or school records, interactions during a clinic visit, etc.). If not recruiting subjects directly (e.g., database query for eligible records or samples) state what will be queried, how and by whom.

StudyFinder:

- If you intend to use StudyFinder (http://studyfinder.psu.edu) for recruitment purposes, include this method in this section.
- Information provided in this protocol needs to be consistent with information provided on the StudyFinder page in your CATS IRB study.

For Penn State Health submissions using Enterprise Information Management (EIM) for recruitment, and for non-Hershey locations as applicable, attach your EIM Design Specification form on in CATS IRB (http://irb.psu.edu). See "HRP-103- Investigator Manual, What is appropriate for study recruitment?" for additional information. **DO NOT** include the actual recruitment material or wording in this protocol.

The coordinator will review charts of patients scheduled for cataract evaluation and determine if they meet eligibility criteria. Response to recruitment materials (pull tab flyer, and STUDYfinder)

4.2 Recruitment process

Describe how potential subjects first learn about this research opportunity or indicate as not applicable if subjects will not be prospectively recruited to participant in the research. Subject recruitment can involve various methods (e.g., approaching potential subjects in person, contacting potential subjects via

email, letters, telephone, ResearchMatch, or advertising to a general public via flyers, websites, StudyFinder, newspaper, television, and radio etc.). **DO NOT** include the actual recruitment material or wording in this protocol.

[Do not type here]

4.2.1 How potential subjects will be recruited.

The coordinator will notify PI which patients on his schedule meet inclusion criteria. After the PI evaluates the patient in clinic and determines patient is eligibility and interest in participating in the study, the coordinator will be notified. The coordinator will discuss the details of the study with the patient and perform the consent process.

Subjects will call the study line at the research site. The coordinator will call and if the subject decides to schedule an appointment the coordinator will schedule a screening visit. The site will utilize the screening form for all potential subjects.

4.2.2Where potential subjects will be recruited.

Potential subjects will be recruited from already scheduled patients in PI's clinic for cataract evaluation. Ophthalmology Eye Center Suite 800 We will be utilizing Studyfinder and flyers as well to recruit potential participants

4.2.3 When potential subjects will be recruited

During the regular scheduled ophthalmology visit for cataract surgery or they will see a flyer and call the number listed to see if they are eligible.

4.2.4Describe the eligibility screening process and indicate whether the screening process will occur before or after obtaining informed consent. Screening begins when the investigator obtains information about or from a prospective participant in order to determine their eligibility. In some studies, these procedures may not take place unless HIPAA Authorization is obtained OR a waiver of HIPAA Authorization when applicable for the screening procedures is approved by the IRB. [*For FDA regulated studies, consent for any screening activities would need to be obtained prior to screening unless specifically waived by the IRB.]*

After the PI evaluates the patient in clinic and determines patient is eligible and has an interest in participating in the study, the coordinator will be notified. The coordinator will discuss the details of the study with the patient and perform the consent process in the research office. Subjects will call the site to be screened. If the subject decides to schedule an appointment the coordinator schedules a screening visit. If the subject declines, the telephone screening is discarded by placing phone screen in the shredder.

5.0 Consent Process and Documentation

Refer to the following materials:

- The "HRP-090- SOP - Informed Consent Process for Research" outlines the process for obtaining informed consent.
- The "HRP-091– SOP - Written Documentation of Consent" describes how the consent process will be documented.
- The "HRP-314- Worksheet - Criteria for Approval" section 7 lists the required elements of consent.

- The "HRP-312- Worksheet - Exemption Determination" includes information on requirements for the consent process for exempt research. In addition, the CATS IRB Library contains consent guidance and templates for exempt research.
- The CATS IRB library contains various consent templates for expedited or full review research that are designed to include the required information.
- Add the consent document(s) to your study in CATS IRB (http://irb.psu.edu). Links to Penn State's consent templates are available in the same location where they are uploaded. **DO NOT** include the actual consent wording in this protocol.

[Do not type here]

5.1 Consent Process:

Check all applicable boxes below:

☒ **Informed consent will be sought and documented with a written consent form *[Complete Sections 5.2 and 5.6]***

☒ **Implied or verbal consent will be obtained – subjects will not sign a consent form (waiver of written documentation of consent) *[Complete Sections 5.2, 5.3 and 5.6]***

☐ **Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception). *[Complete section 5.2, 5.4 and 5.6]***

☐ **Informed consent will not be obtained – request to completely waive the informed consent requirement. *[Complete Section 5.5]***

The following checkbox is for all locations EXCEPT Penn State Health and College of Medicine:

☐ **Exempt Research at all Locations Except Penn State Health and the College of Medicine: If you believe that the research activities outlined meet one or more of the criteria outlined in "HRP-312- Worksheet- Exemption Determination." Please verify by checking this box that if conducting an exempt research study, the consent process will disclose the following (all of which are included in "HRP-590- Consent Guidance for Exempt Research"):**

Penn State affiliation; name and contact information for the researcher and advisor (if the researcher is a student); the activities involve research; the procedures to be performed; participation is voluntary; that there are adequate provisions to maintain the privacy interests of subjects and the confidentiality of the data; and subjects may choose not to answer specific questions.

