Study Protocol and Statistical Analysis Plan for NCT 05265624

The Moran AMD Genetic Testing Assessment Study (MAGENTA)

The following pages contain the IRB approved study protocol and statistical analysis plan at the most recent renewal approved on 12/11/2024.

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IRB_00150093 **Created:** 12/15/2021 2:30 PM

PI: Paul Bernstein M.D. **Submitted:** 1/31/2022

Title: Magenta: The Moran AMD Genetic Testing Assessment Study

IRB_00150093
1. Contacts and Title

1. Study Introduction

1. **Responsible Investigator:**
   Paul Bernstein

Email	Training	CoI Date
paul.bernstein@hsc.utah.edu	7/7/2024 MCG	7/18/2025

a. **Position of the Investigator:**

- (●) **Faculty or** Non-Academic Equivalent
- ( ) Student
- ( ) Staff
- ( ) Resident/Fellow
- ( ) Other

2. **Contact Persons for the Responsible Investigator:**

Name	Email	Training
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Maria Maloney	maria.maloney@hsc.utah.edu	10/25/2022 MCG
Elizabeth Nuttall	Elizabeth.Nuttall@hsc.utah.edu	1/4/2023 MCG
Katie Rogers	katie.rogers@utah.edu	6/5/2025 MCG

3. **Guests of the Responsible Investigator:**

Last Name	First Name	E-Mail

There are no items to display

4. **What type of application is being submitted?**
   New Study Application (or Amendment/Continuing Review)

5. **Title Of Study:**
   Magenta: The Moran AMD Genetic Testing Assessment Study

6. **Study Purposes and Objectives:**

This is a follow up study to our Pilot Study IRB # 60413 - Value of genetic counseling and testing for patients who would like to know more about their personal risk of AMD.

Primary Outcome: Change over 1 year in skin carotenoid status in response to genetic risk disclosure

We hypothesize that disclosure of high AMD risk will motivate subjects to make lifestyle changes that will improve the carotenoid levels in the subjects' skin as assessed by Raman spectroscopy and reflectance relative to lower risk disclosure (primary) or deferred disclosure (secondary). We will also compare disclosure of any AMD risk versus deferred disclosure.

Secondary Outcome: Change over 1 year in ocular and serum carotenoid status in response to genetic risk disclosure

We hypothesize that disclosure of high AMD risk will motivate subjects to make lifestyle changes that will improve the carotenoid levels in the subjects' macula and serum as assessed by autofluorescence intensity and lifetime imaging (macula) and HPLC (serum) relative to lower risk disclosure or deferred disclosure.

Exploratory Outcomes:

a. **Correlations of AMD risk with biomarker and imaging data** - We will conduct exploratory analyses to correlate the various AMD risk alleles singly and in aggregate with our baseline measures of ocular and systemic carotenoid status to ascertain whether or not AMD-associated genetic risk factors influence carotenoid levels. We will also correlate our AMD genetic risk profiles with FLIO imaging to learn if there is a genetic basis for the AMD-associated FLIO patterns that we observe in the long spectral channel (LSC) in up to 1/3 of clinically normal middle-aged individuals and to learn if lifestyle changes alter these patterns.

b. **Psychological and behavioral surveys** - Various standardized surveys (HADS and IES) to evaluate the impact of genetic risk communication and to identify participants who may benefit from psychological counseling

7. Is this a multi-site study, where more than one site needs IRB approval?

○ Yes ● **No**

8. Background and Introduction:

Grant Congruency:

The research goals & objectives, study design, population and procedures as stated in this IRB application are consistent with the grant, as is the funding award.

Background and Introduction:

In the past two decades, we have learned that variants in CFH, ARMS2/HTRA1 and other genetic loci are major risk factors for age-related macular degeneration (AMD) and that nutritional supplementation with AREDS2 antioxidant vitamins, minerals, and carotenoids could slow the progression of this blinding disorder. Despite recommendations by the American Academy Ophthalmology (AAO) against routine genetic testing for AMD risk, many members of the public express an interest in pursuing such testing, and direct-to-consumer laboratories already market them commercially. The AAO's expert panel did not assert that these tests do not accurately reflect eventual risk of visual loss from AMD, but rather that there is no proof that knowledge of AMD risk has any quantifiable impact on behavior that could mitigate the incidence of AMD in their senior years.

A prospective study to show that knowledge of AMD risk could decrease incidence of AMD decades later would settle this controversy and would be consistent with research recommendations of the AAO expert panel, but it is not currently feasible due to the large number of subjects and prolonged time required. Instead, we propose a shorter, Phase 2 randomized clinical trial to study if quantifiable biomarkers of healthy behavior (skin and ocular carotenoid levels) improve in response to knowledge of AMD risk.

We hypothesize that compared to subjects who have deferred disclosure or who are informed of low risk, individuals informed of a high risk of eventual AMD will be more likely to make sustained changes in behavior associated with decreased incidence of AMD later in life. Healthy behaviors include: smoking cessation, weight loss, decreased light exposure, and diets rich in carotenoids. These lifestyle changes all result in increased levels of lutein, zeaxanthin, and other carotenoids, and we have shown in pilot studies that such changes in systemic carotenoid status can be reproducibly and reliably measured in the skin by resonance Raman spectroscopy (RRS) within 1-2 months. Besides RRS, we will also assess ocular and systemic carotenoid status with skin reflectance spectroscopy (RS), macular autofluorescence imaging (AFI) and fluorescence lifetime imaging ophthalmoscopy (FLIO). The results of this study will then be used to design a future Phase 3 multicenter trial.

