DRCR RETINA NETWORK POLICIES

Version 14.0 – Effective Date: February 28, 2024

A. Organizational Structure

The DRCR Retina Network has three central units: the Coordinating Center and two Network Chairs. One of the Network Chairs will provide scientific leadership for diabetic retinopathy studies, and the other will provide scientific leadership for age-related macular degeneration studies and other retinal disease studies. The structure of the Network also includes two Steering Committees, an Executive Committee, and an Operations Committee. In addition, a Data and Safety Monitoring Committee and External Protocol Review Committee are assigned by the National Eye Institute and serve as independent oversight committees for the DRCR Retina Network. Additional sub-committees such as Protocol Development Committees and Manuscript Writing Committees are developed as needed. The central units and committees are responsible for carrying out specific tasks as outlined in the Organizational Structure (Policy Appendix I: DRCR Retina Network Organizational Structure).

B. Investigators, Study Coordinators, and Fellows

1. Qualification of Investigators

The Network maintains select requirements for potential and existing investigators. Investigators should have completed either a 1-2 year retina advanced specialty training program or a 1-2 year retina clinical fellowship program. Investigators should be certified by the American Board of Ophthalmology or its equivalent. Investigators who have passed the written portion of the boards but are pending the oral portion may still participate. Investigators must hold either hospital or surgical privileges or have the ability to control the management of retinal complications that occur as a result of study treatments or retinal conditions observed in Network study participants. Each potential investigator who applies is reviewed by one Network Chair to confirm qualifications are met. Investigators must also have current GCP training before joining an individual protocol. Additional qualifications for individual protocols may be required. There may be exceptions for certain protocols, which will be communicated as part of the study start-up and site certification for that protocol.

2. Principal Investigator

Each site must have a designated Principal Investigator (PI) who will assume overall responsibility for the DRCR Retina Network studies conducted at the site. PIs of DRCR Retina Network clinical sites are expected to be familiar with all aspects of operations at the local DRCR Retina Network site. The PI must understand the responsibilities associated with conducting human subjects research. PIs must comply with federal regulations, state and local laws, the organization policies and, if applicable, the IRBs of their respective entities, as well as the organization policies of the DRCR Retina Network.

During the process of identifying and certifying personnel to participate in the DRCR Retina Network, the PI should discuss with each candidate the importance of conscientious adherence to all aspects of the DRCR Retina Network protocols and accurate reporting of data. Personnel should be assured that no penalty is attached to honest errors. However, the PI should make clear that each individual staff member is expected to promptly report any error discovered.

Periodically, all DRCR Retina Network staff should be reminded of their responsibilities for data quality.

PIs are responsible for training sub-investigators and other study team members and for conducting the research at their respective entities. Delegation of responsibility for the management of DRCR Retina Network activities to other staff does not free the PI of responsibility. Ultimately, he/she is responsible for the safety of the human subjects participating in the study. Each DRCR Retina Network protocol may have a different site PI.

The Network recommends that PIs have routine inter-office communication with sub-investigators, coordinators, and other DRCR Retina Network staff. The PI must make time to meet with key members of the DRCR Retina Network clinical site research team. It may be useful to designate a specific time each week to meet with the DRCR Retina Network site coordinator to take care of pending tasks and to review any operational issues. Such meetings may require only a few minutes but are essential for smooth operations. In addition, the PI must be accessible to the site coordinator in case any issues or problems arise.

Specific responsibilities of PIs of DRCR Retina Network clinical sites regarding research data integrity include, but are not limited to, the following:

- To have a thorough understanding of the DRCR Retina Network policies, protocol designs, and study methods.
- To ensure that local institutional requirements (if applicable) are satisfied and that approvals and assurances are obtained annually.
- To ensure that the required DRCR Retina Network-certified staff, facilities, and equipment are available to meet DRCR Retina Network responsibilities.
- To provide adequate support and guidance to DRCR Retina Network staff so that the DRCR Retina Network studies can be conducted according to protocol.
- To respond promptly to requests from the Coordinating Center and the Network or Protocol Chairs or her/his designates.
- To oversee local DRCR Retina Network documentation and records.
- To conduct periodic meetings of local DRCR Retina Network personnel.
- To cooperate with protocol monitors by making available DRCR Retina Network personnel, DRCR Retina Network records and protocol binders, clinic charts for DRCR Retina Network study participants, and other necessary records needed for on-site or remote clinic monitoring.
- To correspond and maintain accessibility via email and phone with the Coordinating Center and Network Leadership.
- To notify the Coordinating Center if any protocol adherence or data reporting problem is discovered or suspected.
- To review the site visit reports and participate on an annual monitoring call to discuss clinical site performance.
- To attend investigator meetings if meet criteria set by the Operations Committee for attendance.

- To maintain IRB (or other ethics board approval) and to comply with all IRB polices and ensure Good Clinical Practice is followed.

3. Coordinators

Each site must have at least one designated study coordinator who is certified for the DRCR Retina Network studies in which the site is participating. Study coordinators are critical to the success of a study, as they assist with recruiting and retaining study participants. Together with the principal investigator, the coordinator ensures that patients are appropriately consented, only eligible patients are enrolled, study protocols are followed correctly, study procedures are completed accurately, and data is entered accurately on the DRCR Retina Network website. These responsibilities require detailed and complete knowledge of each protocol and complete familiarity with the informed consent process and data collection procedures.

All study coordinators must provide a current CV or other statement of qualifications and have current GCP training before joining an individual protocol. Additional qualifications for individual protocols may be required.

4. Fellows

The Network allows fellows at current Network sites to receive Network communications that investigators normally receive. Fellows will have to complete an application that is reviewed and approved by one of the Network Chairs. They are also required to have a U.S. Medical License, be currently enrolled in a Fellowship program, and submit their current Curriculum Vitae (CV). Fellows cannot perform any investigator-related procedures on their own. However, this would not preclude a site from delegating a fellow to other study tasks if qualified and trained (e.g. imaging) or *assisting* the investigator with exams as would normally be done in clinical practice. As always, the certified investigator is ultimately responsible for performing study exams and signing off on case report forms. Fellows may be invited to attend Study Group Meetings, unmasking meetings/calls, and be sent protocols to review, and other items that are normally sent to investigators to review. Fellows are eligible to be included in publication listings of Network personnel based on the same criteria used for other staff. After their fellowship is completed, fellows can apply to be an investigator.

C. Editorial Policy

1. Manuscripts

DRCR Retina Network will produce one or more manuscripts for each conducted protocol. Investigators retain ownership of the data collected from Network protocols. Datasets are maintained at the DRCR Retina Network Coordinating Center and released for reporting in accordance with the following policies. The National Eye Institute (NEI) of the National Institutes of Health, is granted the opportunity to review and comment on each manuscript. However, it will not have the authority to restrict the publication or presentation of study results. This policy extends to any study Co-Funders.

A manuscript topic proposed by any individual, whether inside or outside of the Network, utilizing the DRCR Retina Network Manuscript Idea Form, is submitted to the relevant Steering Committee for review and approval. The Operations Committee is responsible for prioritizing manuscripts approved by the Steering Committee. If after data analyses are conducted, there is not enough clinical evidence for a manuscript, this will be re-reviewed with the Steering Committee for a decision not to proceed.

Since every investigator cannot have an active role in writing a paper, a Writing Committee will be established by applicable Steering Committees for each paper. Generally, the Protocol Chair will be the lead writer on the Writing Committee of the primary outcome paper. A decision on the authorship listing will be made before the writing of each manuscript by the Steering Committee. The list may be modified by the Steering Committee before manuscript submission to account for the unanticipated contribution effort of any individual. The Executive Committee must approve Network manuscripts; three members are selected to critically review and approve each manuscript; all other members of the committee receive the manuscript for their interest and are not required to provide comment or approval. All comments received from any member, selected or not, are considered.

For the major results manuscript of protocols with oversight by the DSMC, the DSMC must approve the manuscript before submission. The DSMC will be sent secondary manuscripts for comment, but approval will not be required.

Manuscripts are made publicly available as soon as possible in adherence with Journal policies. For each protocol, a dataset will be made available to the public.

Investigators shall have the right to publish the study results, provided that the investigator submits any proposed manuscript, presentation, or other public disclosure of the results of the study to JCHR for review at least thirty (30) days before submitting such proposed manuscript to a publisher or delivering or making such presentation or public disclosure. JCHR may provide comments that the investigator agrees to consider in good faith. However, the investigator will not independently publish, publicly disclose, present, or discuss, any results of or information about the study conducted by the DRCR Retina Network until a multi-center publication of the primary results is published. Any data presentations or publication using DRCR Retina Network data, but not coordinated by DRCR Retina Network must contain the following language: "The source of the data is the DRCR Retina Network (Unique Federal Award Identification Number (FAIN) UG1EY014231 funded by the National Institutes of Health), but the analyses, content, and conclusions presented herein are solely the responsibility of the authors and have not been reviewed or approved by DRCR Retina Network." Additional requirements may be necessary for studies with industry collaborators.

2. Authorship

For manuscripts reporting the primary outcome of a protocol, the DRCR Retina Network will be listed as the author on the by-line if this meets with journal approval. The writing committee for the manuscript will be listed. Group-authored manuscripts will require the Principal Investigator

sign off on behalf of the clinical site. Whenever possible, all investigators and coordinators who actively participated in the protocol (1) will be given an opportunity to review and comment on the manuscript, (2) will be listed in an appendix that accompanies the manuscript and (3) can include the manuscript on their CVs as a co-author. Each manuscript will acknowledge the NIH and NIDDK funding and other sources of funding deemed appropriate by the Executive Committee, if any.

For secondary manuscripts without group authorship, the investigators involved in writing the paper will be listed by name followed by "for the DRCR Retina Network".

For manuscripts written with a collaborator group, the investigators involved in writing the paper will be listed by name followed by "with the DRCR Retina Network".

3. Society Meeting Abstract Submissions and Presentations

The Operations Committee will plan abstract submissions in accordance with manuscripts in preparation. Additionally, any individual may submit an 'Abstract Idea Form' via www.drcr.net for approval by a Steering Committee. Approved topics will receive DRCR staff support for analysis, number verification, and submitting the abstract. The submitter will be responsible for drafting the abstract.