If the research includes the use of student educational records include the following language in this section (otherwise delete): The parent or eligible student will provide a signed and dated written consent that discloses: the records that may be disclosed; the purpose of the disclosure; the party or class of parties to whom the disclosure may be made; if a parent or adult student requests, the school will provide him or her with a copy of the records disclosed; if the parent of a student who is not an adult so requests, the school will provide the student with a copy of the records disclosed.

Note: If this box has been checked, skip the remainder of section 5 and proceed to section 6 of this protocol. If the investigator's assessment is inaccurate, an IRB Analyst will request revision to the protocol and that an informed consent form be submitted for review and approval. Except for exemptions where Limited IRB Review (see "HRP-312- Worksheet- Exemption Determination") is required or where otherwise requested by the IRB, informed consent forms for research activities

determined to be exempt without Limited IRB Review are generally not required to be submitted for review and approval by the University Park IRB.

5.2 Obtaining Informed Consent

5.2.1Timing and Location of Consent

Describe where and when the consent process will take place.

The consent will take place in a private exam room in the Ophthalmology Clinic (Suite 700/800), or the Ophthalmology Research Office, UPC I-RM 501.

5.2.2Coercion or Undue Influence during Consent

Describe the steps that will be taken to minimize the possibility of coercion or undue influence in the consent process.

Subjects will have ample time to read and ask questions about the study. Their involvement in the study will not affect their treatment if they are currently patients of the ophthalmology clinic.

5.3 Waiver of Written Documentation of Consent

Review "HRP – 411 – Checklist – Waiver of Written Documentation of Consent."

5.3.1Indicate which of the following conditions applies to this research:

☒ The research presents no more that minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

OR

☐ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. (*Note: This condition is not applicable for FDA-regulated research. If this category is chosen, include copies of a consent form and /or parental permission form for participants who want written documentation linking them to the research.)*

OR

☐ If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. (*Note: This condition is not applicable for FDA-regulated research.)*

Describe the alternative mechanism for documenting that informed consent was obtained:

[Type protocol text here]

5.3.2 Indicate what materials, if any, will be used to inform potential subjects about the research (e.g., a letter accompanying a questionnaire, verbal script, implied consent form, or summary explanation of the research)

Site will use a screening form to discuss eligibility and study details if a participant calls the research office to inquire about the study.

5.4 Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception).

Review "HRP-410-Checklist -Waiver or Alteration of Consent Process" to ensure that you have provided sufficient information.

5.4.1 Indicate the elements of informed consent to be omitted or altered

NA

5.4.2Indicate why the research could not practicably be carried out without the omission or alteration of consent elements

NA

5.4.3Describe why the research involves no more than minimal risk to subjects.

NA

5.4.4 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

NA

5.4.5If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not be practicably be carried out without using such information or biospecimens in an identifiable format.

NA

5.4.6Debriefing

Explain whether and how subjects will be debriefed after participation in the study. If subjects will not be debriefed, provide a justification for not doing so. Add any debriefing materials to the study in CATS IRB.

NA

5.5 Informed consent will not be obtained – request to completely waive the informed consent requirement

Review "HRP-410-Checklist -Waiver or Alteration of Consent Process" to ensure that you have provided sufficient information.

5.5.1Indicate why the research could not practicably be carried out without the waiver of consent

NA

5.5.2Describe why the research involves no more than minimal risk to subjects.

NA

5.5.3 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

NA

5.5.4If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not be practicably be carried out without using such information or biospecimens in an identifiable format.

NA

5.5.5 Additional pertinent information after participation

Explain if subjects will be provided with additional pertinent information after participation. If not applicable, indicate "not applicable."

NA

5.6 Consent – Other Considerations

5.6.1 Non-English-Speaking Subjects

Indicate what language(s) other than English are understood by prospective subjects or representatives.

If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

Indicate whether the consent process will be documented in writing with the long form of the consent documentation or with the short form of the consent documentation. Review "HRP-091 –SOP- Written Documentation of Consent" and "HRP-103 -Investigator Manual" to ensure that you have provided sufficient information.

NA

5.6.2 Cognitively Impaired Adults

Refer "HRP-417 -CHECKLIST- Cognitively Impaired Adults" for information about research involving cognitively impaired adults as subjects.

5.6.2.1 Capability of Providing Consent

Describe the process to determine whether an individual is capable of consent.

NA

5.6.2.2 Adults Unable to Consent

Describe whether and how informed consent will be obtained from the legally authorized representative. Describe who will be allowed to provide informed consent. Describe the process used to determine these individual's authority to consent to research.