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2. Study Location and Sponsors

1. **Add all locations applying for approval of research via the University of Utah IRB or Human Research Protection Program (HRPP).**

   Click the appropriate button(s) below to add locations:

	Site Name	Investigators Name	Covered Entity	Sub Sites
View	University of Utah	Paul Bernstein	Yes	

2. **Will a Central IRB (CIRB) or Single IRB (SIRB) model be used for review of this study for the sites listed in this application?**
   ○ Yes ● **No**

3. **Indicate the source(s) of funding obtained or applied for to support this study.**

	Sponsor	Sponsor Type	Sponsor Contact Information	Prime Sponsor	Prime Sponsor Type	OrgID
View	HEIDELBERG ENGINEERING GMBH	Industry	Heidelberg Engineering GmbH Max-Jarecki-Straβe 8 69115 Heidelberg Germany www.HeidelbergEngineering.com			00017492
View	NIH NATIONAL EYE INSTITUTE	Federal Government				10164

4. **Does this study have functions assigned to a Contract Research Organization (CRO)?**
   ○ Yes ● **No**

5. **Does this study involve use of the Utah Resource for Genetic and Epidemiologic Research (RGE)?**
   Examples: Utah Population Database (UPDB), Utah Cancer Registry (UCR), All Payers Claims Database (APCD), etc.
   ○ Yes ● **No**

Addition of a Site

1. **Site Name:**
   University of Utah

2. **Site Principal Investigator**
   ☑ **Mark if Same as Responsible Investigator (syncs with investigator on the first page)**
   Paul Bernstein

Email	Training	CoI Date
paul.bernstein@hsc.utah.edu	7/7/2024 MCG	7/18/2025

   a. **Position of the Site Principal Investigator**
   Faculty or Non-Academic Equivalent

   b. **Will the Site PI consent participants?** ○ Yes ● **No**

3. **Site Contact Persons, if different from the Site PI:**
   ☑ **Mark if Same as Contacts for Responsible Investigator (syncs with contacts on the first page)**

Name	Email	Training
Susan Allman	susan.allman@hsc.utah.edu	1/30/2023 MCG
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Maria Maloney	maria.maloney@hsc.utah.edu	10/25/2022 MCG
Elizabeth Nuttall	Elizabeth.Nuttall@hsc.utah.edu	1/4/2023 MCG
Katie Rogers	katie.rogers@utah.edu	6/5/2025 MCG

4. **Site Staff and Sub-Investigators**

Name	Email	Training	Obtaining Consent	CoI Date
Emmanuel Kofi Addo	u1272149@utah.edu	9/13/2022 MG	☐	1/13/2025
Karen Gutierrez	u0740625@umail.utah.edu	4/7/2025 MCG	☐	6/9/2025
Gregory Hageman	gregory.hageman@hsc.utah.edu	6/7/2024 MG	☐	7/16/2025
Mary Elizabeth Hartnett	me.hartnett@hsc.utah.edu	11/16/2022 MCG	☐	12/4/2024
Lucia Lucci	lucia.lucci@utah.edu	8/2/2024 MCG	☑	4/24/2025

Name	Email	Training	Obtaining Consent	CoI Date
Lisa Ord	lisa.ord@hsc.utah.edu	9/18/2024 MG	☐	9/5/2024
Kelliann Ordonez	kellian.farnsworth@hsc.utah.edu	11/26/2024 MCG	☑	4/29/2025
Marcela Pasaye	marcela.pasaye@utah.edu	7/31/2023 SMCG	☐	7/18/2025
Emily Spoth	emily.spoth@hsc.utah.edu	7/8/2024 MG	☐	7/23/2025

5. **Site Guests:**

Name	Email	Training

There are no items to display

6. **Select HIPAA coverage for this study:**
Study procedures will be conducted within a HIPAA Covered Entity at this site (HIPAA Privacy Rule applies)

7. **Select the study procedures that will be conducted at this site:**

- Recruitment
- Consent/Enrollment
- Research observation/intervention with participants
- Data collection
- Data analysis

Do you have an enrollment goal or anticipated enrollment number for this site?

- ● **Yes**
- ○ No

Enrollment Number:
80 evaluable patients

8. **Select the University of Utah department responsible for this research:**
OPHTHALMOLOGY-CLINICAL STUDIES

9. **Add any additional sites that are part of this performance group**
There are no items to display

Sponsor Information

a. Are you receiving award or contract management for the sponsored funds through the University of Utah Office of Sponsored Projects?

◯ Yes ● **No**

If no, indicate how the funds are being received:
Other

If 'Other', please explain how funds are being received:
Heidelberg has provided Dr. Bernstein with a beta version of the macular pigment imaging (MOPD) software and FLIO imaging system at no cost. They must be used under IRB approval as they are not yet FDA approved.

Heidielberg will not be receiving data from this study and has no interest in the conduct of the study.

* **Sponsor:**
HEIDELBERG ENGINEERING GMBH

Previously, the following data was entered on your IRB application:

Sponsor Contact Information:
Heidelberg Engineering GmbH
Max-Jarecki-Straβe 8
69115 Heidelberg
Germany
www.HeidelbergEngineering.com

Sponsor Information

a. Are you receiving award or contract management for the sponsored funds through the University of Utah Office of Sponsored Projects?

● **Yes** ○ No

If yes, select the associated OSP Proposal ID/DSS through eAward to link it to the ERICA system.

You must have a fully approved Proposal ID/DSS number through eProposal which will show up in eAward after OSP has integrated the ID. To access the eAward application, use the instructions on the OSP website.

Link to a Proposal ID/DSS through eAward

Proposal ID/DSS: 10060978
PI: BERNSTEIN,PAUL S
Sponsor: NIH NATIONAL EYE INSTITUTE
Prime Sponsor:
Department:
Short Title: PRESYMPT GENETIC RISK ASSESS
Sponsor Award Number: 5R21EY033579-02
Type: Federal Government
Award Start Date: 5/1/2022
Award End Date: 4/30/2025
Prime Sponsor Type:

3. Participants

1. **Ages of Participants:**

   18 and older (Consent form needed)

2. **Specific age range of participants (e.g., 7-12 years old, 60+, etc.):**
   18-64

3. **Indicate any vulnerable participant groups (other than children) included:**

   None

   If "Other", please specify:

   If "None" and no children are involved, answer the following question.
   Has the participant selection process overprotected potential subjects who are considered vulnerable so that they are denied opportunities to participate in research?
   ○ Yes ● **No**

4. **Number of participants to be included and/or enrolled in this entire study, across all study locations:**
   approximately 85, with a goal of 80 evaluable participants

5. **Characteristics of Participants/Inclusion Criteria:**

   1. Participants must be between 18 and 64 years of age.
   2. They must also be Caucasian as this genetic test is only validated in Caucasians.
   3. They can have a positive family history of AMD but this is not necessary.

