

1 **DIABETIC RETINOPATHY CLINICAL RESEARCH NETWORK**

2  
3 **ORGANIZATIONAL STRUCTURE**

4  
5  
6 **I. Organizational Structure**

7 **A. Introduction**

8 The permanent central units of the project include the Coordinating Center and the Operations  
9 Center.

10  
11 The committee structure includes an Executive Committee and the Operations Group, as well as  
12 two National Eye Institute appointed committees: the Data and Safety Monitoring Committee  
13 (DSMC), which is advisory to the Coordinating Center and the National Eye Institute (NEI), and  
14 an External Protocol Review Committee, which is advisory to the NEI. Sub-committees will be  
15 created by the Executive Committee as necessary.

16  
17 The Executive Committee is responsible for providing scientific oversight of Network activities,  
18 including scientific oversight of both the Operations Center and the Coordinating Center as well  
19 as oversight of Network policies within the confines of the NIH terms and conditions for  
20 cooperative agreements. The Executive Committee can be considered analogous but not  
21 synonymous to a board of directors with respect to making policy decisions that are necessary  
22 for the scientific aspects of the Network, providing advice regarding Operations Group activities,  
23 selecting the Network Chair (subject to approval of the National Eye Institute) and Vice Chairs,  
24 and providing members who serve as part of periodic review of the Coordinating Center and  
25 Operations Center. The Operations Group is responsible for implementing the daily scientific  
26 operations of the Network and providing recommendations to be approved by the Executive  
27 Committee, analogous to senior officers (e.g., chief executive officer, chief operations officer,  
28 and other key positions) of a company. The Network investigators serve in an analogous role as  
29 “employee shareholders” of the Network, whose participation are needed to implement  
30 protocols; for example, implementation of protocols recommended by the Executive Committee  
31 and major publications of Network protocol results can occur only with buy-in and enthusiasm of  
32 Network clinical sites.

33  
34 **B. Central Units**

35 **1. Coordinating Center**

36 Adam R. Glassman, M.S. is Principal Investigator and director of the DRCR.net Coordinating  
37 Center, located at the Jaeb Center for Health Research in Tampa, Florida. Specific  
38 responsibilities of the Coordinating Center include:

- 39
- 40 • Solicit ideas for new studies from investigators
  - 41 • Assist the Operations Group with the development of study protocols and the protocol  
42 development committees
  - 43 • Obtain and maintain INDs and IDEs
  - 44 • Develop study documents such as protocols, operating procedures manuals, and data  
collection forms

- 45 • Maintain version control of all protocols, study documents, publications, presentations, and  
46 the like
- 47 • Coordinate and monitor the conduct of study protocols
- 48 • Develop and implement a data management system capable of supporting multiple projects
- 49 • Develop and maintain a multi-functional website for use by the Coordinating Center, clinical  
50 centers, retinal imaging reading centers, Operations Center, and committee members
- 51 • Develop procedures for patient enrollment and randomization
- 52 • Develop and implement a system for adverse event reporting
- 53 • Develop and implement a quality assurance program that includes training and certification  
54 of clinic staff, monitoring of adherence to the protocol, reporting of quality control data,  
55 validation of collected data, assessments of retinal imaging reading center(s), and assessment  
56 of drug packaging and labeling
- 57 • Coordinate the selection process of clinical centers in conjunction with the Network Chair
- 58 • Develop procedures and materials for certification of clinical centers and associated staff
- 59 • Develop systems to assist the clinical centers in maintaining a high rate of patient retention
- 60 • Develop and maintain a system to facilitate communication between the central units, clinical  
61 centers, and committees
- 62 • Develop and maintain a system for drug distribution and accountability
- 63 • Coordinate site visits, prepare site visit agendas, and prepare site visit reports
- 64 • Develop and maintain a system for semiannual collection, review, and reporting of financial  
65 disclosures for investigators, coordinators, and other key personnel as defined in the  
66 Network's Financial Disclosure policy
- 67 • Develop a system, if needed, for integration of a central laboratory into the project
- 68 • Develops and oversees implementation of subcontracts with clinical sites to participate in  
69 DRCR Network protocols
- 70 • Develop contracts with other centralized resource groups utilized in DRCR Network  
71 protocols, such as imaging reading centers for grading and transmission of imaging data to  
72 the Coordinating Center
- 73 • Develops contracts with industry collaborators following the DRCR Network's Industry  
74 Collaboration Guidelines
- 75 • Develops processes to accept unrestricted gifts within regulations and approval of the  
76 National Eye Institute
- 77 • Implement subcontracts with the participating clinical centers
- 78 • Develop materials for IRB submissions by the clinical centers
- 79 • Track IRB approvals and expirations