Proposed abstract topics that do not have an associated approved manuscript must be reviewed and approved by the relevant Steering Committee prior to being submitted to any society. Abstracts that already have an approved manuscript will be approved by the applicable Network Chair and Principal Investigator of the Coordinating Center as part of the Operations Committee, provided that the abstract is not appreciably different from the approved manuscript.

When possible, authorship will include the presenter 'for the DRCR Retina Network'. On a case-by-case basis, as determined by the Operations Committee, the lead statistician or another individual with substantial input also may be listed as an author.

4. Non-DRCR Retina Network Presentations

Investigators or coordinators presenting published DRCR Retina Network data at institutional, local, and regional meetings are strongly encouraged to use the slides available on the DRCR Retina Network website but are not required to submit their slides for approval to the applicable Steering Committee. Any data presentations or publication using DRCR Retina Network data, but not coordinated by DRCR Retina Network must contain the following language "The source of the data is the DRCR Retina Network (Unique Federal Award Identification Number (FAIN) UG1EY014231 funded by the National Institutes of Health), but the analyses, content, and conclusions presented herein are solely the responsibility of the authors and have not been reviewed or approved by DRCR Retina Network."

D. Publicity

The Steering Committee must approve any DRCR Retina Network press release or other publicity about study results that are not yet in the public domain and public use of the DRCR Retina Network Name; or formerly, Diabetic Retinopathy Clinical Research Network.

To present uniform messages to the public from the DRCR Retina Network, all other publicity and press releases for the DRCR Retina Network are to have prior approval of the Operations Committee or relevant Network Chair and Coordinating Center Director unless otherwise specified below. Drafts of proposed publicity or press releases should be sent to the Coordinating Center for review.

Publicity includes the use of the current or former DRCR Retina Network logo or name on office stationery, slides, and the like.

While investigators are free to speak as individuals concerning communications with the press, investigators, and other Network personnel (other than the Network Chairs) should decline to answer questions on behalf of the Network and refer the media, in writing, to the Coordinating Center and applicable Network Chair. The Network Chairs are the designated spokespersons for the Network, and in general, will communicate with the press orally or in writing only following discussions and agreement with the appropriate Network group (e.g., the Operations Committee, or the Executive Committee, or Principal Investigator of the Coordinating Center). At times, other Network personnel may be designated to speak on behalf of the Network. In general, all questions to the Network from the media must be in writing and the Network will respond in writing. This will not interfere with the Network policy to be open, and transparent, and deal with the scientific process with the highest integrity. Approaching responses in writing should help ensure that the Network has made all reasonable attempts to have information presented to the media to be free of scientific errors and accurate in every regard.

It is recognized that when information is sought from an individual investigator or staff by the local press or others in their community, it is sometimes necessary or desirable for that investigator to handle the request. In such an event, the investigator should speak as an individual and not as the official representative of the DRCR Retina Network. This perspective should be made clear to the audience at both the beginning and the end of any oral presentation, as well as in writing whenever feasible. Also, the investigator should ask to be sourced accordingly, that is, as an individual, and not as a spokesperson for the Network. Ideally, the information provided to the press should be accurate and should reflect the general policy and views of the Network. If an investigator is unsure about what is appropriate to say, it is better to refrain and refer the media to the Coordinating Center, in writing.

Of note, it sometimes is not obvious that someone inquiring about Network information is from the media. Therefore, it is wise to consider carefully what one says to individuals outside of the Network regarding information about the Network, especially information that might be confidential within a teleconference or in-person Network meeting, or information involving the design (protocol development committees), conduct (enrollment numbers and outcomes from

clinical sites), or reporting (presentations or publications in draft form) of Network protocols that are not in the public domain.

Items that do not require approval include the following:

- Notation on letterhead of participation in the Network (although such letterhead only can be used by active sites and by active investigators at those sites and may only list active investigators).
- Presentation of recruitment slides for studies previously created and approved by the Network (available on the Network website).
- Presentation of slides presenting information published in peer-reviewed literature.

E. Patient Confidentiality

Individual participant medical information obtained as a result of this project is considered confidential and disclosure to third parties other than those noted below (or on the informed consent form) is prohibited. Consistent with an institution's policies, medical information may be given to the patient's physician or to other appropriate medical personnel responsible for the patient's welfare.

Data generated because of this study are to be available for inspection upon request by the Coordinating Center, the NIH, and auditors of regulatory agencies.

All DRCR Retina Network clinical sites must conform to HIPAA regulations.

F. Policy for Email and Website Use

All investigators and coordinators must have a unique email address that is checked regularly. All study personnel must log onto the DRCR Retina Network website only using their individually created password and must not share their password with others. Under no circumstances may an investigator delegate the signing of study forms to an assistant who logs in using the investigator's password.

1. Electronic Signature

An electronic signature on an electronic case report form indicates that the data have been reviewed and accepted by the signatory. Electronic signatures will consist of the combination of the individually assigned DRCR Retina Network personnel identification number and password. It is unlawful to forge an electronic signature.

Additional information regarding website use can be obtained in the DRCR Website User's Manual.

G. Retention of Study Records

Each center will archive all relevant study data and keep them on file for the period of time specified by the Coordinating Center, US law, or by the center's institutional requirements, whichever is greater. Per NIH requirements, study records must be kept for at least three years

following the end of the grant cycle during which a study is completed. Additional record retention requirements may apply to studies conducted under an IND or IDE, which will be documented via a document retention plan.

H. Study Participant Retention

The goal for the Network is to have as few losses to follow-up as possible. A study participant has the right to withdraw from a study at any time. If a study participant is considering withdrawal from a study, the investigator must attempt to speak personally to the study participant about the reasons and make every effort to accommodate the study participant. The Coordinating Center will assist in the tracking of study participants.

I. Participation of Investigators in 'Competing' Studies

A 'competing' study is defined as one in which subject eligibility criteria overlap with that of a DRCR Retina Network study. If the site is involved in a competing study, the site should determine a management plan for competing studies internally. Investigators should strive to not have competing studies or have strategies of how to allocate patients in competing studies. Although typically sites will not be required to submit a proposed management plan to the Coordinating Center, sites will be provided with the Network's Competing Studies Document that provides guidance on managing competing studies. In addition, assistance from the applicable Network Chair will be available for sites that would like advice on how to manage their competing studies.

If deemed necessary for a given protocol, sites will be required to inform the Coordinating Center of studies in which they are participating that have eligibility criteria that overlap with the DRCR Retina Network protocol in which they are concurrently participating.

J. Women and Race/Ethnic Minorities

It is expected that men and women will be equally represented in all protocols of the project. Efforts will be taken to assure diverse gender as well as race/ethnic representation.

K. Funding

The DRCR Retina Network is funded through a Cooperative Clinical Research Agreement from the Department of Health and Human Services, National Institutes of Health, National Eye Institute to the Jaeb Center for Health Research Foundation, Inc. Additional funding may be provided to the Jaeb Center for Health Research Foundation, Inc. by other NIH institutes, industry, foundations, or unrestricted gifts following approval of the NEI and the Executive Committee.

1. Clinical Centers

Clinical centers will be funded through subawards with the Jaeb Center for Health Research Foundation, Inc. Funding is expected to be partially on a fixed-cost basis for completion of milestones such as certification for a protocol and primarily on a per-patient (fixed rate) basis for the conduct of a protocol. A payment schedule will be established for each protocol.

Research funds will pay for clinical and other procedures that are purely for research and otherwise would not have been performed on the patient (as distinct from usual care activities that would occur if the research did not exist). Additionally, per-visit funding will be provided to the site and is expected to cover the additional time necessary on the part of the investigator and his/her office staff to perform research activities. This per-visit funding is also expected to cover the costs of maintaining an internet connection and usage time and study-directed time on the part of the investigator in areas such as promoting recruitment, screening patients who would otherwise not be examined, educating eligible patients about the trial and obtaining informed consent, responding to calls from participants during the study, and responding to edits and queries from the Coordinating Center.

2. Patient Costs

Grant funds are intended to pay for study procedures that are for research purposes. Each study will identify which procedures are paid by the study and which should be billed to the patient or their insurance company as part of standard care.

Funds may be available for certain protocols to cover unreimbursed costs from insurance or for uninsured participants with a financial hardship. Funds also may be available to cover up to 80% of copay or deductible costs for study participants with a financial hardship. Such instances will be reviewed on a case-by-case and procedure-by-procedure basis. If a financial hardship does not exist, the DRCR Retina Network cannot reimburse.

Study participants may be compensated for their participation, subject to IRB approval.

3. Coordinating Center

The Coordinating Center is funded through a Cooperative Clinical Research Agreement from the Department of Health and Human Services, National Institutes of Health, National Eye Institute to the Jaeb Center for Health Research Foundation, Inc. Additional funding may be provided to the Jaeb Center for Health Research Foundation, Inc. for Coordinating Center activities by industry, foundations, or unrestricted gifts following approval of the NEI and the Executive Committee.

4. Network Chair Positions

The Network Chair positions are supported through a subaward between the Jaeb Center for Health Research Foundation, Inc. and the Chair's institution.

5. Committees Members and Other Investigator Positions

Committee members (including Protocol Chairs) and other Investigator Working Positions are funded through written agreements with the Coordinating Center to partially compensate them for the time they devote to the study in attending meetings, participating in conference calls, review of materials, pilot testing study procedures, etc.

L. Selection of Protocols

1. Process

The following process outlines the evaluation and prioritization of protocols within the DRCR Retina Network.