6. **Participant Exclusion Criteria:**

   1. Personal history of AMD
   2. Non Caucasian
   3. Employee of the Moran or other eye care practice (likely to have more knowledge about AMD than a layperson)
   4. Personal history of prior genetic testing results for AMD risk

5. Anticipated cataract surgery in the upcoming year (can affect Macular Pigment measurement)

6. Major psychiatric disorder

7. **Is a substantial percentage of the participant population anticipated to be non-English speaking?**

○ Yes ● **No**

4. Study Information

1. **Design of Study (select all that apply):**

   ☐ **Non-Experimental and/or Descriptive Research Design:**

   There are no items to display

   ☑ **Experimental and/or Interventional Research Design:**

   Prospective Social/Behavioral Intervention or Experiment

   Is the prospective social/behavioral intervention or experiment intended to evaluate a health-related outcome?
   ● **Yes** ○ No

   ☐ **Development of a research resource (repositories, databases, etc.)**

   There are no items to display

   ☐ **Other**

2. **Does your study involve the use of any placebo?**
   ○ Yes ● **No**

3. **Length of entire study, from initiation through closeout:**
   3 years

4. **How will participants be recruited or identified for inclusion in the study?**

   a. **Select all methods that will be used:**

   In-person contact (e.g., patients, students, etc.)

   Referrals

   Written or electronic record review

   Written advertising (flyers, brochures, website postings, newspaper ads, etc.)

   From a database or participant pool for which participants have given prior permission to be contacted for research studies

   b. **Describe the recruitment/participant identification process in detail (e.g. who will review charts or records, who can refer participants to the study, where will flyers be posted, how often will recruitment letters be sent, when will follow-up phone calls be made, etc.):**

   Flyers will be placed around the Moran Eye Center in waiting areas as well as clinics. Patients and family members can self-refer, or the treating physician can refer them to the study. Flyers will be placed in university non-ophthalmological clinics as well. Also, flyers will be given to local eye centers, newspapers, and social media that are not necessarily university affiliates.

   Some patients have asked about a study of this nature in the past, and they will be re-contacted from our list to see if they are still interested in participating.

   Interested participants will be referred to the study coordinator who will contact them to explain the study and determine if the patient meets initial eligibility requirements.

5. **How will consent be obtained?**

Informed Consent Process (with or without a document)

6. **Describe all the procedures chronologically, from screening/enrollment through study closeout, which will be completed in the research project.**

Screening Visit (by telephone)

Participants who agree to participate in the study will complete a telephone-based screening to ensure they meet inclusion criteria. If eligible, individuals will be asked to schedule an in-person baseline visit.

Baseline Visit - Month 0 (In person)

a. An authorized member of the study staff will obtain written informed consent.

b. Participants height and weight measurements will be recorded for body mass index (BMI).

c. Participants will complete nutritional and social surveys. Participants may choose to complete the surveys electronically or on paper either at their study visits or in advance of each visit.

   a. Two validated instruments will be used to evaluate the psychological impact of genetic risk communication and identify participants who may benefit from psychological counseling. The Hospital Anxiety and Depression Scale (HADS) is a frequently used measure of levels of anxiety and depression in non-psychiatric patients. The second measure, the Impact of Events Scale (IES) evaluates the distress impact of a specific event (Horowitz et al., 1979), in this case genetic risk knowledge, may evoke. Both scales are based on feelings and actions over the past week, and both have been used extensively in genetic counseling research (Kasparian et al., 2007).

   b. The Tufts LZQ Screener will be used to assess dietary carotenoid intake.

   c. Additional Survey Questions regarding AMD knowledge and lifestyle will be administered.

d. Participants will have skin carotenoid measurements taken by Resonance Raman Spectroscopy (RRS) and Reflectance Spectroscopy (RS). The RSS instrument is an investigational device. The RS instrument is commercially available.

e. Participants will have ocular carotenoid imaging by Macular pigment imaging and Fluorescense Lifetime Imaging Ophthalmoscopy (FLIO). Macular pigment images are taken with the standard clinical camera, but uses a software program that is not FDA approved. The FLIO camera is also investigational.

f. Participants will have Color Fundus Photography, Autofluorescence (AF) and optical coherence tomography (OCT) performed on standard clinical imaging systems. Images will be reviewed after the visit to rule out AMD or other macular pathology that would preclude eligibility.

g. Participants will have High-Resolution OCT Imaging. This camera uses a slightly different wavelength than the standard OCT camera and is not FDA approved.

h. Participants eyes will be dilated for the imaging.

i. Participants will have their blood drawn for genetic testing (10mL) and to measure serum carotenoid levels (10mL). Genetic samples will be analyzed in the Hageman research lab. Carotenoid samples will be analyzed in the Bernstein research lab. Results from these tests will not be entered into the medical record. These types of testing are not available at commercial CLIA-certified labs.

j. Study Coordinator will review AMD risk factors and reduction strategies with participants.

Disclosure - Month 1 (in person)

a. Participants who are eligible after review of ophthalmic images will be randomized in a 3:1 ratio to the immediate disclosure or deferred disclosure group.

b. The licensed ophthalmic genetic counselor will meet with subjects to inform them of their disclosure assignment, review the AMD risk factors and reduction strategies with participants and address any questions or concerns. The genetic counselor will also ask participants to complete the Impact of Genetic Counseling Survey.

c. The genetic counselor will disclose and discuss genetic testing results with subjects who were assigned to immediate disclosure.

d. The study coordinator will inform participants which eye has been assigned as their study eye.

e. Participants in both groups will have skin carotenoid measurements taken by RRS and RS.

f. Participants in both groups will complete the Nutritional, Lifestyle, HADS and IES surveys.

Month 3 Visit (in person)

a. Participants in both groups will complete the Nutritional, Lifestyle, HADS and IES surveys.

b. Participants in both groups will have skin carotenoid measurements taken by RRS and RS.

Month 6 Visit (in person)

a. Participants in both groups will complete the Nutritional, Lifestyle, HADS and IES surveys.

b. Participants in both groups will have skin carotenoid measurements taken by RRS and RS.

c. Participants will have dilated ocular carotenoid imaging by Macular Pigment and Fluorescense Lifetime Imaging Ophthalmoscopy (FLIO).

d. Participants will have height and weight measured for body mass index (BMI)

e. Participants will have their blood drawn (10mL) to measure serum carotenoid levels.