For research conducted in the state of Pennsylvania, review "HRP-013 -SOP- Legally Authorized Representatives, Children and Guardians" to be aware of which individuals in the state of Pennsylvania meet the definition of "legally authorized representative."

For research conducted outside of the state of Pennsylvania, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "children" in "HRP-013 - SOP- Legally Authorized Representatives, Children, and Guardians."

NA

5.6.2.3 Assent of Adults Unable to Consent

Describe the process for assent of the subjects. Indicate whether assent will be required of all, some or none of the subjects. If some, indicate which subjects will be required to assent and which will not.

If assent will not be obtained from some or all subjects, provide an explanation of why not.

Describe whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.

NA

1. Subjects who are not yet adults (infants, children, teenagers)

5.6.3.1 Parental Permission

Describe whether and how parental permission will be obtained. If permission will be obtained from individuals other than parents, describe who will be allowed to provide permission. Describe the process used to determine these individual's authority to consent to each child's general medical care.

For research conducted in the state of Pennsylvania, review "HRP-013-SOP- Legally Authorized Representatives, Children and Guardians" to be aware of which individuals in the state of Pennsylvania meet the definition of "children."

For research conducted outside of the state of Pennsylvania, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "children" in "HRP-013-SOP- Legally Authorized Representatives, Children, and Guardians."

NA

5.6.3.2 Assent of subjects who are not yet adults

Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent. When assent of children is obtained describe whether and how it will be documented.

NA.

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

This section is about the access, use or disclosure of Protected Health Information (PHI). PHI is individually identifiable health information (i.e., health information containing one or more 18 identifiers) that is transmitted or maintained in any form or medium by a Covered Entity or its Business Associate. A Covered Entity is a health plan, a health care clearinghouse or health care provider who transmits health information in electronic form. See "HRP-103 -Investigator Manual" for a list of the 18 identifiers.

If requesting a waiver/alteration of HIPAA authorization, complete sections 6.2 and 6.3 in addition to section 6.1. The Privacy Rule permits waivers (or alterations) of authorization if the research meets certain conditions. Include only information that will be accessed with the waiver/alteration.

[Do not type here]

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☒ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☒ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2.Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Include the following statement as written – DO NOT ALTER OR DELETE unless this section is not applicable because the research does not involve a waiver of authorization. **If the section is <u>not</u> applicable, <u>remove</u> the statement and <u>indicate as not applicable</u>.**

Information is included in the "Confidentiality, Privacy and Data Management" section of this protocol.

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research. Include when and how identifiers will be destroyed. If identifiers will be retained, provide the legal, health or research justification for retaining the identifiers.

All study materials that have identifiable information will be kept until notified by the sponsor. If the subject doesn't qualify from a phone call, the screening form will be placed in the shredder due to PHI.

6.2.2Explanation for why the research could not practicably be conducted without access to and use of PHI

Provide an explanation for why the research could not practicably be conducted without access to and use of PHI.

Research team has access to participant's medical record after the ICF is signed. Research needs to use PHI to ensure subject meets eligibility criteria.

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

Provide an explanation for why the research could not practicably be conducted without the waiver or alternation of authorization.

Participants are screened prior to performing ICF process to help determine if the patient is potentially eligible for the study. This helps sift through candidates for appointments so patient's time is not wasted.

6.3 Waiver or alteration of authorization statements of agreement

By submitting this study for review with a waiver of authorization, you agree to the following statement – DO NOT ALTER OR DELETE unless this section is not applicable because the research does not involve a waiver or alteration of authorization. **If the section is <u>not</u> applicable, <u>remove</u> the statement and <u>indicate as not applicable.</u>**

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

Data collection materials that will be seen or used by subjects in your study must be uploaded to CATS IRB (http://irb.psu.edu). **DO NOT** include any actual data collection materials in this protocol (e.g., actual survey or interview questions)

7.1 Study Design

Describe and explain the study design.

This is a prospective, single-center, patient and assessor-blinded, double-arm clinical study. Subjects will be enrolled at the Penn State Eye Center. Eligible subjects must be anticipated to undergo bilateral sequential cataract surgery. Both eyes from each patient will be considered study eyes.

Candidate patients who give written consent to participate in the study will be enrolled and screened to determine study eligibility, then examined to obtain their medical and ophthalmic history and establish their baseline ocular condition. Qualified subjects will be randomized to receive one of two study devices in both eyes. Post-operatively, subjects will undergo examination at 4 protocol-specific visits at regularly scheduled intervals through 3 months post-operatively, as shown in **APPENDIX 1: SCHEDULE OF CLINICAL ASSESSMENTS/PROCEDURES.**

7.2 Study Procedures

Provide a step by step description of all research procedures being conducted (broken down by visit, if applicable) including such information as below (where and when applicable); describe the following:

- HOW: (e.g., data collection via interviews, focus groups, forms such as surveys and questionnaires, medical/school records, audio/video/digital recordings, photographs, EKG procedures, MRI, mobile devices such as electronic tablets/cell phones, observations, collection of specimens, experimental drug/device testing, manipulation of behavior/use of deception, computer games, etc.)
- WHERE: (e.g., classrooms, labs, internet/online, places of business, medical settings, public spaces, etc.)