- A protocol proposal form is available on the DRCR Retina Network public website.
- Any DRCR Retina Network investigator or individual outside of the Network may submit a protocol idea using this form at any time.
- Submitted protocol ideas will be saved and tracked by the Coordinating Center. Tracking will document the protocol ideas progress through the entire review process, and all submitted ideas will be provided to the Executive Committee at a semi-annual meeting.
- Investigators will be routinely solicited for protocol ideas. Ideas will be reviewed by the applicable Steering Committee. If an idea might be applicable to both of the Steering Committees, the Operations Committee will preliminarily review the idea and decide which Steering Committee is to review.
- A separate New Protocol Idea call may be held with select members of both Steering Committees with the purpose of reviewing new protocol ideas if necessary due to time constraints of regularly scheduled calls.
- The submitter of the protocol idea will be invited to join part of the New Protocol Idea Call or applicable Steering Committee call, via phone or video, to present the idea. The NEI Project Officer will also be invited to join the new protocol idea discussion. A Steering Committee member will be selected in advance to review the idea in detail and research any additional background information as needed to support the Steering Committee's discussion. Based on scientific merit and feasibility the Steering Committee will select the proposed concepts for presentation to the full investigator group. The applicable Steering Committee will conduct initial review of each idea as it is submitted and decide on degree of merit and public health importance for presentation to investigators at the semiannual Coordinator/Investigator meetings and recommendation to the Executive Committee. If the Steering Committee deems a protocol proposal has extremely high public health importance or is time sensitive, it may be reviewed expeditiously by the Executive Committee as detailed below.
- The selected ideas will be presented, typically by the submitter, to the investigators at the Coordinator/Investigator meetings to gauge interest and feasibility. Ideas may also be circulated to investigators via email for feedback. Typically feedback at the meeting will be solicited during the large full group session, within small breakout sessions, and via written or web survey.
- After the idea has been presented to the investigators, the applicable Steering Committee should re-review the idea and decide if they believe the idea should move forward based on the discussions at the meeting. Submitters may be invited to be a part of the Steering Committee discussion after presenting at the Coordinator/Investigator Meeting if the Steering Committee has additional questions about the proposal. If the Steering

Committee decides the idea should not move forward, the original idea and Steering Committee decision will be sent to the Executive Committee via email to review and determine if they agree with the Steering Committee's recommendation. If the Executive Committee agrees with the Steering Committee's recommendation, the submitter will be notified of the Executive Committee's decision. If the Executive Committee disagrees with the Steering Committee's recommendation, the idea will be presented at the following Executive Committee meeting.

- For proposals being presented to the Executive Committee, the Network Chairs, or members of the Steering Committee, in consultation with the primary proponents of each proposal, will develop a brief protocol outline (6-8 pages) that addresses the following:
  - Background, significance, public health importance
  - Protocol outline (including flow diagram, if applicable)
  - Outcome measures
  - Sample size and statistical considerations
  - Recruitment potential
  - Budget (to be drafted by the Coordinating Center)
- At the Executive Committee meeting:
  - A member of the Coordinating Center and/or the applicable Steering Committee member will present the materials. The submitter will not be present during the presentation and discussion of ideas at the Executive Committee but may be available by phone/video in case questions arise.
  - If the submitter is an Executive Committee member, they may participate in the presentation and discussion of their idea. They will recuse themselves for the vote. They may also participate in the discussion of other protocol ideas, as well as scoring the ideas and the decision of whether the ideas should proceed to a protocol development committee, however, they will not be allowed to rank their idea amongst other ideas.
  - The Executive Committee will score the protocol ideas based on public health significance, impact on clinical practice, alignment with Network mission/priorities, risk/benefit ratio for the participant, existing scientific evidence, experimental design feasibility and innovation.
  - Based on the score and budgetary constraints the Executive Committee will determine which studies should have full protocols developed and the timeline for their development.
- Feedback will be given to the proponents of each protocol. Those protocols that were not selected potentially could be brought forward for consideration in future cycles.
- A protocol development committee (PDC) will be formed for each selected protocol to develop a full protocol.
- Each developed full protocol will be circulated to all DRCR Retina Network investigators and fellows for input prior to final review and approval by the DRCR Retina Network Executive Committee and the Data Safety and Monitoring Committee, if applicable. An

additional step of external review may be necessary prior to review by the DSMC, at the discretion of the NEI.

2. Supplementary Studies

A supplementary, or ancillary study, is one in which procedures not part of the primary protocol are performed on a subject participating in a current DRCR Retina Network protocol. Any supplementary studies not part of the protocol that are performed on a DRCR Retina Network subject require pre-approval. The purpose of the approval is to assure that the supplementary study will not interfere with the objectives of the primary study. A DRCR Retina Network Ancillary Protocol Idea Form can be used to propose supplementary study. The editorial policy for a supplementary study is the same as for any other DRCR Retina Network manuscript.

- Submitted ancillary protocol ideas will be saved and tracked by the Coordinating Center. Tracking will document the ancillary protocol ideas progress through the review process.
- As they are submitted, the ancillary ideas will be reviewed by the applicable Steering Committee on biweekly calls. If the submitter is a Steering Committee member, they may participate in the presentation and discussion of their idea. They will recuse themselves for the vote.
- Based on the requirements above, feasibility and scientific merit, the Steering Committee will recommend which ancillary studies should be move forward.

There are two main types of supplementary studies:

- Additional testing for research purposes at a single site where both study resources and the Coordinating Center are not involved
- A formal protocol to be carried out at one or multiple sites

General Principles

- Any supplementary study must not interfere with the objectives of the primary protocol
- Participation must be optional for study subjects
- Approval by the Executive Committee is required
- If the primary study is already overseen by the Data and Safety Monitoring Committee, approval by the Data and Safety Monitoring Committee, is required prior to initiation
- Approval by the IRB is required prior to initiation

M. Patient Protection and Data Quality

1. Institutional Review Board (IRB)

For DRCR Retina Network studies beginning January 1, 2018, all Network sites in the United States will be required to use the central IRB located at the Jaeb Center for Health Research Foundation, Inc. as their IRB of record in order to comply with the NIH policy to use a central IRB of record for multi-site research. The site must abide by reporting requirements of the JCHR and local IRB. Each site must obtain approval from the JCHR IRB for each protocol in

which it participates before it can begin to enroll patients. All changes in the research activities and all significant deviations and unanticipated problems involving risks to patients must be immediately reported. Significant protocol changes require IRB approval before implementation, except when required to eliminate apparent immediate hazards to patients.

IRB coverage must remain current. The Coordinating Center will send a reminder to each site about two months prior to the expiration of IRB coverage for a protocol (a protocol update for the IRB will be included). If IRB coverage lapses, the site cannot enroll any new patients and cannot submit data forms to the Coordinating Center for any established study patients until IRB coverage is back in effect.

2. Informed Consent

An informed consent form must be signed by a potential study participant before any procedures are performed that are specific to a study (i.e., not part of a patient's routine care). If IRB-approved, some protocols may allow verbal consent only. The Informed Consent Form will contain information about the objectives of the study, the procedures followed during the study, and the risks and restrictions of the study, with special reference to possible side effects of the treatments. The form will be in compliance with the guidelines of the Office for Human Research Protections (OHRP) and the IRB. In general, the ICF will automatically be translated into Spanish. For sites with a large population of patients speaking another language, additional translations may be available upon request.

Consent must be obtained according to IRB procedures. In addition to any IRB procedures, consent only may be obtained by a DRCR Retina Network investigator and coordinator who is certified through the Coordinating Center for the protocol for which consent is being obtained. Sites will either electronically or manually redact all except the first initials of the first and last name of the participant before the consent is faxed or uploaded to the Coordinating Center.

3. Data Quality and Site Visits

Each site is monitored for adherence to the protocol and good clinical practices. Sites or study group members with excessive protocol deviations and/or quality issues may be placed on probation for a period of time and/or dismissed from DRCR Retina Network at the discretion of the Steering Committees.

Site visits will be conducted to ensure quality. The site visit policy may vary from protocol to protocol and may include in-person or remote site visits. The site visits will be coordinated by the Coordinating Center but may include other individuals from both within and outside the study group.

Site visits may be performed on a routine schedule for sites participating in major IND/IDE protocols. In general, a site visit will be performed (1) whenever there are concerns about data quality or (2) when an investigator (or site, if there are multiple investigators at the same site) enrolls or is projected to enroll at least 10% of the patients in a protocol, (3) when required by a regulatory agency or (4) when a site is participating in a major IND/IDE protocol. All

investigators are subject to in-person site visits and must agree to cooperate with in-person or remote site visits in order to participate in DRCR Retina Network protocols.

4. Research Misconduct

Consistent with the NIH Grants Policy Statement, research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in research records or reports. Fabrication is making up data or results and recording or reporting them. Examples include (1) altering information collected from a patient that would have excluded the patient so that the patient appears to be eligible for the study, (2) randomization of patients prior to obtaining informed consent and changing the date on the informed consent form to conform with the randomization date, (3) changing examination dates so that they appear to be in the time windows specified in the protocol, and (4) altering outcome measurements. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit. Research misconduct includes the destruction of, absence of, or accused person's failure to provide research records accurately documenting the questioned research.

Research misconduct does not include honest errors or honest differences of opinion. Perfect compliance with a protocol is not expected. Study participant adherence to protocol will never be 100%. Some problems with medication compliance (where applicable) and missed visits are expected in any trial. Some misclassification of outcome is also possible. In fact, in determining a sample size estimate for a study, an adjustment is made to account for the expected losses to follow up, number of misdiagnosed study participants, and number of study participants who do not comply with their treatment assignment.

Clinic staff members, including investigators, do make mistakes. Unintentional errors that occur in data collection are not scientific fraud. They may be signs of poor clinic performance and such errors are tabulated by the Coordinating Center, but they do not imply fraud. This is monitored by the Coordinating Center and becomes a concern when a clinic is making more mistakes than expected, particularly major ones (e.g. entering ineligible patients).

An investigator has the responsibility of assuring that the protocol is carried out properly at his/her site and assumes responsibility for staff involved in the care of and data collection for study participants. An investigator who suspects data irregularities should report this to the Coordinating Center immediately.

5. Good Clinical Practice Training

Good Clinical Practice training is required every three years by active investigators, coordinators, and Coordinating Center personnel.

6. Provision of Care if a Study-Related Injury Occurs

In general, the DRCR Retina Network does not have a program to pay for study participants who have an adverse event or injury as a result of being in a DRCR Retina Network study. However, DRCR Retina Network investigators, to the best of their abilities, should arrange for necessary medical care for study participants with study-related injuries and provide any medical records from the study they judge are relevant or needed to treat the injury.

N. Confidentiality

Study data, protocols, other documents, and proceedings of meetings and conference calls are considered confidential information until such time that they are reported publicly or placed in the public domain. This includes information that has been received from an outside entity by the Network and labeled as confidential.

Network investigators and staff agree to take all reasonable care to maintain confidential information as secret and confidential, such efforts to be no less than the degree of care employed by the Network investigator or staff to preserve and safeguard his or her own confidential information. The confidential information shall not be disclosed or revealed to anyone except employees of the Network investigator or staff who have a need to know the confidential information for Network activities and who agree to be bound by the Network's policies of confidentiality.