Month 9 Visit (in person)

a. Participants in both groups will complete the Nutritional, Lifestyle, HADS and IES surveys.

b. Participants in both groups will have skin carotenoid measurements taken by RRS and RS.

Month12 Visit (closeout) (in person):

a. Participants will complete the Nutritional, Lifestyle, HADS, IES and AMD Risk surveys.

b. Participant skin carotenoid levels will be measured by RRS and RS.

c. Participant ocular carotenoid levels will be measured by dilated Macular Pigment and FLIO imaging.

d. Participants will have their blood drawn (10mL) to measure serum carotenoid levels.

e. Height and weight measurements will be taken for BMI.

f. The ophthalmic genetic counselor will meet all participants and have them complete the Impact of Genetic Counseling Survey. She will meet with the participants in the late disclosure group to discuss their test results and address any questions or concerns.

Adverse Events

Any unexpected adverse events and all serious adverse events will be evaluated by the PI and reported to the DSMB. S/AEs will also be reported to the IRB per IRB reporting guidelines.

Visit	**Screening/ Baseline**	**Disclosure**	**Monitoring**			**Closeout**
Month	**0**	**1**	**3**	**6**	**9**	**12**
Informed Consent	X					
Review of AMD fact sheet	X	X				
Blood or saliva collection for genetic testing	X					
Color fundus photography, Autofluorescence and OCT to confirm eligibility	X					
Randomization		X				
Disclosure (or deferral) of genetic testing results		X				X
Impact Value of Genetic Counseling Survey		X				X
Skin carotenoid levels by RRS and RS	X	X	X	X	X	X
Ocular carotenoid levels by Macular Pigment and FLIO	X			X		X
High-Resolution OCT imaging	X					
AMD knowledge survey	X					X
Lifestyle Questions	X	X	X	X	X	X
LZQ^{TM} Questionnaire	X	X	X	X	X	X
Hospital Anxiety & Depression Scale (HADS)	X	X	X	X	X	X
Impact of Events (IES)	X	X	X	X	X	X
Serum carotenoid levels	X			X		X

Height and weight measurement for BMI	X			X		X

Participants will be provided a letter notifying them of their carotenoid skin level results after study completion.

7. **Are all procedures for research purposes only (non-standard or non-standard of care procedures)?**
   ● **Yes** ○ No

   If no, list the procedures that are performed for research purposes only (non-standard or non-standard of care procedures):

8. **Is there a safety monitoring plan for this study?**
   ● **Yes** ○ No

9. **Provide a summary of the statistical methods, data analysis, or data interpretation planned for this study. Factors for determining the proposed sample size (e.g., power) should be stated.**

   Feasibility Aim: We will monitor the proportion of people who complete the monitoring and closeout visits by trial arm assignment and provide estimates and 95% confidence intervals for those rates.

   Analytic Aim: Our primary analysis will compare follow-up carotenoid level between the randomized early and late disclosure groups while accounting for AMD risk (categorized as high, medium or low) and baseline carotenoid level under the longitudinal model:

   Sample Size and Power: Our power calculation for the primary and secondary comparisons utilizes the pilot study data. We found that with 60 patients (after 25% drop-out from 80 enrolled patients) and an allocation ratio of 3:1 to early and late disclosure groups, there is 80% power to detect a 40.5% difference for our primary comparison. This compares favorably with the >100% changes achievable with diet alone.

   Specific Aim 2: AMD risk alleles will be individually tested for associations with skin carotenoid status and MPOV using simple linear regression. We will use this step as a variable selection for a multivariable regression. Alleles with p-values less than 0.05 in the univariable analyses will be included in the final multivariable regression, which will additionally control for baseline measures of ocular and systemic carotenoid status.

   Effect of Gender as a Biological Variable: Since men and women are anticipated to be enrolled in a 50:50 ratio, gender as a biologic variable will be assessed in all analyses.

   Missing data: To assess risk of bias due to missing data, patterns of missing measurements across follow-up visits will be displayed for the primary and secondary outcomes. Reasons for missing measurements will be tabulated with a focus on differentiating missed measurements for logistical reasons from dropout or intermittent missingness potentially related to the condition of the patient.

   Because we are using restricted maximum likelihood estimation, our statistical inferences for the primary and the numeric secondary outcomes will remain valid if missing data follows a missing at random (MAR) pattern (Little & Rubin, 2014). Nonetheless, if more than 10% of subjects have missing outcome measurements for any of the follow-up visits, i.e. we have less than 80 complete patients, or if comparisons of baseline characteristics between patients with missing and non-missing measurements indicate significant imbalances, we will apply multiple imputation (MI) to further address missing outcome scores (Rubin, 2004). MI incorporates baseline and follow-up factors beyond the variable being analyzed into imputation models to account for dependence of missing data on other factors. We will use the fully sequential imputation method to generate imputed values (Van Buuren, 2007).

Consent Process

1. **The following investigators and internal staff will obtain consent (as indicated on the Study Location and Sponsors Page):**

Lucia Lucci	University of Utah
Kelliann Ordonez	University of Utah

List by name, role, and affiliation any others who will obtain consent (e.g. Dr. John Smith, Co-Investigator, etc.).

2. **Describe the location(s) where consent will be obtained.**
   At the Moran Eye Center

3. **Describe the consent process(es), including the timing of consent. Describe whether there is a waiting period between the consent process and obtaining consent from the participant (i.e., any time between informing participants and actually obtaining consent).**
   Participants who meet pre-screening criteria will be invited to schedule a baseline visit where written informed consent will be obtained. There will be adequate time between pre-screening and baseline for the participant to review the consent.

4. **Describe what measures will be taken to minimize the possibility of coercion or undue influence.**
   It will be explained to participants that they may not benefit directly from participating and that they can still receive the same standard of care should they decide not to participate.

5. **Describe the provisions that are made to allow adequate time to exchange information and questions between the investigator and participant.**
   The investigators will allow as much time as needed when obtaining consent and will encourage the participants to ask questions before they decide whether or not to participate.