All potential participants will complete all of the pre-operative assessments as part of Standard of Care treatment. At that time, the Principle Investigator will introduce the study to the potential participants and go over each lens that could be implanted. If patient agrees to move forward with study participation, the coordinator will complete screening and perform the consent process. The study participants will be provided two questionnaires to complete that ask about how much difficulty they presently have seeing things at distance, intermediate and near. It will also assess which specific visual disturbances (eg blurry vision, glare) they are experiencing before surgery takes place.

Randomization, the IOL randomization code list will be provided by the Dept. of Public Health Sciences. This determines which IOL would be implanted for each patient and will be assigned once the consent is

signed and it is determined that the subject has met all eligibility criteria. The PI will be unblinded to the lens that will be implanted as he will be doing the surgical procedure.

Post-operative assessments that occur for eye #1- Day 1 and week 1 as well as eye #2- Day 1 will be performed by Dr. Pantanelli as part of standard of care. During this time, if an AE or SAE is identified, it would be reviewed and causality/IOL relationship will be determined by another Ophthalmologist, Dr. Sundstrom who will be unblinded. At the 1 month and 3 month follow-up visits, assessments would be performed by the Blinded investigator, Dr. O'Rourke. At study completion, after all study procedures are completed the coordinator will then pull the subject envelope containing the wallet card that reveals which IOL lens was implanted in both the right and left eye.

Table 1: Schedule of Clinical Assessments / Procedures

Assessment / Procedure	Protocol Visit							
	Pre-operative/ Visit 1	Operative #1/ Visit 2	1 Day #1/ Visit 3	1 Week / Visit 4	Operative #2/ Visit 5	1 Day #2/ Visit 6	1 Month/ Visit 7	3 Month/ Visit 8
Medical and ophthalmic history	SOC							
Slit lamp examination	SOC		SOC	SOC		SOC	SOC	SOC
Dilated fundus examination	SOC						SOC	
Intraocular pressure	SOC		SOC	SOC		SOC	SOC	SOC
Pre-operative biometry	SOC							
Macular optical-coherence tomography	SOC							
Corneal topography	SOC							
Informed consent	R							
Randomization to study arm	R							
Cataract extraction with IOL implantation		SOC			SOC			
Manifest refraction				SOC			SOC	SOC
Snellen uncorrected distance acuity	SOC		SOC	SOC		SOC	SOC	SOC
Uncorrected distance visual acuity (UDVA) monocular and binocular							R	R
Corrected distance visual acuity (CDVA) monocular and binocular							R	R
Uncorrected intermediate visual acuity (UIVA) monocular							R	R

and binocular								
Distance corrected intermediate visual acuity (DCIVA) monocular and binocular							R	R
Uncorrected near visual acuity (UNVA) monocular and binocular							R	R
Distance corrected near visual acuity (DCNVA) monocular and binocular							R	R
Defocus Curve Testing (binocular only)								R
Un-blinding								R
Patient Reported Outcomes	R							R
Adverse Event Monitoring	R	R	R	R	R	R	R	R
Urine Pregnancy test	R							

SOC = standard-of-care; R = research

7.2.1 Visit 1/Pre-Operative

Provide a description of what procedures will be performed on visit 1 or day 1 or pre-test in order of how these will be done. If your study only involves one session or visit, use this section only and indicate 7.2.2 as not applicable.

Preoperative (research related procedures only listed below):

- Eligibility screening
- Informed consent
- Randomization to study group
- Patient reported outcomes; 2 questionnaires

7.2.2 Visit 2 / Operative #1

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

Operative Day #1:

- Cataract surgery with implantation of intraocular lens

Visit 3/1 Day #1

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

One Day Post-Op #1:

- Standard of care visual acuity, intraocular pressure, and slit lamp examination

Visit 4/ 1 Week

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

One Week Post-op #1

- Standard of care visual acuity, intraocular pressure, and slit lamp exam
- Standard of care manifest refraction

Visit 5 / Operative #2

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

Operative Day #2:

- Cataract surgery with implantation of intraocular lens

Visit 6 / 1 Day #2

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

One Day Post-op #2:

- Standard of care visual acuity, intraocular pressure, and slit lamp examination

Visit 7 / 1 Month

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

One Month Post-op:

- Standard of care visual acuity, intraocular pressure, and slit lamp examination
- Standard of care manifest refraction
- Research related ETDRS visual acuity testing at distance, intermediate, and near, both monocularly and binocularly, uncorrected and best-distance corrected
- Standard of care dilated fundus examination

Visit 8 / 3 Month

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.).