Except as required by law, obligations under Paragraphs 1 and 2 above shall not extend to any part of the confidential information wherein:

- the disclosed information was previously known to the party to whom the disclosure is made as evidenced by written documents; or
- the substance of the disclosure was or becomes general public knowledge; or
- the substance of the disclosure is made known by a third party who by such disclosure is not in breach of any duty or obligation toward the party whose confidential information is being disclosed; or
- the party providing the confidential information agrees to its disclosure.

Network investigator or staff obligations under Paragraphs 1 and 2 above shall extend for a period of five (5) years from the effective date of receipt of confidential information unless otherwise specified for a specific protocol or committee assignment.

O. Financial Disclosure and Conflict of Interest

All DRCR Retina Network investigators, coordinators, committee members, and other key staff personnel will be required to disclose all financial interests and working relationships with any entity whose financial interests potentially could be affected by the conduct or outcome of DRCR Retina Network research. This disclosure will be required on an annual basis by completion of an electronic financial disclosure form on the DRCR Retina Network website and must be updated within 30 days when there is a change in related financial interest or a new financial interest is acquired (such as by marriage, purchase of stock, or payment from a related

entity). Each disclosure will cover the previous 12 months. Additional reporting requirements may be required by the IRB or as part of FDA regulated studies.

Any person serving as a member of the Executive Committee (or other committees, such as the Steering Committees, as applicable) who has financial disclosures relevant to a company involved in discussions to collaborate with the Network will forego voting privileges regarding decisions on the collaboration. This policy will prevent putting any DRCR Retina Network investigator in an inappropriate position and will ensure that financial biases are eliminated when voting takes place.

Further details of the Network policy appear in a separate document (Policy Appendix II: Financial Disclosure Policies for the DRCR Retina Network).

P. Guidelines for Remaining as an Active Clinical Site in the Network

The principal responsibility of a site is to have at least one investigator who is enrolling and following study participants. It is recognized that some effort is needed to maintain a Clinical Site in the Network, including, for example, site visits, contracts, and IRB issues.

Definitions:

- Fully Active: able to enroll study participants and complete follow-up visits on study participants in the Network.
- Active, Follow-up Only: unable to enroll study participants in the Network or participate in future studies, but able to follow existing active study participants in the Network.
- Dropped: unable to enroll or follow study participants in the Network; not considered part of the Network from the time the Clinical Site is dropped.

In general, the following minimum activity is expected to maintain a clinical site as active in the Network:

1. Sites that have been in the Network for at least one year must meet the enrollment minimum as determined and set each year by the DRCR Retina Network Executive Committee. This number will be based on the number of actively recruiting protocols anticipated for the year. Sites new to the Network that have been active less than one year are required to meet the recruitment minimum in the second year of activity.
    - Sites that do not meet the enrollment minimum in Network protocols during a calendar year may receive a warning notification that if the site reaches 18 months of insufficient participation, the site will be reviewed by the Steering Committees again and may no longer have fully active status within the Network.
    - In addition, sites must maintain certification of a clinic coordinator and visual acuity examiner for the site and any certified technician (e.g., photographer, OCT examiner) needed for participation in protocols in which the site is participating.
        - Sites that do not have sufficient certified personnel will be placed on active: follow-up only status for new enrollments until the deficiency is corrected.

- Sites who haven't participated in any active Network protocols for 12 months and who have not indicated they are interested in upcoming protocols will be contacted by the Coordinating Center or designee. If the PI indicates that they are not interested in any current or upcoming protocols, the site will be dropped. If the PI indicates they are interested, the site will need to be certified for a protocol within 6 months to remain in the Network.

Sites with insufficient participation over the 12 month period as described above will have a status change from Fully Active to one of the following:

- Active, Follow-up Only: if the site has any active study participants in follow-up
- Dropped: if the site has no active study participants in follow-up and has completed all research activities for any ongoing trials including data closeout and any regulatory documentation.
    - Note, sites which are Active, Follow-up Only will be changed to Dropped when the site no longer has active participants.

In general, "Dropped" or "Active, Follow-up Only" sites may reapply for DRCR Retina Network fully active site status six months after the drop date.

Individual protocols may have additional criteria for a site to remain active for the protocol.

Q. Guidelines for Remaining as an Active Investigator in the Network

The principal responsibility of an investigator at a clinical site is to enroll (and follow) study participants. It is recognized that some effort is needed to maintain investigator participation in the Network. For example, the Directory needs to be kept up to date; financial disclosure forms must be maintained. Investigators may have had the best of intentions to participate in the Network but then demonstrate little or no activity in any given year.

Definitions:

- Active: certified for at least one active Network protocol
- Dropped: not certified for a Network protocol and thus unable to enroll or follow study participants in the Network or participate in Network activities, including committees, conference calls and meetings; the Investigator is not considered part of the Network from the time that the Investigator is dropped

In general, the following minimum activity is expected to maintain active Investigator participation in the Network:

1. Maintain protocol certification for at least one active Network protocol each calendar year.
    - Investigators who do not maintain certification for an active Network protocol during a 12 month period may receive a warning notification that if they reach 18 months of insufficient participation, the investigator will be dropped from the Network.

2. Adherence to Network policy including timely signoff on manuscripts (generally one week) and submission of financial disclosure forms (according to DRCR Retina Network policy).

In general, dropped investigators may reapply for DRCR Retina Network fully active status six months after the drop date.

Individual protocols may have additional criteria for an investigator to remain active for the protocol.

R. Industry and Other Entity Collaborations

The DRCR Retina Network collaborates with related industries and other entities in a manner that appreciates the needs of those industries or other entities with regard to drug, biologic, or device development while maintaining clinical trial design, investigational ethics, and rigorous implementation consistent with academic standards. The DRCR Retina Network has policies related to these collaborations, including protocol development, study data, publications, presentations, and publicity, data integrity, clinical sites, site monitoring, adverse event reporting, efficacy and safety reviews, study drug, laboratory measurements, FDA or other regulatory registration and submission, study committees and oversight, legal agreements, and cost sharing. (See Policy Appendix III: DRCR Retina Network Industry Collaboration Policies for detailed information.)

Appendices

Appendix I: DRCR Retina Network Organizational Structure

Appendix II: Financial Disclosure Policies for the DRCR Retina Network

Appendix III: DRCR Retina Network Industry Collaboration Policies

POLICY APPENDIX I – ORGANIZATIONAL STRUCTURE

Version 12.0 – Effective Date: February 28, 2024

A. Introduction

The central units of the DRCR Retina Network are the Coordinating Center (CC) and Network Chair positions. The CC plays a role in all aspects of DRCR Retina Network trials including protocol development and implementation, quality control, statistical analyses, reporting and dissemination of results. The DRCR Retina Network Chairs assume overall responsibility for the scientific direction of the Network and serve as Network spokespersons to the public, industry, FDA, NIH and research foundations.

The DRCR Retina Network committee structure includes an Executive Committee, two Steering Committees and the Operations Committee, as well as two National Eye Institute appointed committees: the Data and Safety Monitoring Committee (DSMC) and an External Protocol Review Committee (EPRC) which are both advisory to the Network and the National Eye Institute (NEI). Sub-committees are created by the Executive Committee as necessary.

The Executive Committee (EC) is responsible for providing scientific oversight of Network activities and prioritizing Network resources. The EC oversees the Steering Committees, Operations Committee, and the Coordinating Center. The EC also provides final approval for Protocol Chair appointments and for Network policies within the confines of the NIH terms and conditions for cooperative agreements. The Operations Committee is responsible for implementing the daily oversight, management, and operations for the Network. There are two Steering Committees. A Diabetic Retinopathy Steering Committee that is responsible for overseeing diabetic retinopathy initiatives, and a Retina Steering Committee that is responsible for overseeing initiatives in other areas outside of diabetic retinopathy. If an initiative spans across both diabetic retinopathy and other retinal diseases, the Operations Committee will determine which Steering Committee will be responsible for the oversight of that initiative. The Steering Committees are responsible for the daily scientific operations of the Network, including making key decisions regarding aspects of protocol development, reviewing new protocol ideas, and manuscript development and providing recommendations to be approved by the Executive Committee such as amendments to ongoing protocols. Some of these responsibilities may be delegated to the Network Chairs and Coordinating Center Principal Investigator. The Network Investigators are needed to implement protocols and disseminate results which can occur only with buy-in and enthusiasm of Network clinical sites. Ad hoc committees for protocol development, manuscript writing, and advisory capacities are created with membership drawn from DRCR Retina Network Investigators and external experts as needed. Details of the specific role and function of each of these entities are included below.

B. Central Units

1. Coordinating Center

The DRCR Retina Network Coordinating Center is located at the Jaeb Center for Health Research Foundation, Inc. in Tampa, Florida. Specific responsibilities of the Coordinating Center include:

- Solicit ideas for new studies from investigators

- Assist the Steering Committees and protocol development committees with the development of study protocols
- Obtain and maintain INDs and IDEs
- Develop study documents such as protocols, informed consent forms, operating procedures manuals, and data collection forms
- Maintain version control of all protocols, study documents, publications, presentations, and the like
- Develop and implement a data management system capable of supporting multiple projects
- Develop and maintain a multi-functional private website for use by the Coordinating Center, clinical centers, retinal imaging reading centers, and committee members
- Develop and maintain a website for public use
- Provide datasets of studies for public use as per the guidance on NIH's policy on the dissemination of NIH funded trials
- Develop procedures for study participant enrollment and randomization
- Develop and implement a system for adverse event reporting
- Develop and implement a quality assurance program that includes training and certification of clinic staff, monitoring of adherence to the protocol, reporting of quality control data, validation of collected data, assessments of retinal imaging reading center(s), and assessment of drug packaging and labeling
- Coordinate and monitor the conduct of study protocols
- Coordinate the selection process of clinical centers in conjunction with the Network Chair(s)
- Develop procedures and materials for certification of clinical centers and associated staff
- Develop systems to assist the clinical centers in maintaining a high rate of study participant retention
- Develop and maintain a system for drug/device distribution and accountability
- Develop and maintain a system to facilitate communication between the central units, clinical centers, and committees
- Coordinate site visits, prepare site visit agendas, and prepare site visit reports
- Develop and maintain a system for collection, review, and reporting of financial disclosures as well as Financial Conflicts of Interests (FCOI) for investigators, coordinators, and other key personnel as defined in the Network's Financial Disclosure policy
- Develop a system for integration of central laboratories into the project
- Develop and oversee implementation of subawards with clinical sites to participate in DRCR Retina Network protocols
- Develop agreements with other centralized resource groups utilized in DRCR Retina Network protocols, such as imaging reading centers for grading and transmission of imaging data to the Coordinating Center