6. **Will a legally authorized representative (LAR) be used?**
   ○ Yes ● **No**

7. **Will a language other than English be used to obtain consent?**
   ○ Yes ● **No**

8. **Are you requesting that documentation of informed consent be waived by the IRB (a consent process in place, but no documentation of consent, e.g. questionnaire cover letter, web-based consent, consent without signature, etc.)?**
   ○ Yes ● **No**

   If yes, complete the following:

   a. **Explain why the waiver of consent documentation is being requested.**

   b. **Justification for the waiver is one of the following:**
   There are no items to display

5. Data Monitoring Plan

1. **Privacy Protections:** Privacy refers to persons and to their interest in controlling access of others to themselves. Privacy can be defined in terms of having control over the extent, timing and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. **What precautions will be used to ensure subject privacy is protected?**

Select all that apply:

The research intervention is conducted in a private place

Discussing the study with participants individually instead of in front of a group

Other or additional details (specify):

We will not discuss genetic results with anyone other than the participant to whom they belong or authorized members of the study team.

2. **Confidentiality Precautions:** Confidentiality is an extension of the concept of privacy; it refers to the subject's understanding of, and agreement to, the ways identifiable information will be stored and shared. Identifiable information can be printed information, electronic information or visual information such as photographs. **What precautions will be used to maintain the confidentiality of identifiable information?**

Select all that apply:

Storing research data on password protected computers or in locked cabinets or offices

Other or additional details (specify):

The Genetic testing in this study is done by a research lab that is not CLIA certified. Results from the research lab will be kept in the research record and be disclosed to participants, but will not be included in the electronic medical record.

Genetic testing for AMD risk is not available through a CLIA-certified lab so we will be unable to refer participants for confirmatory testing.

The research lab will not identify incidental genetic findings.

3. **Will photos, audio recordings, or video recordings, or medical images of participants be made during the study?**

● **Yes** ○ No

If yes, describe the recording/images and what will become of them after creation (e.g., shown at scientific meetings, stored in the medical/research record, transcribed, erased, etc.):

Ophthalmic images obtained on standard clinical devices will be stored in the electronic medical record. Ophthalmic images obtained on the investigational devices will be stored on the device.

4. **How will study data and documentation be monitored throughout the study?**

Select all that apply:

Periodic review and confirmation of participant eligibility

Periodic review of informed consent documentation

Periodic review of the transfer/transcription of data from the original source to the research record

Confirmation that all appropriate information has been reported to the sponsor, oversight agencies (such as the FDA), and/or IRB

Other additional details (specify):

5. **Who will be the primary monitor of the study data and documentation?**

Select all that apply:

Study Coordinator or Research Nurse

Data (and safety) Monitoring Board or Committee

Other or additional details (specify):

6. **How often is study data and documentation monitoring planned (e.g., monthly, twice a year, annually, after N participants are enrolled, etc.)?**
Data and safety monitoring will occur every 6 months.

Safety Monitoring Plan

1. **Describe the safety monitoring entity for this study:**

   a. **Select all that apply:**

   Principal Investigator

   Data and Safety Monitoring Board or Committee

   Please specify:

   b. **Describe the expertise and affiliation of the individual(s) selected above who will monitor the study:**

   Although this study does not require a Safety Monitoring plan, in order to fulfill NIH requirements, we will recruit a data safety monitoring committee consisting of an ophthalmologist and a social worker not otherwise involved in recruitment or study procedures who will review all serious adverse events (SAEs) every six months and who will recommend early termination of the study if any concerning safety signals are discerned.

2. **Describe the data and events that will be monitored and reviewed (e.g., vital signs, safety blood labs, depression scales, neurological exams, types of adverse events, etc.):**

   Unexpected adverse events and all serious adverse events

3. **Describe the types of reports that will be produced by the monitoring entity (e.g., safety, study progress, interim analysis, etc.):**

   DSMB reports

4. **Describe the specific triggers or stopping rules for the study:**

   a. **Under what conditions will a participant be withdrawn from the study?**

   - Patient withdrawal of consent at any time.
   - Investigator determines it is in the best interest of the patient.
   - Patient non-compliance with study visits or testing.

   b. **Under what conditions will the study be modified or stopped?**

   If any concerning safety signals are discerned

5. **How often will the data and events be reviewed by the monitoring entity (e.g., after every 5 submits, monthly, quarterly, twice a year, etc.)?**
   Every 6 months

6. Risks and Benefits

1. Describe the reasonable foreseeable risks or discomforts to the participants:

There is a risk of loss of confidentiality from medical record review, but procedures are in place to prevent any such loss.

There will be brief discomfort from the needle stick. It is possible that there will be bruising or oozing of blood afterwards. Rarely, there is a risk of infection.

There are no expected side effects from the light exposure for the skin measurement. It is important not to look at the laser directly for a long period of time.

Participants eyes will be dilated for ophthalmic imaging and macular pigment measurements. Dilation causes mild blurry vision and light sensitivity for several hours. Rarely there can be an allergic reaction to or closed angle glaucoma from the dilating drops, or a corneal scratch from rubbing the eyes. High blood pressure, irregular heartbeat or glaucoma may worsen when dilating drops are used. This can be managed and participants are counseled to discuss this with the study coordinator. Participants are advised to wear sunglasses after their visit to help with comfort.

Light levels projected on the retina in this study for macular pigment measurements and ophthalmic photos are well within established safety limits. Participants may notice a central dark spot in their vision similar to the afterimage generated by a camera flash. This afterimage will fade away within approximately 5 minutes.

Some subjects may experience anxiety or distress upon learning their genetic risk of AMD or their assignment to the deferred disclosure group. A trained genetic counselor is available to address any subject questions or concerns about their genetic testing results. If subjects experience significant distress or anxiety, they will be referred to Dr. Lisa Ord for psychological counseling at no cost to the participant.

2. Describe the potential benefits to society AND to participants (do not include compensation):

Knowledge of genetic risk for AMD could encourage the subjects to make positive lifestyle changes that could lower their risk of vision loss later in life.

Positive results from this study could lead to wider use of validated AMD genetic risk testing that would encourage high-risk individuals to make lifestyle changes that could lower their risk of vision loss later in life. If negative results are obtained, then we will have provided further evidence that the AAO's stance against routine genetic testing for AMD risk in asymptomatic individuals is correct.