- 80 • Develop study close-out procedures and materials
- 81 • Develop statistical analysis plans
- 82 • Coordinate the preparation and publication of study manuscripts, including drafting the initial
- 83 manuscript draft
- 84 • Conduct data analyses for Data and Safety Monitoring Committee review as well as for
- 85 manuscripts, abstracts, presentations, and ancillary studies
- 86 • Coordinate activities with the Operations Center, Executive Committee, Operations Group
- 87 and any other committees
- 88 • Coordinate activities of the Data and Safety Monitoring Committee
- 89 • Arrange conference calls
- 90 • Arrange meetings, including semiannual Protocol Review Committee/Operations Group
- 91 Quality Control meetings, semiannual Coordinator/Investigator meetings, semiannual
- 92 Executive Committee/Protocol Prioritization & Planning meetings, semiannual Data and
- 93 Safety Monitoring Committee meetings, and Protocol Development Committee meetings
- 94 • Develop and disseminate agendas and summaries of committee conference calls and
- 95 meetings in coordination with the Operations Center
- 96 • Assist with communication with NIH, JDRF, regulatory agencies, and the public
- 97 • Develop clinical center budgets in conjunction with the Executive Committee
- 98 • Develop and maintain directory of project personnel
- 99 • Develop and maintain a public Network website

100

## 101 **2. Operations Center**

102 Neil M. Bressler, M.D., is the Principal Investigator of the Operations Center, which serves as  
 103 the office of the Network Chair. The Network Chair, within the Operations Center, works closely  
 104 with, but independently of, the Coordinating Center for the following specific responsibilities:

105

- 106 • Assume overall scientific responsibility and direction for Network protocols
- 107 • Chair the Operations Group to manage day-to-day Network scientific activities
- 108 • Provide input and assist with preparation of all manuscripts, abstracts, and slide set
- 109 presentations
- 110 • Provide initial review of Network financial disclosures with the PI of the Coordinating
- 111 Center or senior member of the Coordinating Center designated by the PI to determine if a
- 112 financial conflict exists per the Network's policies based on disclosures (subject to review
- 113 and final decision of the Executive Committee) and to recommend plans to manage any
- 114 financial conflicts (subject to review and final decision of the Executive Committee)
- 115 • Serve as spokesperson of the Network to the public
- 116 • Chair monthly investigator calls

- 117 • Represent the Network with regulatory agencies such as the FDA
- 118 • Assist the Coordinating Center with communication with IRBs when ophthalmic expertise is
- 119 needed
- 120 • Assist and back-up Protocol Chairs
- 121 • Participate with the Coordinating Center in coordination of activities between the Network
- 122 and the NEI
- 123 • Assist with communication with NIH, JDRF, regulatory agencies, and the public
- 124 • Participate and serve as spokesperson in coordination of activities between the Network and
- 125 industry (for-profit) sponsors, other not-for-profit sponsors (e.g., Juvenile Diabetes Research
- 126 Foundation, International), and third party payers
- 127 • Identify potential funding sources
- 128 • Assist the Coordinating Center with oversight of the Network annual budget including
- 129 determining amounts available for new protocols
- 130 • Review and approve new site/investigator Network applications
- 131 • Communicate with international sites interested in participating in the Network
- 132 • Work with the Coordinating Center to coordinate and back-up the activities of the Vice-
- 133 Chair(s) and other funded “working” positions (e.g., investigators funded to work on protocol
- 134 development or manuscripts or presentations)
- 135 • Provide support to other researchers desiring to use methodology developed for Network
- 136 operations or protocols, such as financial disclosure procedures and competing studies
- 137 procedures
- 138 • Review of ‘competing studies’ proposals, with regard to impact on existing or planned
- 139 DRCR.net protocols
- 140 • Serve as an ex officio representative to the Data and Safety Monitoring Committee and the
- 141 External Protocol Concept Review Committee as needed
- 142 • Oversee consultant expertise when needed for a specific protocol for which expertise is not
- 143 available within the Network.