Three Month Post-op:

- Standard of care visual acuity, intraocular pressure, and slit lamp examination
- Research related ETDRS visual acuity testing at distance, intermediate, and near, both monocularly and binocularly, uncorrected and best-distance corrected
- Binocular defocus curve testing (visual acuity testing through blur)
- Patient un-blinding

- Patient reported outcomes; 2 questionnaires

7.3 Duration of Participation

Describe how long subjects will be involved in this research study. Include the number of sessions and the duration of each session - consider the total number of minutes, hours, days, months, years, etc.

The duration of each subject's study participation is estimated to be approximately 18 weeks; however, duration of participation is affected by the time lapse between the Pre-operative Visit, which may occur between Day -30 and Day 0, and the Operative Day #1 Visit on Day 0. Each subject will be followed for approximately 12 weeks after the Operative Visit #2.

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

Indicate the maximum number of subjects to be accrued/enrolled. Distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures if applicable (i.e., numbers of subjects excluding screen failures.)

70

8.2 Sample size determination

If applicable, provide a justification of the sample size outlined in section 8.1 to include reflections on, or calculations of, the power of the study.

The FDA Summary of Safety and Effectiveness Data on the Alcon Vivity IOL compared the Alcon Vivity IOL to the Alcon Acrysof IQ SN60WF. It demonstrated binocular DCIVA's of 0.054 (SD = 0.09) and 0.196 (SD 0.113) logMAR units, respectively (Table 25; difference of 0.142). The difference between the DCNVAs was similar.[8] We hypothesize that the neutral asphericity of the B&L enVista IOL will result in a slightly improved DCIVA and DCNVA as compared with that of the SN60WF. As such, we assumed that the mean difference in the DCIVA or DCNVA between the two study devices will be ≥ 0.12 logMAR units and that the standard deviation on these measurements will be approximately 0.10.[8,11]

A 2019 ASCRS abstract by Dr. Dee Stephenson also described the MX60E as having monocular UCIVA and UCNVA of 0.17 ± 0.17 and 0.44 ± 0.33 D, respectively.[12] Binocular UCIVA and UCNVA for the Alcon Vivity IOL was 0.058 ± 0.083 and 0.208 ± 0.104 D, respectively (monocular logMAR not reported).[8] Although monocular and binocular acuities are not typically compared, the difference between the Vivity and MX60E IOLs might be approximately 0.11 for intermediate and 0.24 logMAR units, based upon this above information. The higher SDs are likely due to the uncorrected astigmatism in this population.

The sample size calculation was performed using http://clincalc.com. Based on a difference in binocular DCIVA of 0.12 logMAR units and a SD of 0.10, we calculated that for an α of 0.05 and power of 0.80, 22 bilaterally implanted patients would be required in each group. However, 28 patients were included to more closely approximate a normal distribution and ensure adequate numbers after accounting for screen failures and patients lost to follow-up.

8.3 Statistical methods

Describe the statistical methods (or non-statistical methods of analysis) that will be employed.

Descriptive data will be used for demographic characteristics as well asvisual and refractive outcomes, A Shapiro-Wilk test will be used to assess the normality of the data. Visual acuities will be converted to logMAR notation to facilitate averaging and analysis.

The paired sample t-test or nonparametric Wilcoxan signed-rank test will be used to compare monocular and binocular visual acuity under uncorrected and distance-corrected conditions. Comparisons between patients with different IOLs will be evaluated with independent sample t-tests or the nonparametric Mann-Whitney test for visual acuity and refractive outcomes, depending on the normality of the data. The level of significance will be set at $p < 0.05$.

9.0 Data and Safety Monitoring Plan

This section is required when research involves more than Minimal Risk to subjects as defined in "HRP-001 SOP- Definitions."

Minimal Risk is defined as the probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For research involving prisoners, Minimal Risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Please complete the sections below if the research involves more than minimal risk to subjects, otherwise indicate each section as not applicable.

[Do not type here]

9.1 Periodic evaluation of data

Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Outcome measures will be reviewed after 10, and again after 20 subjects have completed all study related assessments.

Adverse events and SAEs will be monitored continuously by the blinded examiner. The expected or unexpected adverse events will not unblind the examiner because everyone receives an IOL The examiner would not be able to decipher which lens could be related to an event.

9.2 Data that are reviewed

Describe the data that are reviewed, including safety data, untoward events, and efficacy data.

Refractive outcomes and mean best-corrected distance visual acuity will be reviewed to ensure mean prediction errors (MPEs) and logMAR visual acuities are in line with what is reported in the peer-reviewed literature and FDA Summary of Safety and Effectiveness for the Alcon Vivity IOL.

AEs and SAE's will be reviewed on a case-by-case basis by the blinded examiner.

9.3 Method of collection of safety information

Describe the method by which the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls and with subjects).

Paper forms will be used to collect study related data, which will be transferred to the EDC (RedCAP). The sponsor is not providing case report forms.