3. Are there any costs to the participants from participation in research?

○ Yes ● **No**

If yes, specify:

4. Is there any compensation to the participants?

● **Yes** ○ No

a. **If yes, answer the following:**

Specify overall amount:
$200.00

b. **Specify when participants will be paid (e.g. at each visit, at end of study, etc.):**
Participants will be paid at the first 2 study visits, then at their final study visit.

c. **If applicable, please specify payment by visit or other time interval (e.g. $10 per visit, etc.):**
$40.00 for the first 2 visits. $30.00 for the remaining 4 visits.

d. **If applicable, explain plan for prorating payments if participant does not complete the study:**
Participants will receive payment for each visit completed.

7. HIPAA and the Covered Entity

1. **Does this study involve Protected Health Information (PHI) or de-identified health information?**
   ● **Yes** ○ No

   a. **Select the method(s) of authorization that will be used:**

   (Consent and) Authorization Document

   Waiver or Alteration of Authorization

   b. **Will PHI be disclosed outside the Covered Entity?**
   ● **Yes** ○ No

   To whom?
   NIH, FDA, Heidelberg Engineering

   And for what purposes?
   The NIH, FDA and Heidelberg have the right to inspect the research record, although we do not plan to send PHI directly to them.

   Heidielberg will not be receiving data from this study and has no interest in the conduct of the study.

Does this study involve any of the following:

2. **The investigational use of a drug?**
   ○ Yes ● **No**
   Mark yes, for an expanded access application.

3. **The investigational use of a medical device or humanitarian use device?**
   ● **Yes** ○ No
   Mark yes, for an expanded access application.

4. **The investigational use of a dietary supplement, food, or cosmetic?**
   ○ Yes ● **No**

5. **Is this an investigator-initiated drug or device trial lead by the Principal Investigator'**
   ● **Yes** ○ No
   All investigator-initiated drug or device trials are required to have a full research protocol attached to the Documents and Attachments page.

6. **Will this study involve the use of an imaging modality from the department of Radiology?**
   ○ Yes ● **No**

7. **Exposure to radioisotopes or ionizing radiation?**
   ○ Yes ● **No**

8. **Genetic testing and/or analysis of genetic data?**
   ● **Yes** ○ No

9. **Creating or sending data and/or samples to a repository to be saved for future research uses?**
   ○ Yes ● **No**

10. **Are you:**
    - **Collecting samples of blood, organs or tissues from participants for research purposes;**
    - **Introducing Recombinant or Synthetic Nucleic Acids (e.g. viral vectors, oligonucleotides) or cells containing recombinant nucleic acids (e.g. CAR-T) into participants; OR**
    - **Introducing other biological materials (e.g. bacteria, viruses) into participants.**

    ● **Yes** ○ No

11. **Does this study involve any of the following?**
    - **Cancer Patients**
    - **Cancer Hypothesis**
    - **Cancer risk reduction**
    - **Cancer prevention**

    ○ Yes ● **No**

12. **Any component of the Clinical and Translational Science Institute (CTSI)?**
    ● **Yes** ○ No

    The Clinical Research Unit (CRU)?
    ○ Yes ● **No**

IRB_00150093 **Created:** 12/15/2021 2:30 PM

PI: Paul Bernstein M.D. **Submitted:** 1/31/2022

Title: Magenta: The Moran AMD Genetic Testing Assessment Study

Request for Waiver or Alteration of Authorization

Request for Waiver of Authorization for Recruitment Only

This option must only be used if you are reviewing PHI in order to identify eligible participants BEFORE approaching them to obtain consent and authorization. All other waiver requests must be entered below.

Waiver of Authorization for Recruitment Requested

Other Requests for Waivers of Authorization:

- *Click "Add" below to add a new waiver request to this application.*
- *Click the waiver name link to edit a waiver that has already been created.*
- *To delete a waiver request, contact the IRB.*

Date Created	Type of Request	Purpose of Waiver Request
There are no items to display		

Request for Waiver or Alteration of Authorization

Request for Waiver of Authorization for Recruitment Only

The PI must agree to the terms of this waiver request as described on this page. When the PI uses the "Submit" activity to submit the application for IRB review, a checkbox to accept the terms will be available in the "Submit" activity window.

This waiver request includes justification for waivers of consent for recruitment only, according to 45 CFR 46.116(d).

Terms for the Waiver of Authorization:

- The purpose of this waiver of authorization is to allow for the use of PHI in order to identify and recruit individuals who may be eligible to participate in the specific research described in this IRB application. The waiver of authorization is necessary to accommodate this minimal-risk research activity prior to seeking a full authorization from research participants.
- Methods for identifying individuals may include the following:
  - Reviewing medical charts
  - Reviewing databases that include PHI
  - Reviewing other medical- or health-based documents that include PHI
- Identifiable information used under this waiver may include the following, as this is the minimum necessary for identifying eligible individuals:
  - Name
  - Contact information, such as phone number, address, or email address
  - An ID number, such as MRN or SSN
  - Date of birth
  - Medical and health information that may determine study eligibility
- Any PHI recorded by the study team will only be used for recruitment and determining study eligibility. After this has been completed, the PHI must be removed from the research record or destroyed, unless the participants have given authorization for continued use of the PHI.
- PHI will only be viewed by approved members of the study team and will not be disclosed for research purposes to any individual or institution without the participants' authorization for such use and disclosure of the PHI.
- PHI will be stored in a secure manner according to HIPAA privacy and security provisions.

Investigational Use of a Device

1. What is the initial risk determination of the device study according to the investigator and/or sponsor?

The study is a non-significant risk (NSR) device study.

a. Provide IDE (or HDE) Number(s) for significant risk devices:

IDE/HDE #	Device Name	IDE/HDE Holder

There are no items to display

b. Attach verification of the IDE (or HDE) number for significant risk devices to the Documents and Attachments page. Please check the method by which you choose to verify the IDE (or HDE) number:

There are no items to display

2. Describe the plan to control, store, and dispense the investigational device or humanitarian use device. This plan should ensure that the device is only used by qualified investigator(s) for the participants enrolled in this research project.

There are four investigational devices being used in this study. The first is the Heidelberg MOPD module software program, the second is the Heidelberg FLIO system and the third is the Heidelberg High-Resolution OCT system. Dr. Bernstein personally oversees the use of the Heidelberg systems. He does not allow use of these devices for routine medical care.