- Develop contracts with industry collaborators following the DRCR Retina Network's Industry Collaboration Guidelines
- Develop materials for IRB submissions by the clinical centers
- Track IRB approvals and expirations
- Develop study close-out procedures and materials
- Develop statistical analysis plans
- Coordinate the preparation and publication of study manuscripts, including drafting the initial manuscript draft
- Conduct data analyses for Data and Safety Monitoring Committee review as well as for manuscripts, abstracts, presentations, and ancillary studies
- Coordinate activities with the Operations Committee, Steering Committees, Executive Committee, and any other committees
- Coordinate activities of the Data and Safety Monitoring Committee
- Prepare submission to the NEI External Protocol Review Committee
- Arrange conference calls
- Arrange meetings, including semiannual Coordinator/Investigator meetings, semiannual Executive Committee/Protocol Prioritization & Planning meetings, semiannual Data and Safety Monitoring Committee meetings, and Protocol Development Committee meetings
- Develop and disseminate agendas and summaries of committee conference calls and meetings
- Assist with communication with NIH, JDRF, regulatory agencies, the public, and with industry/foundations
- Develop clinical center budgets in conjunction with the Steering Committees
- Develop and maintain directory of project personnel
- Maintain direct contact with study participants
- Develop and coordinate grant submissions, reporting, and modification requests
- Develop and coordinate Press releases in conjunction with the NEI, Network Chairs, and Protocol Chairs

2. Network Chairs

The Network Chairs work closely with, but independently of, the Coordinating Center for the following specific responsibilities:

- Assume overall scientific responsibility and direction for Network protocols
- Assist CC in managing day-to-day Network scientific activities
- Provide input and assist with preparation of all manuscripts, abstracts, and slide set presentations
- Serve as spokesperson of the Network to the public
- Chair investigator calls, as needed
- Represent the Network with regulatory agencies such as the FDA

- Assist the Coordinating Center with communication with IRBs when ophthalmic expertise is needed
- Assist and back-up Protocol Chairs for protocol related questions and site contact related to specific protocols
- Participate with the Coordinating Center in coordination of activities between the Network and the NEI
- Participate and serve as spokesperson in coordination of activities between the Network and industry (for-profit) sponsors, other not-for-profit sponsors (e.g., JDRF), and third-party payers
- Identify potential funding sources and assist with grant writing and review
- Assist the Coordinating Center with oversight of the Network annual budget including determining amounts available for new protocols
- Review and approve new site/investigator/fellow Network applications
- Communicate with new clinical centers
- Review of 'competing studies' proposals, with regard to impact on existing or planned DRCR Retina Network protocols
- Serve as an ex officio representative to the Data and Safety Monitoring Committee and the External Protocol Concept Review Committee as needed
- Oversee consultant expertise when needed for a specific protocol for which expertise is not available within the Network.
- Serve on the Operations, Steering, and Executive Committees
- Work with the Coordinating Center staff to develop and evaluate manuscript proposals
- Work with the Coordinating Center staff to develop, review, refine analyses for the proposals
- Draft, edit, and review manuscript outlines and drafts, literature reviews, and final manuscripts
- Assist in drafting responses to journal reviewer comments
- Assist in development of analyses, abstracts, and final presentation materials for meeting presentations
- Maintain communication with designated sites' investigators to resolve issues, encourage enrollment, and discuss other protocol- or site-related issues, particularly when issues span across multiple protocols.
- Provide direction for future study protocols

The DRCR Retina Network will have two Network Chairs. One Chair will oversee studies on diabetic eye disease and the other Chair will oversee studies for AMD, vein occlusions, and retinal diseases other than diabetic retinopathy. The Network Chairs will be selected through a broad solicitation of Network participants and non-Network parties. The Network Chairs will serve no more than two 5-year terms (refer to separate document, Process for Selection of DRCR Retina Network Chair, for more details).

3. Other Network Investigator Positions(s)

The Network may create other Investigator Positions as needed. The Executive Committee is responsible for creating and approving other Investigator Positions.

C. Clinical Sites

The clinical sites will be responsible for carrying out the study protocols. A participating clinical site must have at least one individual who meets criteria to be a Network Investigator (refer to a separate document, DRCR Personnel and Site Requirements, for additional information). One investigator at the site must be designated as the Principal Investigator, who will have overall responsibility for all Network-related activities. For each protocol, a protocol Principal Investigator will be designated who is responsible for protocol-related activities and data collection. Additional clinical site staff include sub-investigators, clinic coordinators, and other personnel as needed for the project/protocol. Appropriate backup must be available for all positions. Clinical site investigators will have the opportunity to have a role in all aspects of each project including protocol development, data analyses, and publication of results.

D. Protocol Chairs and Protocol Development Committees

Each primary protocol will have a designated Protocol Chair or Co-Chairs. Multi-phase protocols may have a separate Protocol Chair for each phase. Each Protocol Chair will be proposed by the Operations Committee and approved by the Executive Committee.

The Protocol Chair's role will focus on both scientific aspects of the protocol and communicating with sites to ensure high quality protocol adherence. Protocol Chairs will work with CC staff to develop protocol materials during all stages of development. Protocol Chairs will also oversee site monitoring and protocol monitoring and help develop and maintain methods for quality assurance. Each Protocol Chair will work closely with CC Protocol Monitors to maintain communication with site investigators to resolve issues, encourage enrollment, and discuss other protocol- or site-related issues. Protocol Chairs will also be involved in the development of manuscripts. Protocol Chairs will attend their respective Steering Committee calls.

The responsibilities of the Protocol Chair include, but are not limited to:

- Conduct review and perform background research as needed for submitted protocol and ancillary protocol concepts for discussion with the Steering Committee
- Work with the Network Chairs, Coordinating Center staff, and Protocol Development Committees on protocol development
- Develop drafts of new protocols
- Assist Coordinating Center in developing materials for a protocol, including Informed Consent Form, Statistical Analysis Plan, Procedure Manual, certification materials including Q and A and, case report forms (including review of website application, and site budget)
- Review of data to be collected in Network protocols, including case report forms, imaging (e.g., OCT, photos, FA) and other types of data collection
- Serve on a Steering Committee

- Maintain communication with designated sites' investigators to resolve issues, encourage enrollment, and discuss other protocol- or site-related issues.
- Review quality assurance reports regarding Network performance, comprehensively on a semiannual basis, and at any other times that issues arise
- Monitor adherence to protocols through review of collected data regarding performance and site visits
- Monitor the performance of all participating sites and central units
- Conduct protocol review and certification calls with investigators at the commencement of a protocol
- Lead in and encourage study enrollment
- Respond to protocol queries received from clinical sites
- Respond to protocol treatment deviations by clinical sites
- Consider modifications to the protocol, as necessary
- In general, chair writing development committee for the primary manuscript from the study
- Assist in proposing and developing secondary manuscript ideas from the study
- In general, provide initial public presentation of main outcomes of the study

In general, an investigator should not serve as Protocol Chair for more than one major project at a time. Each Protocol Chair provides at least 5% effort for Network-related activities.

A Protocol Development Committee will be formed for each protocol. This will include the Protocol Chair (when already appointed), Network Chairs, other selected investigators and coordinators, representatives of the Coordinating Center and, when appropriate, external experts and representatives of reading centers or other resource sites. The activities of each Protocol Development Committee will be coordinated by the Coordinating Center.

The responsibilities of the Protocol Development Committee include, but are not limited to:

- Attendance on regular video conference calls and generally one in-person meeting to design the protocol
- Development of the final protocol
- Pilot testing of study forms and procedures prior to commencement of study participant recruitment, if needed

Some protocols in development may require specialists from outside of the Network where additional expertise is needed. The Operations Committee will select specialists for such protocols. The specialists will join the designated Protocol Development Committee(s) and will focus on aspects of the protocol(s) that fall within their specific expertise.

E. Committees

1. Operations Committee

The Operations Committee includes the current Network Chairs, Network Chair(s) Emeritus, the Coordinating Center Director and Associate Director.

Specific functions of the Operations Committee include, but are not limited to:

- Oversee scientific direction of the Network
- Responsibility for day-to-day oversight, management, and operational issues for the Network
- Contribute to final drafting of new protocols
- Prioritize manuscripts to be written, including secondary manuscripts and manuscript ideas solicited from investigators or other individuals approved by Steering Committee
- Plan for abstract submissions and meeting presentations
- Assist with drafting of manuscripts
- Oversee manuscript planning and ensure timely completion of manuscript tasks
- Review of posters and presentations of already published data
- Develop plan for dissemination of study results as indicated

A weekly conference call of the Operations Committee will be held.

2. Steering Committees

There are two Steering Committees, one responsible for studies on diabetic eye disease and the other will oversee studies for AMD, vein occlusions, and all other retinal diseases. The standing members of the Steering Committees will include all members of the Operations Committee, a senior investigator, and the respective Protocol Chairs.

In general, Protocol Chairs will serve on the appropriate Steering Committee while their respective protocol is active. Protocol Chairs will generally rotate off the Steering Committee after the study is complete, and the primary manuscript and other key manuscripts are accepted for publication, unless their term is extended by vote of the Operations Committee.

Whereas the Executive Committee is responsible for issues related to the Network in general, Steering Committees are responsible for issues specific to protocols. The Steering Committees are responsible for protocol specific monitoring and oversight. Committee members will assist Network Chairs and the Coordinating Center with key decision-making regarding protocol related issues.