SAEs will be recorded on case report forms, at study visits, and/or at unscheduled visits. The sponsor is not collecting AE/SAE's.

9.4 Frequency of data collection

Describe the frequency of data collection, including when safety data collection starts.

Data collection will be performed at study visits as described above.

9.5 Individuals reviewing the data

Identify the individuals who will review the data. The plan might include establishing a data and safety monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

A non-conflicted co-investigator (Dr. Tara O'Rourke) will perform the periodic review of data, described above. Coordinator will be responsible for reportable information to be submitted to the IRB.

9.6 Frequency of review of cumulative data

Describe the frequency or periodicity of review of cumulative data.

As described above, after 10 and 20 patients have completed study related assessments.

9.7 Statistical tests

Describe the statistical tests for analyzing the safety data to determine whether harms are occurring.

The paired sample t-test or nonparametric Wilcoxan signed-rank test will be used to compare monocular and binocular visual acuity under distance-corrected conditions. Comparisons between patients with different IOLs will be evaluated with independent sample t-tests or the nonparametric Mann-Whitney test for visual acuity and refractive outcomes, depending on the normality of the data. The level of significance will be set at $p < 0.05$.

9.8 Suspension of research

Describe any conditions that trigger an immediate suspension of research.

Research will be suspended at the discretion of the Principal Investigator if periodic review of the data suggests that safety or efficacy outcomes are significantly different than what would be expected during the routine provision of care of patients not enrolled in the research study.

10.0 Risks

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration and reversibility of the risks. Consider all types of risk including physical, psychological, social, legal, and economic risks. Note: Loss of confidentiality is a potential risk when conducting human subject research.

- If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.
- If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.

- If applicable, describe risks to others who are not subjects.

The risks to study subjects are the same risks as those patients would normally incur before, during, and after cataract surgery.

Intraocular lenses that seek to provide intermediate or near vision without glasses may be associated with additional risks that include blurry vision not correctable with glasses or contact lenses and subjective visual disturbances including starbursts, haloes, glare, hazy or blurry vision. In an FDA trial that compared similar lenses to the ones being evaluated in this study, these visual phenomena were severe or very bothersome in 3-4% of patients. This specific risk has been explained in detail in the informed consent form, and will also be reviewed verbally at the time of consent for surgery.

There is a small risk to the subjects of loss of confidentiality. Safeguards as described in the Data Management Plan are in place to minimize these risk.

11.0 Potential Benefits to Subjects and Others

11.1 Potential Benefits to Subjects

Describe the potential benefits that individual subjects may experience from taking part in the research. If there is no direct benefit to subjects, indicate as such. Compensation is not considered a benefit. Compensation should be addressed in section 13.0.

There is no direct benefit from participating in this research study. 11.2 Potential Benefits to Others

Include benefits to society or others.

Results of the study may benefit other people in the future by helping us learn more about the differences and benefits of the both lens used in the study.

12.0 Sharing Results with Subjects

Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how information will be shared.

There is no plan to share study related outcome measures / results with individual patients.

13.0 Subject Payment and/or Travel Reimbursements

Describe the amount, type (cash, check, gift card, other) and timing of any subject payment or travel reimbursement. If there is **no** subject payment or travel reimbursement, indicate as not applicable.

Extra or Course Credit: Describe the amount of credit **and** the available alternatives. Alternatives should be equal in time and effort to the amount of course or extra credit offered. It is not acceptable to indicate that the amount of credit is to be determined or at the discretion of the instructor of the course.

Approved Subject Pool: Indicate which approved subject pool will be used; include in response below that course credit will be given and alternatives will be offered as per the approved subject pool procedures.

Study subjects will receive $60 for participating in the 1 month Post-op Visit at the completion of the visit and $60 for participating in the 3 month Post-op visit at the completion of the visit. They will be reimbursed utilizing the GreenPhire system

14.0 Economic Burden to Subjects

14.1 Costs

Describe any costs that subjects may be responsible for because of participation in the research.

NA

14.2 Compensation for research-related injury

If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

If there is no sponsor agreement that addresses compensation for medical care for research subjects with a research-related injury, include the following text as written - DO NOT ALTER OR DELETE:
It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

For sponsored research studies with a research agreement with the sponsor that addresses compensation for medical care for research-related injuries, include the following text as written - DO NOT ALTER OR DELETE:
It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Such charges may be paid by the study sponsor as outlined in the research agreement and explained in the consent form.

It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

15.0 Resources Available

15.1 Facilities and locations

Identify and describe the facilities, sites and locations where recruitment and study procedures will be performed.

If research will be conducted outside the United States, describe site-specific regulations or customs affecting the research, and describe the process for obtaining local ethical review. Also, describe the principal investigator's experience conducting research at these locations and familiarity with local culture.

Recruitment will occur in the Ophthalmology Clinic, located in UPC 1 Suite 700/800 and Ophthalmology Research Office 501.