The third investigational device to be used in this study is the RSS skin scanner. Dr. Bernstein previously held a patent for the scanner and controls access to the scanner and trains study staff in it's use. He does not allow use of the skin scanner for routine medical care, not would it be relevant to standard care.

IRB_00150093 **Created:** 12/15/2021 2:30 PM

PI: Paul Bernstein M.D.

Submitted: 1/31/2022

Title: Magenta: The Moran AMD Genetic Testing Assessment Study

IRB_00150093
- - Non Significant Risk Device

Non-Significant Risk Device

Review the following definition of a non-significant risk (NSR) device:

1. The medical device is not a significant risk device, because all of the following are true:
    a. The medical device is NOT intended as an implant that presents a potential for serious risk to the health, safety, or welfare of a subject.
    b. The medical device is NOT purported or represented to be for a use in supporting or sustaining human life that presents a potential for serious risk to the health, safety, or welfare of a subject.
    c. The medical device is NOT for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health that presents a potential for serious risk to the health, safety, or welfare of a subject.
    d. The medical device is does NOT otherwise present a potential for serious risk to the health, safety, or welfare of a subject.
2. The medical device is not banned.

1. **Provide justification of why the investigational medical device used in this study meets the definition of a NSR device.**

In this study, we are using the Heidelberg MultiColor Spectralis instrument to measure and image macular pigment optical density (MPOD). This commercial device is FDA cleared for use in eye clinics throughout the United States to image the retina in various ways. Heidelberg has provided us with a beta version of a software package which analyzes autofluorescence images to measure MPOD. Since this software has not yet been submitted to the FDA for approval, we can use it only under an IRB approved protocol. This software analyzes collected images in a new way, but the actual collection of the images is done in the usual manner for the instrument, so there are no significant risks of harm to the subjects.

Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO), developed by Heidelberg Engineering, is a new imaging technique that may provide more information than current fundus autofluorescence imaging. FLIO allows "reproducible measurements of fluorescence lifetimes of the macular in healthy subjects" (Dysli, C. et al) FLIO is a non-significant risk device exempt from IDE approval. It is not approved for any diagnostic or therapeutic decision and must be used under IRB approval and agreement from Heidelberg.

The Heidelberg high-resolution OCT (HR-OCT) uses a diode light source that more than doubles the axial resolution of the images, allowing unprecedented imaging of the layers of the retina. The Heidelberg Engineering SPECTRALIS HighRes OCT is considered to be a Non-Significant Risk (NSR) device for the following reasons: (1) The technical safety of the device corresponds to the international state of the art for medical devices. It is a variant of the SPECTRALIS, an ophthalmic diagnostic medical device that has been marketed in the USA, the EU and other regions and countries since 2007. During this time there have been no recalls or serious incidents with the SPECTRALIS due to technical hazards. (2) The SPECTRALIS HighRes OCT does not otherwise affect the risk to the user or the study subject: a. Information of the investigational SPECTRALIS HighRes OCT device will not be used to drive clinical decisions in the study. (3) The SPECTRALIS HighRes OCT is non-contact medical device. SPECTRALIS HighRes OCT is not an implant. The SPECTRALIS HighRes OCT does not support or sustain human life. The SPECTRALIS HighRes OCT is a non-contact ophthalmic imaging and analyzing device that supports the user in diagnosing. It uses existing technology and specialized software and does not present an increased risk to health, safety, or welfare of a subject. There is no other potential for serious risk.

The resonance Raman skin scanner measures carotenoids in the skin by shining a blue light on the palm of the hand for about 30 seconds. It is a higher sensitivity research version of the commercially available BioPhotonic scanner made by

NuSkin/Pharmanex. The laser power is less than many laser pointers and is completely safe for prolonged skin exposure, so it poses no significant risk to the subjects.

Genetic Research

1. **Describe the risks to participants in regard to genetic testing, including applicable risks to privacy and confidentiality, as well as psychological and social risks.**

   There is a risk of loss of confidentiality from medical record review, but procedures are in place to prevent any such loss.

   There will be brief discomfort from the needle stick. It is possible that there will be bruising or oozing of blood afterwards. Rarely, there is a risk of infection.

   There are no expected side effects from the light exposure for the skin measurement. It is important not to look at the laser directly for a long period of time.

   Participants eyes will be dilated for ophthalmic imaging and macular pigment measurements. Dilation causes mild blurry vision and light sensitivity for several hours. Rarely there can be an allergic reaction to or closed angle glaucoma from the dilating drops, or a corneal scratch from rubbing the eyes. High blood pressure, irregular heartbeat or glaucoma may worsen when dilating drops are used. This can be managed and participants are counseled to discuss this with the study coordinator. Participants are advised to wear sunglasses after their visit to help with comfort.

   Light levels projected on the retina in this study for macular pigment measurements and ophthalmic photos are well within established safety limits. Participants may notice a central dark spot in their vision similar to the afterimage generated by a camera flash. This afterimage will fade away within approximately 5 minutes.

   Some subjects may experience anxiety or distress upon learning their genetic risk of AMD or their assignment to the deferred disclosure group. A trained genetic counselor is available to address any subject questions or concerns about their genetic testing results. If subjects experience significant distress or anxiety, they will be referred to Dr. Lisa Ord for psychological counseling at no cost to the participant.

2. **Describe the privacy protections in place for participants in regard to genetic testing. This includes how family member privacy will be protected.**
   We will not discuss genetic results with anyone other than the participant to whom they belong or authorized members of the study team.

3. **Are you performing whole genome or whole exome sequencing?**
   ● **Yes** ○ No

4. **Describe the confidentiality protections in place for participants' genetic information. Discuss if and how data will be shared and protected outside the local study team.**
   The Genetic testing in this study is done by a research lab that is not CLIA certified. Results from the research lab will be kept in the research record and be disclosed to participants, but will not be included in the electronic medical record.

   Genetic testing for AMD risk is not available through a CLIA-certified lab so we will be unable to refer participants for confirmatory testing.

   The research lab will not identify incidental genetic findings.