Responsibilities of the Steering Committee include, but are not limited to:

- Contribute to early and mid-stage drafting and review of new protocols
- Consider changes or modifications to the protocol as necessary or desirable
- Review and determine which visits are considered research visits and paid for by the study and which visits are considered standard care visits and billed to the patient or the patient's insurance for each protocol
- Recommend amendments to ongoing protocols as needed
- Advise and assist the Coordinating Center on operational matters related to protocol implementation and adherence
- Monitor the performance of all participating sites

- Review quality assurance reports regarding Network performance, comprehensively on a semiannual basis, and at any other times that issues arise
- Monitor adherence to protocols through review of collected data regarding performance and site visits (accompanied by outside, independent, unconflicted consultants as needed)
- Review quality metrics across all sites and DRCR Retina Network studies approximately twice per year
- Advise and assist the Coordinating Center on operational matters related to protocol implementation and adherence
- Address imaging issues for Network protocols
- Review and approve abstract ideas, statistical analysis ideas, and manuscript ideas.
- Review and approve of protocol amendments unless there is a significant change in budget ($50,000 or greater than 20% of the study budget).
- Review and approve ancillary protocols/sample analyses ideas with direct costs of no more than $100,000 each and totaling up to no more than $300,000 annually. Total costs exceeding $100,000 each or $300,000 in aggregate will have to be reviewed approved by the Executive Committee. CC staff time, priorities, and available resources will also be considered before deciding to proceed with an idea.
- Review and approve abstracts, posters, presentations of data not already publicly available
- Determine journal selection for manuscripts and approve dissemination plan
- Resolve any disagreement regarding authorship listing for manuscripts
- Conduct initial review of submitted protocol and ancillary study ideas
- Select protocol specific committees including protocol development committees and writing committees

In general, two biweekly calls will be held each month. The two committees will have separate calls.

Members of the Steering Committees will be invited to conduct initial review of submitted protocol concepts from investigators in and outside the Network as they are submitted. The Steering Committee responsible for studies on diabetic eye disease will review ideas related to diabetic eye disease and the other will review ideas for AMD, vein occlusions, and all other retinal diseases. The Steering Committees will decide on degree of merit and public health importance for presentation to investigators at the semiannual Coordinator/Investigator meetings and recommendation to the Executive Committee.

3. Executive Committee

The standing members of the Executive Committee will include all members of the Operations Committee (listed in a separate section), past Coordinating Center Principal Investigators, Steering Committee members, a NEI representative, select Reading Center representatives, and other members of Network leadership. An investigator from a site on probation is not eligible for nomination to the Executive Committee. If a site is placed on probation, any investigators from that site serving on the Executive Committee may be asked to resign.

The Executive Committee has overall responsibility for providing scientific oversight of the activities of the project. This Committee also formulates all policy decisions related to the maintenance and conduct of the project.

Responsibilities of the Executive Committee include, but are not limited to:

- Primary responsibility for the scientific oversight of the Network
- Provide input on issues related to the Network, including issues brought to the Committee by the Operations Committee
- Develop requirements for the participation of clinical sites and investigators and other site personnel
- Review recruitment reports on active protocols across sites
- Develop and enforce Network policies
- Select Network Chairs
- Select Protocol Chairs following recommendation of the Operations Committee
- Select and prioritize protocols to be developed following recommendation of the Steering Committee and buy-in from investigators
- Review and approve all ancillary studies utilize Network funds
- Review and approve primary outcome and secondary outcome manuscripts
- Review recommendations of the Operations Committee of imaging needs and reading center(s) for each protocol
- Review progress and monitor performance of imaging reading centers
- Monitoring the performance of central units
- Prioritize studies for protocol development
- Provide input to the Coordinating Center and Network Chairs on Network budgets
- Review and approve all protocols, including protocol budgets, and any budgetary increases larger than $50,000 or greater than 20% of the study budget after initial approval. Any protocol amendments or other sources of budgetary increases less than $50,000 or less than 20% of the study budget are approved by the appropriate Steering Committee
- Review and approve ancillary protocols/sample analyses with direct costs more than $100,000 each or totaling more than $300,000 annually. CC staff time, priorities, and available resources will also be considered before deciding to proceed with an idea.
- Review and approve collaborations and funding, including unrestricted grants or gifts from Industry or foundations
- Review and approve of any other communications on behalf of the Network.

Items that are reviewed and approved by the Executive Committee will be considered approved if the majority of the Committee approves and there are no disapprovals. In the case of a disapproval, a conference call or meeting will be held before moving forward. In general, two in-person Executive Committee meetings will be held each year. Conference calls will be held as needed.

4. Advisory Committees and Other Subcommittees

Advisory Committees and other subcommittees may be developed as needed for non-Network areas where additional expertise is desired (e.g. genetics, optical coherence tomography angiography studies).

5. Data and Safety Monitoring Committee (DSMC)

The DSMC is an independent group composed of individuals not directly involved in patient care or data collection for the study. The DSMC is responsible for reviewing the ethical conduct of the study, for monitoring the safety of the participants, assessing data for evidence of adverse or beneficial treatment effects and providing recommendations about stopping or continuing a trial. The DSMC may also formulate recommendations to enhance the trial's scientific integrity and timeliness including recommendations relating to the selection/recruitment/retention of participants, their management, improving adherence to protocol-specified treatments, and procedures for data management and quality control. The Data and Safety Monitoring Committee is advisory to the Network.

The members of the DSMC will be based on recommendations from the Study Leadership and the NEI program staff. The National Eye Institute will select one of the DSMC members to serve as the Chair. The voting members will include individuals with expertise in clinical trials, biostatistics, ophthalmology, diabetes, and bioethics. The NEI Project Officer will be considered an ex-officio nonvoting member.

Prior to the initiation of recruitment for a protocol, the DSMC must approve the study protocol, including the informed consent procedure and form. Subsequent protocol changes that are substantive must be approved by the DSMC prior to implementation. Minor changes that do not impact study participant safety or the assessment of efficacy do not require prior DSMC approval and will be reported to the DSMC at its semi-annual meetings. At its discretion, the DSMC may recommend to the Executive Committee that a protocol change be considered.

The DSMC will periodically review the progress of each protocol involving study participant safety (at least twice each year either at a meeting or via a conference call) and any other protocol they deem would benefit from their monitoring. In conjunction with the Coordinating Center, the Committee will determine specific plans for evaluating adverse effects and efficacy, including deciding whether a formal interim analysis should be performed.

Recommendations made by this Committee relating to the protection of patient rights and/or resulting from data analyses are forwarded to the National Eye Institute. For randomized clinical trials, results are not available to the participating investigators involved in patient care until the DSMC recommends that this information be released.

DSMC financial disclosures will be reviewed by Coordinating Center designee annually and follow the Network's Financial Disclosure Policy.

Further details of the role of the DSMC appear in the DSMC Standard Operating Procedures.

6. External Protocol Review Committee

The External Protocol Review Committee (EPRC) is an independent review group formed by the NEI. The responsibility of the EPRC is to review the Network protocols and their comments are advisory to the NEI as well as the Network investigators. The EPRC is developed and managed by the NEI and is advisory to the Network.

POLICY APPENDIX II – FINANCIAL DISCLOSURE POLICIES

Version Date: October 31, 2025

The policy will be reviewed for potential revisions at least annually by the Executive Committee.

A. Financial Disclosure Policy Overview

Based on U.S. Public Health Service regulations (42 CFR Part 50 Subpart F), the DRCR Retina Network has developed a policy to promote objectivity in research by establishing a policy that provides a reasonable expectation that the design, conduct, and reporting of DRCR Retina Network research is free from bias resulting from investigator financial conflicts of interest. For the purposes of this policy, the term "investigator" means any member of the DRCR Retina Network who is expected to disclose financial interests.

Investigators are expected to be discriminating in the selection of outside commitments in order to avoid impairment of the Network's reputation as a leading research entity within the ophthalmic community. Investigators should avoid commitments that could compromise the basic scholarly independence and freedom of action that are central to the Network.

Investigators at an institution without a 42 CFR Part 50 compliant Financial Conflict of Interest Policy must follow the Jaeb Center for Health Research Foundation, Inc. (JCHR) Financial Conflict of Interest Policy and are required to be trained on the Policy. The DRCR Retina Network policy is consistent with and complimentary to the JCHR IRB Conflict of Interest Policy (https://wiki.jaeb.org/SOP/index.php/Conflict_of_Interest). Training must occur no less than every four (4) years and whenever the JCHR COI SOP is revised with major changes.

B. Definitions

1. Institutional Responsibilities

Institutional responsibilities refer to the responsibilities related to the investigator's position. These may include professional responsibilities such as teaching, consulting, research, professional practice, institutional committee membership, and service on panels such as IRBs or Data and Safety Monitoring Boards.

2. Significant Financial Interest

As defined by 42 CFR Part 50, a significant financial interest (SFI) consists of one or more of the following interests of the investigator (or those of the investigator's spouse and dependent children):

- With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the 12 months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure exceeds $5,000.00. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value.
- With regard to any non-publicly traded for-profit entity, a SFI exists if the value of any remuneration received from the entity in the 12 months preceding the disclosure exceeds

$5,000.00. A SFI also exists when the investigator (or the investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest) in a non-publicly traded entity.

- Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

In addition, an SFI exists whether remuneration is paid directly to the investigator OR to the investigator's institution/legal entity on the investigator's behalf.

The term significant financial interest does not include the following types of financial interests:

- Salary, royalties, or other remuneration paid by Jaeb Center for Health Research Foundation, Inc. (JCHR) to the investigator if the investigator is currently employed or otherwise appointed by JCHR, including intellectual property rights assigned to JCHR and agreements to share in royalties related to such rights;
- Income from investment vehicles, such as mutual funds and retirement accounts, as long as the Employee does not directly control the investment decisions made in these vehicles.
- Income from seminars, lectures, or teaching engagements sponsored by
  - a Federal, state, or local government agency,
  - an Institution of higher education as defined at 20 U.S.C. 1001(a),
  - an academic teaching hospital,
  - a medical center, or
  - a research institute that is affiliated with an Institution of higher education;
- Income from service on advisory committees or review panels for
  - a Federal, state, or local government agency,
  - an Institution of higher education as defined at 20 U.S.C. 1001(a),
  - an academic teaching hospital,
  - a medical center, or
  - a research institute that is affiliated with an Institution of higher education.

3. Financial Conflict of Interest

A SFI is considered to be a financial conflict of interest (FCOI) if it is related to the research and could directly and significantly affect the design, conduct, or reporting of research. See section D for DRCR Retina Network policy on avoiding FCOI.