Surgeries will occur at the Hershey Outpatient Surgery Center

Follow-up visits that include only standard-of-care assessments will occur in the Ophthalmology Clinic, located in UPC 1 Suite 700/800.

Follow-up visits that include research related assessments will occur in the Ophthalmology Research office UPC I– Room 501.

Recruitment phone calls will take place in the research office UPCII Rm 2301.

15.2 Feasibility of recruiting the required number of subjects

Indicate the number of potential subjects to which the study team has access. Indicate the percentage of those potential subjects needed for recruitment.

We anticipate 20% of patients being seen for cataract evaluations will qualify for and ascent to participation in the research study.

The Principal Investigator will see an average of 10 cataract evaluations per week. It is estimated that this will generate 2 study subjects per week.

The Sponsor was advised that study recruitment would last 36 weeks. This is enough time to recruit as many as 72 study subjects, but only 56 subjects are to be enrolled.

15.3 PI Time devoted to conducting the research

Describe how the PI will ensure that a sufficient amount of time will be devoted to conducting and completing the research. Please consider outside responsibilities as well as other on-going research for which the PI is responsible.

The Principal Investigator has one academic day per week. He has no clinical responsibilities during this time.

15.4 Availability of medical or psychological resources

Describe the availability of medical or psychological resources that subjects might need as a result of their participation in the study, if applicable.

Medical and psychological resources are available at the Penn State Milton S. Hershey Medical Center, at the same site if needed.

15.5 Process for informing Study Team

Describe the training plans to ensure members of the research team are informed about the protocol and their duties, if applicable.

All study team members will attend a training session prior to start of study. If not available to attend they will be trained individually prior to collecting any data for the study. All training will be documented on a training log.

16.0 Other Approvals

16.1 Other Approvals from External Entities

Describe any approvals that will be obtained prior to commencing the research (e.g., from engaged cooperating institutions IRBs who are also reviewing the research and other required review committees, community leaders, schools, research locations where research is to be conducted by the Penn State investigator, funding agencies, etc.).

Not applicable.

16.2 Internal PSU Committee Approvals

Check all that apply:

☐ Anatomic Pathology – **Penn State** Health **only** – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of "HRP-902 - Human Tissue For Research Form" in CATS IRB.

☐ Animal Care and Use – **All campuses** – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – **All campuses** – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – **Penn State Health only** – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes but are no longer needed for clinical use. Upload a copy of "HRP-901 - Human Body Fluids for Research Form" in CATS IRB.

☐ Clinical Research Center (CRC) Advisory Committee – **All campuses** – Research involves the use of CRC services in any way.

☒ Conflict of Interest Review – **All campuses** – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – **Penn State Health only** – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of "HRP-903 - Radiation Review Form" in CATS IRB.

☐ IND/IDE Audit – **All campuses** – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☒ Scientific Review – **Penn State Health only** – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Health Cancer Institute (PSCI) Protocol Review Committee or the PSCI Disease Team is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website.

17.0 Multi-Site Study

If this is a multi-site study (i.e., a study in which two or more institutions coordinate, with each institution completing all research activities outlined in a specific protocol) and the Penn State PI is the lead investigator, describe the processes to ensure communication among sites in the sections below.

17.1 Other sites

List the name and location of all other participating sites. Provide the name, qualifications and contact information for the principal investigator at each site and indicate which IRB will be reviewing the study at each site.

NA

17.2 Communication Plans

Describe the plan for regular communication between the overall study director and the other sites to ensure that all sites have the most current version of the protocol, consent document, etc. Describe the process to ensure all modifications have been communicated to sites. Describe the process to ensure that all required approvals have been obtained at each site (including approval by the site's IRB of record). Describe the process for communication of problems with the research, interim results and closure of the study.

NA

17.3 Data Submission and Security Plan

Describe the process and schedule for data submission and provide the data security plan for data collected from other sites. Describe the process to ensure all engaged participating sites will safeguard data as required by local information security policies.

NA

17.4 Subject Enrollment

Describe the procedures for coordination of subject enrollment and randomization for the overall project.

NA

17.5 Reporting of Adverse Events and New Information

Describe how adverse events and other information will be reported from the clinical sites to the overall study director. Provide the timeframe for this reporting.

NA

17.6 Audit and Monitoring Plans

Describe the process to ensure all local site investigators conduct the study appropriately. Describe any on-site auditing and monitoring plans for the study.

NA

18.0 Adverse Event Reporting

18.1Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

By submitting this study for review, you agree to the following statement – DO NOT ALTER OR DELETE:

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1)

unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

19.1 Auditing and Inspecting

By submitting this study for review, you agree to the following statement – DO NOT ALTER OR DELETE:

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

20.0 Future Undetermined Research: Data and Specimen Banking

If this study is collecting **identifiable** data and/or specimens that will be banked for future **undetermined research**, please describe this process in the sections below. This information should not conflict with information provided in section 22 regarding whether or not data and/or specimens will be associated with identifiers (directly or indirectly). If **NOT applicable**, indicate as such below in all sections.