5. **Will incidental findings relevant to individuals or families be communicated to the participants?**
   ○ Yes ● **No**
   If yes, answer the questions below:

   a. **Describe the process for determining which incidental findings will be returned to the participants. Describe the information and expert consultation that will be used to make this determination.**

   b. **Indicate the process that will be used to return information about incidental finding to participants:**
   There are no items to display
   If Other, describe and justify the process that will be used:

6. **Will genetic information or samples be submitted to a national or international database because of this research?**

- ○ Yes
- ● **No**

8. Resources and Responsibilities

1. * **State and justify the qualifications of the study staff:**

   The PI and physician sub-investigators have a medical license to allow them to make medical decisions and provide patient care. They are qualified by certification and experience to conduct the study.

   Study Coordinators have experience in conducting clinical studies and receive protocol specific training from the investigator and other study team members.

   Ophthalmic imagers are qualified by experience and/or certification to conduct protocol specified procedures.

   The genetic counselor is licensed in the state of Utah and experienced in clinical research.

   A graduate student from the Nutrition department with a background in optometry will perform the serum carotenoid analyses and the Spectralis AFI and FLIO imaging and will participate in data analysis and manuscript preparation.

2. * **Describe the training that study staff and investigators will receive in order to be informed about the protocol and understand their research-related duties and functions:**

   Study specific training includes study-specific or staff meetings, e-mail correspondence, and teleconferences. All study staff members and investigators agree to conduct the study according to good clinical practices and the ethical conduct of research. Training documentation, including but not limited to study meetings, GCP certificates and CITI certificates will be maintained in the study file.

3. * **Describe the facilities where the research activities will be performed (e.g. hospitals, clinics, laboratories, classrooms/schools, offices, tissue banks, etc.).**

   Research visits and data analysis will be conducted at the Moran Eye Center.

   Genetic analysis will be conducted at the Moran Eye Center in the Hageman Lab. Serum carotenoind analysis will be conducted at the Moran Eye Center in the Bernstein Lab.

4. * **Describe the medical or psychological resources available at this site (and other participating sites, if applicable) that participants might require as a consequence of the research. If not applicable, please state.**

   Lisa Ord, PhD, LCSW, Associate Professor of Ophthalmology and Visual Sciences at the University of Utah, is Director of the Moran Eye Center's Patient Support Program. She will counsel any subjects who experience anxiety or distress from learning of their genetic risk of AMD or from their assignment to deferred disclosure.

PI: Paul Bernstein M.D. Submitted: 1/31/2022

Title: Magenta: The Moran AMD Genetic Testing Assessment Study

Documents and Attachments

If any of your documents (such as investigational brochures, sponsor protocols, advertisements, etc.) are not available in an electronic format, please scan and save them as PDF files or contact our office for assistance.

Naming Documents: Please use the title field to clearly indicate the content of each form. The name you enter will be listed on your approval letter. Use names that will differentiate from earlier versions.

Examples:
Consent Document Control Group 04/14/05
Consent Document Treatment Group 4/14/05
Sponsor Protocol 04/14/05 Version 2
Assent Document(Highlighted Changes)

Apple/Macintosh Users:MS Word documents must have a .doc file extension. See ERICA home page for instructions.

Print View: IRB Draft Protocol Summary

eProtocol Summary:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Consent Documents, Consent Cover Letters, Consent Information Sheets, Consent Scripts, etc.:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Parental Permission Documents:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Assent Documents:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

VA Consent Documents:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Surveys, Questionnaires, Interview Scripts, etc.:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Full Protocol (company protocol, sponsor protocol, investigator-initiated protocol, etc.):

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Investigational Brochure (IB) for Investigational Drug or Drug/Device Package Insert:

Name	Version	Date Created	Date Modified	Date Approved
There are no items to display				

Grant Application:

The Federal Government is a direct or indirect sponsor of your research. You are required to provide a copy of the grant proposal, grant award, or sub-award.

By submitting to the IRB, you are confirming the grant and the study protocol are consistent (Design, Study Population, Study Objectives and Goals, Test Interventions and Procedures, etc.)

Name	Version	Date Created	Date Modified	Date Approved

There are no items to display

Literature Cited/References:

Name	Version	Date Created	Date Modified	Date Approved

There are no items to display

Principal Investigator's Scholarly Record (CV/Resume):

Name	Version	Date Created	Date Modified	Date Approved
Bernstein CV 13 May 2015.pdf(0.01)	0.01	5/14/2015 1:10 PM	5/14/2015 1:10 PM	
Bernstein CV 13 Sep 2017.pdf(0.01)	0.01	1/9/2018 3:49 PM	1/9/2018 3:49 PM	
Bernstein CV exp 9.13.2021.pdf(0.01)	0.01	4/19/2021 12:42 PM	4/19/2021 12:42 PM	

Faculty Sponsor's Scholarly Record (CV/Resume):

Name	Version	Date Created	Date Modified	Date Approved

There are no items to display

Other Stamped Documents:

Name	Version	Date Created	Date Modified	Date Approved

There are no items to display

Recruitment Materials, Advertisements, etc.:

Name	Version	Date Created	Date Modified	Date Approved

There are no items to display

Other Documents:

Name	Version	Date Created	Date Modified	Date Approved

There are no items to display

Biosafety Registraion

Biosafety Office Registration

Are you manipulating unfixed human samples (blood, tissues, organs, cells, etc.) in a University of Utah research laboratory (for storage or work in a diagnostic lab select "No"):

Yes: already registered and approved by the Biosafety Office.

Biosafety Office Registration Number

BOR_00000356

Institutional Biosafety Committee Registration

Are you introducing recombinant or synthetic nucleic acids (such as viral vectors, plasmids, or oligonucleotides, or cells containing recombinant or synthetic nucleic acids) or human pathogens (e.g., Viruses, Bacteria, Fungi or Parasites) into Research Subjects:

No

PI: Paul Bernstein M.D. **Submitted:** 1/31/2022

Title: Magenta: The Moran AMD Genetic Testing Assessment Study

Finish Instructions

Finish Instructions

1. **To view errors, select the "Validate" option at the top-left of the page. If you have errors on your application, you won't be able to submit it to the IRB.**
2. **Selecting the Finish button will NOT submit the application to the IRB.**
   You MUST select the "Submit" option on the workspace once you've selected the "Finish" button.
3. **If your study has a faculty sponsor: Once the PI submits the application, it will be sent to the faculty sponsor for final approval. The IRB cannot review the study until the faculty sponsor submits the application to the IRB.**