4. Related Research

Related to DRCR Retina Network research means an entity that provides funding or support for DRCR Retina Network research or whose financial interest would reasonably appear to have the potential to be directly or indirectly materially affected by the outcome or conduct of the DRCR Retina Network research. Examples include, but are not limited to, companies that hold patent rights for discoveries, drugs, or devices being studied in DRCR Retina Network protocols or companies that provide financial or in-kind support for research projects. This term includes

companies that compete with any companies that collaborate with the DRCR Retina Network or compete with the manufacturer of the investigational product, if the DRCR Retina Network investigator knows that the financial interests of such a company would reasonably appear to be affected by DRCR Retina Network research. This term also includes any entity acting as the agent of a financially interested company (e.g., a contract research organization). If there is any ambiguity as to whether the company is related to DRCR Retina Network research, the company must be disclosed. In these cases, by examining the company's business and the scope of research conducted by the DRCR Retina Network, the Network Chair and the Director of the Coordinating Center (or Executive Committee, where applicable) will judge whether the investigator's interest is with a “financially interested company."

5. Involved Entity

An entity whose product is being evaluated in the planned or ongoing DRCR study.

C. Reporting Financial Disclosures

1. Personnel Required to Report

All DRCR Retina Network investigators, coordinators, committee members, and other individuals who are responsible for the design, conduct, or reporting of research (e.g., collaborators or consultants), are required to report financial interests according to this policy (note: throughout the remainder of this document, wherever the term “investigator” is used, it also should be considered as indicative of committee members and other individuals in the Network required to report this information). Being responsible for the conduct of research is not the same as performing a study procedure. For instance, a study staff member who conducts visual acuity testing on a study participant is not considered an investigator. Financial interest of an investigator’s dependent(s), domestic partner, or spouse also must be disclosed. In general, clinical site staff other than study investigators and study coordinators are not required to report financial interests according to this policy unless participating on a Network committee (e.g., Writing Committee, Executive Committee, etc.).

2. Financial Interests to Disclose

All significant financial interests (SFI) from an entity related to DRCR Retina Network Research must be disclosed. Additionally, per the NIH Grants Policy Statement 4.1.10, foreign SFIs (which includes income from seminars, lectures, or teaching engagements, income from service on advisory committees or review panels, and reimbursed or sponsored travel) received from any foreign entity, including foreign Institutions of higher education and foreign governments (which includes local, provincial, or equivalent governments of another country) must be disclosed, whether or not related to DRCR Retina Network research. Disclosure is required whether remuneration is paid directly to the investigator OR to the investigator’s institution/legal entity on the investigator’s behalf. Relationships unrelated to DRCR Retina Network research that are not from a foreign entity do not require disclosure.

3. Frequency of Reporting

Investigators are required to complete the DRCR Retina Network financial disclosure form:

a. annually,
b. within 30 days of discovering or acquiring (e.g. through purchase, marriage, or inheritance) a new SFI or a substantial change to an SFI.
    - A substantial change is defined as when a previously reported SFI increases to a higher category level defined as follows: $10,000–$19,999; amounts between $20,000–$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000.

IRB requirements for reporting SFI prior to initiation of a new protocol will be followed.

Additional FDA reporting requirements may also be required. If an investigator is participating in a study that is FDA regulated, disclosure must also be made when a substantial change occurs to a financial interest.

- A substantial change is defined as when a previously reported SFI increases to a higher category level defined as follows: $10,000–$19,999; amounts between $20,000–$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000.

4. Disclosure Process Details

Financial disclosures are completed on the DRCR Retina Network study website Financial Disclosure Form.

Financial disclosures are made separately for the following categories:

- Prospective Clinical or Epidemiological Research Grant – a grant from the entity paid to an organization for the conduct of a prospective clinical study or epidemiologic study that receives IRB approval
- Basic Science Laboratory Research Grant – a grant from the entity paid to an organization for the conduct of basic science laboratory research
- Other Research Grant – Investigator-initiated research not meeting criteria above that is conducted for scientific or public health purposes and not considered Work for Hire for the benefit of the company. A research grant in this category should be money that is paid for a specific research purpose with the intent that the results will be reported in a scientific publication. In general, this research would be investigator-initiated, would have a budget, protocol, statistical analysis plan, or similar document describing the research and would receive IRB review with either IRB approval of the activity or designation as exempt research.
    - Details (e.g., protocol, statistical analysis plan, IRB approval, or similar document) of activities conducted in this category may be requested for clarification of appropriate reporting.
- Professional Fees– monies paid to an individual or to an organization for services rendered, including honoraria, or fees for consulting, lectures, speakers' bureaus, expert testimony, employment, board membership, office positions, or other affiliations.

- Royalties
- Intellectual Property Rights Patents (planned, pending, or issued)
- Stock/stock options
    - Equity Interest (publicly or non-publicly traded entity; stock, stock option, or other ownership interest
    - Investment vehicles, such as mutual funds and retirement accounts, controlled by the Investigator)
- Reimbursed or sponsored travel
- Other including non-financial support –equipment, supplies, or anything else not covered in the above categories.

Any listing on Open Payments as a General Payment but not reported to the Network as a professional fee should be reconciled on request by revising the prior DRCR disclosure or by submitting a written as to why the Open Payments reporting is incorrect.

All classifications above are irrespective of whether receipt of the financial support is directly to the investigator or to the investigator's institution/legal entity. The investigator will indicate whether he/she has equity in the institution/legal entity.

Support paid to the investigator and support paid to the institution for research will be reported within the following categories: $0-$4,999; $5,000-$9,999; $10,000-$19,999; $20,000-$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000, a statement that a value cannot readily be determined, or a statement that the value cannot be disclosed (e.g. confidentiality agreement with entity). Only support related to the Investigator's Institutional responsibilities should be counted as support paid for research, otherwise the value should be reported as not for research.

D. Managing Financial Disclosures

Ultimately it is the responsibility of JCHR and the investigator's institution, if the institution has a FCOI policy conformant to 42 CFR 50 Subpart F, to manage financial interests; however, DRCR Retina Network has developed a policy to avoid FCOI within the Network.

1. Policy to Avoid Financial Conflict of Interest

The DRCR Retina Network policy aims to avoid FCOI whenever possible. The following policy ensures that any SFI could not directly and significantly impact the design, conduct, or reporting of research. If exceptions are granted to the below criteria, the Investigator's financial interests will be considered and if needed, managed via a management plan and reported to the NIH as a managed FCOI. The Executive Committee reserves the right to assess all disclosures as to whether a potential FCOI exists. The Executive Committee also reserves the right to confirm for each protocol if this policy is appropriate. The following policies are in place to avoid FCOI within the Network.

- No Investigator in the network, regardless of financial interests, may enroll more than 10% of the study participants into any DRCR Retina Network study.

    - In rare cases, an exception may be made for small scale or feasibility studies. In those cases, an Investigator may be allowed to enroll more than 10% of participants.
- The Principal Investigator of the DRCR Retina Network Coordinating Center and a Network Chair(s) are presumptively prohibited from having a non-research, SFI with an entity *involved* in DRCR Retina Network research or a *related* entity that has an FDA approved product for an indication being evaluated in current studies or studies in development.
    - Note: The Network Chair(s) and Coordinating Center PI are presumptively prohibited from owning stock, being an employee, or having ownership rights in an involved company or a company related to current DRCR research or studies in development.
- No more than 25% of the members of any writing committees will have a non-research SFI with an entity related to the work being conducted for the specific DRCR Retina Network research during their committee term. No lead author on a DRCR Retina Network manuscript will have a non-research SFI of $20,000 annually or more with an entity involved in the work being conducted for the specific DRCR Retina Network protocol/publication.
- No more than 25% of the members of any protocol development committees should have a non-research SFI with an entity related to the work being conducted for the specific DRCR Retina Network research during their committee term.
- The Protocol Chair for a study is presumptively prohibited from having a non-research SFI exceeding $20,000 annually with an entity *involved* in the work being conducted for the specific DRCR Retina Network protocol (e.g. funder or manufacturer of the investigational product) or a related entity that has an FDA approved product for the indication being studied in the protocol. Protocol Chairs will have their disclosures for other related companies reviewed by the Executive Committee before approval and annually while the study is ongoing. If a non-research SFI with a related company has the potential to influence the work of the Protocol Chair, the Executive Committee can require the Protocol Chair to divest their SFI or give up their Protocol Chair position.
- All Executive Committee members will have their non-research SFI disclosures for related and involved entities reviewed by the Executive Committee annually.
- Members of the Data and Safety Monitoring Committee are presumptively prohibited from having a non-research SFI with an entity *related* to DRCR Retina Network research for which the DSMC is monitoring.

The determination of whether a FCOI exists in certain instances can be a matter of judgment involving all the facts of the situation. The Network Chairs and Director of the Coordinating Center (or Coordinating Center designee) will oversee review of potential FCOI. If the investigator disagrees with the management plan proposed by the Network Chair and Coordinating Center Director (or Coordinating Center designee), the investigator can make an appeal to the Executive Committee, which will delegate review of the disclosure to a sub-

Committee of the Executive Committee. When necessary, the sub-Committee will provide final decisions on behalf of the Network.

2. Investigator Options When a Presumptive Prohibition is Identified to Avoid a FCOI

If a presumptive prohibition above is identified, a management plan will be developed. The following are examples of how unique instances might be managed.

- Preclude participation in the design or reporting of the study
- Divestiture – allow arrangements to go forward contingent upon the sale or disposal of specified financial interests to eliminate or reduce the financial conflict of interest by a certain date
- Severance of relationships that heighten or create actual or potential conflicts – investigators may be required, as example, to relinquish a seat on a board of directors or terminate a consulting arrangement with an outside entity in order to reduce the financial or fiduciary conflict of interest

The Network Chairs and Coordinating Center Director, or the Executive Committee members (when cases are overseen by the Executive Committee) may recommend other conditions or restrictions on the proposed arrangements if such conditions or restrictions will contribute to the elimination, reduction, or management of the conflict of interest.

If an IRB separately determines that an FCOI exists that does not meet the above definitions, a management plan may also be required.

E. Public Disclosure of Reported Financial Interests

All reported financial disclosures are available on the DRCR Retina Network public website. Only the relationship, not the amount of the relationship, is publicly disclosed. In addition, investigators are required to disclose any FCOI in all applicable presentations and publications.

F. Additional Requirements for Investigators Covered Under JCHR Financial Conflict of Interest Policy

Investigators covered under the JCHR financial conflict of interest policy must abide by this DRCR Retina Network policy as well as the JCHR policy (see policy https://wiki.jaeb.org/SOP/index.php/Conflict_of_Interest).