[Do not type here]

20.1 Data and/or specimens being stored

Identify what data and/or specimens will be stored and the data associated with each specimen.

Clinical and demographic data collected throughout the entire the study duration.

20.2 Location of storage

Identify the location where the data and/or specimens will be stored.

Clinical and demographic data associated with this study will be stored in hard copy in the Ophthalmology Research Office (UPCII 2300) during the study recruitment and preliminary analyses. This data will also be stored electronically within the HMC secured server; RedCap.

20.3Duration of storage

Identify how long the data and/or specimens will be stored. If data and/or specimens will be stored indefinitely, indicate as such.

Data from the study will be stored until completion of the study. .

20.4 Access to data and/or specimens

Identify who will have access to the data and/or specimens.

Study team members will have access to data from the study.

20.5 Procedures to release data or specimens

Describe the procedures to release the data and/or specimens, including: the process to request a release, approvals required for release, who can obtain data and/or specimens, and the data to be provided with the specimens.

At the completion of this study, de-identified data will be published within a peer-reviewed journal.

20.6 Process for returning results

Describe the process for returning results about the use of the data and/or specimens.

NA

22. Study Monitoring, Auditing and Inspecting

23.Future Undetermined Research: Data and Specimen Banking

If this study is collecting **identifiable** data and/or specimens that will be banked for future **undetermined research**, please describe this process in the sections below. This information should not conflict with information provided in section 22 regarding whether or not data and/or specimens will be associated with identifiers (directly or indirectly). If **NOT applicable**, indicate as such below in all sections.

NA

24. References

List relevant references in the literature which highlight methods, controversies, and study outcomes.

1. Allen ED, Burton RL, Webber SK, et al. Comparison of a diffractive bifocal and a monofocal intraocular lens. J Cataract Refract Surg 1996; 22(4): 446-51.
2. Alio JL, Tavolato M, De la Hoz F, et al. Near vision restoration with refractive lens exchange and pseudoaccomodating and multifocal refractive and diffractive intraocular lenses: comparative clinical study. J Cataract Refract Surg 2004; 30(12): 494-503.
3. Calladine D, Evans JR, Shah S, et al. Multifocal versus monofocal intraocular lenses after cataract extraction. Cochrane Database Syst Rev 2012; 9: CD003169.
4. Cochener B, Lafuma A, Khoshnood B, et al. Comparison of outcomes with multifocal intraocular lenses: a meta-analysis. Clin Ophthalmol 2011; 5:45-56.
5. Yeu E, Wang L, Koch DD. The effect of corneal wavefront aberrations on corneal pseudoaccommodation. Am J Ophthalmol 2012; 153(5): 972-981.e2.
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7. Bellucci R, Curatolo MC. A New Extended Depth of Focus Intraocular Lens Based on Spherical Aberration. J Refract Surg 2017; 33(6): 389-394.
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9. Steinberg EP, Tielsch JM, Schein OD. The VF-14. An index of functional impairment in patients with cataract. Arch Ophthalmol 1994; 112:630-8.
10. Carneros-Llorente AM, Carneros AM, Carneros-Llorente PM, et al. Comparison of visual quality and subjective outcomes among 3 trifocal intraocular lenses and 1 bifocal intraocular lens. J Cataract Refract Surg 2019; 45: 587-594.
11. Stephenson PDG. Objective and Subjective Assessment of Functional-Range-of-Vision in Patients Implanted with Aberration-Free Monofocal IOL. https://ascrs.org/clinical-education/abstracts/2019/objective-and-subjective-assessment-of-functionalrangeofvision-in-patients-implanted-with-aberration. Accessed May 30, 2020.

25.0 Confidentiality, Privacy and Data Management

IMPORTANT: The following section is required for all locations EXCEPT Penn State Health and the College of Medicine. Penn State Health and College of Medicine should skip this section and complete "HRP-598 Research Data Plan Review Form." In order to avoid redundancy, for this section state "See the Research Data Plan Review Form" if you are conducting Penn State Health research. Delete all other sub-sections of section 22.

For research being conducted at Penn State Health or by Penn State Health researchers only: The research data security and integrity plan is submitted using "HRP-598 – Research Data Plan Review Form."

Refer to Penn State College of Medicine IRB's "Standard Operating Procedure Addendum: Security and Integrity of Human Research Data," which is available on the IRB's website. In order to avoid redundancy, for this section state "See the Research Data Plan Review Form" if you are conducting Penn State Health research. Delete all sub-sections of section 22.

For all other research: complete the following section. Please refer to PSU Policy AD95 for information regarding information classification and security standards and requirements. It is recommended that you work with local IT staff when planning to store, process, or access data electronically to ensure that your plan can be carried out locally and meets applicable requirements. If you have questions about Penn State's Policy AD95 or standards or need a consultation regarding data security, please contact security@psu.edu.