The following additional requirements are required for investigators covered under JCHR policy:

1. Travel Reporting

Investigators must disclose the occurrence of any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), not reimbursed directly by JCHR, whether related to their institutional responsibilities or not (e.g., travel related to consulting performed while the investigator has taken annual leave time must be reported); however, this disclosure requirement does not apply to travel that is reimbursed or sponsored by:

- a Federal, state, or local government agency,

- an Institution of higher education as defined at 20 U.S.C. 1001(a),
- an academic teaching hospital,
- a medical center, or
- a research institute that is affiliated with an Institution of higher education.

The JCHR FCOI policy requires that the investigator disclose the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with the JCHR FCOI policy, the institutional official will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes an FCOI with the investigator's research.

The disclosure must be reported within 30 days of travel.

POLICY APPENDIX III – INDUSTRY COLLABORATION POLICIES

Version 7.0 – Effective Date: April 15, 2021

DRCR Retina Network is committed to:

- performing rigorous multi-center clinical trials to address timely critical needs in diabetic retinopathy, diabetic macular edema, and other retinal diseases
- collaborating with industry in a manner that appreciates the needs of industry with regard to drug development while maintaining clinical trial design, investigational ethics and rigorous implementation consistent with academic standards

The sections below outline the DRCR Retina Network guidelines regarding industry collaboration. Depending on the type of collaboration, some of the guidelines below may not apply. The DRCR Operations Committee will approve any collaboration with parameters that differ substantially from the guidelines below.

A. Protocol Development

1. The DRCR Retina Network will develop the protocol according to Network standards (including associated procedures, CRFs, statistical plan, etc.).
2. The industry partner may provide input, especially with regard to regulatory issues when the protocol is being conducted under an IND or IDE.
3. The DRCR Retina Network will accommodate industry partner needs required for drug or device registration as long as they are feasible and maintain clinical trial design and implementation consistent with academic standards.
4. The DRCR Retina Network will consider expanding protocols with additional industry support to provide adequate size such that industry can analyze data as two definitive trials according to FDA guidance if so requested by the industry partner.
5. All final decisions regarding protocol design, development and implementation will be made by the DRCR Retina Network.
6. The protocol will be placed in the public domain at the commencement of the study. The protocol will be posted on the DRCR Retina Network public website (drcr.net) and summarized on public websites such as clinicaltrials.gov.

B. Study Data

1. The DRCR Retina Network will have ownership of the study data.
2. The final dataset will be placed in the public domain.
3. At the completion of the study, the DRCR Retina Network will distribute a final dataset to the industry partner for its needs regarding FDA submission (as a general rule, the DRCR Retina Network does not intend to prepare FDA submissions itself) and its internal use. The dataset may not be used for any other purpose unless approved by the DRCR Retina Network.

C. Publications, Presentations, and Publicity

1. The DRCR Retina Network is free to publish and present the study data without restriction.

2. The DRCR Retina Network will provide the industry partner with the opportunity to review and comment on the primary manuscript and any secondary manuscript that provides information related specifically to the treatment under study that is not already in the public domain. This policy also applies to abstracts and presentations that are made prior to the information having already been publicly disseminated. Unless the DRCR Retina Network and the industry partner agree on different time intervals, the industry partner will be given 14 days to comment on manuscripts and up to an additional 30 days if there is a need for the industry partner to submit patent application materials to obtain patent protection.
3. The DRCR Retina Network will have the opportunity to review and comment on all press releases of the industry partner related to the study prior to their release. The industry partner will not release information about the study without the review and comment from the DRCR Retina Network.
4. The industry partner may not publish or present any study results that have not already been publicly disseminated by the DRCR Retina Network.

D. Data Integrity

1. The DRCR Retina Network Coordinating Center will oversee data collection, data cleaning, data lock, data maintenance, etc. The DRCR Retina Network utilizes electronic data capture such that the electronic capture is the source documentation.
2. The DRCR Retina Network will provide the industry partner with details of these procedures for the industry partner to verify that these procedures meet regulatory requirements.
3. The industry partner may conduct a yearly site visit of the Coordinating Center to evaluate issues related to maintaining the database and other Coordinating Center procedures as they pertain to meeting regulatory requirements.

E. Clinical Sites

1. The DRCR Retina Network will select the participating sites and establish the procedures for their certification. Certification includes the review and approval of regulatory documents such that the clinical site is approved to receive investigational product and subsequently enroll patients.
2. The industry partner may review these procedures to verify that they are in accord with regulatory requirements.
3. The DRCR Retina Network Coordinating Center will be responsible for the certification of the sites.

F. Site Monitoring

1. The DRCR Retina Network will determine those monitoring needs it deems critical for the study and provide the support needed.

2. The industry partner may review the DRCR Retina Network site monitoring plan to verify that it meets regulatory requirements.
3. The industry partner will not be permitted to contact the clinical sites, request data or conduct monitoring visits without approval from the DRCR Retina Network. Permission may be granted in the event of a pending FDA audit.
4. If the industry partner determines that additional monitoring is needed for regulatory purposes, the DRCR Retina Network will consider this request but will have the right to reject the request. Support for any additional monitoring will be provided by the industry partner.
5. The monitoring will be overseen by the the DRCR Retina Network Coordinating Center, which will have the option of conducting this monitoring itself.

G. Adverse Event Reporting

1. The DRCR Retina Network will establish a system for adverse event reporting, review, and coding.
2. The industry partner may review this plan to verify that it is in accord with regulatory requirements and will meet the industry partner's needs for its FDA submission.

H. Efficacy and Safety Reviews, Stopping Decisions

1. The DRCR Retina Network will be responsible for developing the statistical analysis plan.
2. The industry partner may review this plan to verify that it is in accord with regulatory requirements and will meet the industry partner's needs for its FDA submission.
3. An independent Data and Safety Monitoring Committee (DSMC) will review all data (masked or unmasked) as appropriate and make suggestions to the DRCR Retina Network regarding protocol modifications and stopping a study for efficacy or safety. The industry partner will not be provided with the study data (other than the aforementioned masked adverse event data) until either the conclusion of the study or the DSMC's decision that such data can be provided.
4. The DRCR Retina Network will provide the industry partner with monitoring reports related to study progress (such as a recruitment report by month).

I. Investigational Product

1. The industry partner will be responsible for providing the investigational product, placebos (when applicable), packaging of the investigational product, all necessary manufacturing information for the IND or IDE and any related materials. The industry partner will agree to provide the investigational product and related materials for the duration of the study.

2. Investigational drug will be manufactured in accordance with Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) standards. Investigational devices will be manufactured in accordance with GMP standards.
3. The DRCR Retina Network will develop procedures for supplying the investigational product to the clinical sites, maintaining accountability of the investigational product at the site, and disposal or return of the investigational product. The industry partner will pay for the costs of supplying investigational product to the clinical sites and returning investigational product for disposal, if required. The industry partner, if requested, will supply the investigational product and related materials directly to the clinical sites.

J. Laboratory Measurements

1. The DRCR Retina Network will determine those laboratory measures it deems necessary for the study.
2. The industry partner may identify those additional laboratory measures required for regulatory or other purposes. The DRCR Retina Network will attempt to accommodate these needs as long as they do not adversely affect the conduct, data validity or safety of the study.
3. The DRCR Retina Network will have the final decision on the use of a central laboratory.

K. FDA Registration and Submission

1. The DRCR Retina Network will have the option of applying for and maintaining the IND or IDE. The industry partner will assume this function if requested by The DRCR Retina Network.
2. The industry partner will perform registration and submission specific analysis and preparation as needed.
3. The DRCR Retina Network and the industry partner will provide one another with a copy of all documents submitted under the IND or IDE.
4. Should there be a need to conduct a second trial specifically for the purpose of the FDA submission, the industry partner will have the option of conducting the second trial independently from the DRCR Retina Network or may contract with the DRCR Retina Network to conduct the second trial as long as the DRCR Retina Network agrees that such a trial is an appropriate use of the DRCR Retina Network resources at that time.

L. The DRCR Retina Network Policies

1. The industry partner will be provided with a copy of the DRCR Retina Network policies and the Terms and Conditions of the NEI Cooperative Agreement.

M. Study Committees and Oversight

1. The industry partner will appoint an individual to serve as the liaison with the DRCR Retina Network.
2. The liaison will receive recruitment reports on the progress of the study.

N. Legal Agreements

1. A legal agreement will be established between the industry partner and the Coordinating Center.
2. A legal agreement will be established between the Coordinating Center and each participating site for the site's participation in the study.
3. The legal agreement will contain an indemnification section that specifies, the situations in which the industry partner will provide indemnification, a confidentiality section agreeable to both parties, and an intellectual property section agreeable to both parties.

O. Cost Sharing

1. The DRCR Retina Network will usually provide funding along with collaborators, for studies that are:
   - associated with one definitive efficacy trial per specific intervention that meets the DRCR Retina Network standards
   - associated with earlier stage trials (e.g. dose-ranging) or other trial designs as deemed appropriate by the DRCR Retina Network
2. The DRCR Retina Network will usually not support clinical trial costs that are:
   - not necessary for optimal academic clinical trial design and implementation (eg. additional monitoring, special laboratory analyses, etc.)
   - associated with additional patient numbers required by the industry partner (eg. to have enough power to analyze data as two definitive trials according to FDA guidance)
   - second trials required for IND or IDE registration submission, etc. that do not add significant additional academic scientific information to that provided by prior trials.
3. The DRCR Retina Network funding, in general, will provide for the Coordinating Center, Network Chairs, Protocol Chairs, Steering Committees, Executive Committee, Data and Safety Monitoring Committee, and certain infrastructure costs at the clinical centers.
4. In general, the industry partner will be expected to provide funding for:
   - All costs for the clinical sites to conduct the protocol, through a subcontract with the Jaeb Center, including IRB costs
   - All costs involved with the manufacture, labeling, distribution, and disposal of investigational product and any other related costs associated with the intervention
   - All costs associated with image grading or other protocol-approved analyses (e.g., pathology, genetic, pharmacokinetic)
   - All laboratory costs
   - Site monitoring costs for site visits and other activities over and above what the DRCR Retina Network will be performing
   - All costs involved related to FDA and other regulatory agencies
   - All costs involved for PK study or other preclinical or ancillary studies mutually agreed upon by the DRCR Retina Network and the industry partner