144  
 145 The Network Chair will be selected through solicitation of Network participants. The Network  
 146 Chair will serve no more than two five-year terms coincident with the funding cycle of the  
 147 DRCR.net Operations Center.  
 148

### 149 **3. Network Vice-Chair(s)**

150 The Network Vice-Chair(s) will work closely with the Network Chair and Coordinating Center  
 151 to oversee site monitoring and protocol monitoring, develop and maintain quality assurance, and  
 152 backup Network Chair and Protocol Chairs when needed. Each Vice-Chair works with his or her  
 153 Protocol Monitor and is responsible for maintaining communication with their designated sites’  
 154

155 investigators to resolve issues, encourage enrollment, and discuss other protocol- or site-related  
156 issues. For a complete listing of responsibilities, see Operations Group.

157  
158 The Network Vice-Chair(s) will be selected through solicitation of Network participants. The  
159 Vice-Chair(s) will serve one-year renewable terms, up to three years with the exception of the  
160 inaugural Vice-chairs. For the inaugural Vice-Chairs, at least one will rotate off after years two,  
161 three, and four, so one member will have the opportunity to serve as Vice-Chair for two years  
162 and one member for up to four years. One or more Vice-Chairs will be selected (see separate  
163 document, Process for Selection of Network Vice-Chair, for more details).

#### 164 165 **4. Other Network Investigator Positions(s)**

166 The Network creates other Investigator Positions as needed, for example, for manuscript and  
167 protocol development. Investigator members serving in these positions will serve one-year terms  
168 renewable throughout each NIH grant period and will work closely with the Network Chair and  
169 Coordinating Center for new protocol development and implementation and manuscript  
170 preparation with the following specific responsibilities:

- 171 • Conduct initial review of submitted protocol concepts for discussion with the Operations  
172 Group
- 173 • Work with the Protocol Chairs, Network Chair, Coordinating Center staff, and Protocol  
174 Development Committees on protocol development
- 175 • Develop drafts of new protocols
- 176 • Review data to be collected for each protocol
- 177 • Assist Coordinating Center in developing materials for a protocol, including Procedure  
178 Manual, certification materials including Q and A, case report forms (including review of  
179 website application, and site budget
- 180 • Review of data to be collected in network protocols, including case report forms, imaging  
181 (e.g., OCT, photos, FA) and other types of data collection
- 182 • Conduct initial review of submitted ancillary study concepts from investigators, research the  
183 topic when needed, and decide on degree of merit and priority for recommendation to the  
184 Executive Committee
- 185 • Work with the Coordinating Center staff to develop and evaluate manuscript proposals
- 186 • Work with the Coordinating Center staff to develop, review, refine analyses for the proposals
- 187 • Review manuscript outlines, initial data, and manuscript drafts
- 188 • Write parts of manuscripts including literature reviews
- 189 • Draft responses to journal reviewer comments
- 190 • Development of analyses, abstracts, and final presentation materials for meeting  
191 presentations
- 192 • Provide oversight to meeting presentations

- 193 • Assist the Coordinating Center and Operations Group members with manuscript  
194 writing/reviewing

195  
196

### 197 **C. Clinical Centers**

198 The clinical centers will be responsible for carrying out the common study protocols. Clinical  
199 center staff include a principal investigator, co-investigators, clinic coordinators, and other  
200 personnel as needed for the project. Appropriate backup must be available for all positions.  
201 Principal investigators will have overall responsibility for all study-related activities and all data  
202 collection at the center. Clinical center investigators will have an active role in all aspects of the  
203 project including protocol development, data analyses, and publication of results.

### 204 **D. Protocol Chairs and Protocol Development Committees**

205 Each protocol, including primary protocols and ancillary studies, will have a designated Protocol  
206 Chair. Multi-phase protocols may have a separate protocol chair for each phase. Each Chair will  
207 be proposed by the Operations Group and approved by the Executive Committee.  
208

209  
210 The Protocol Chair's role will focus on scientific aspects of a protocol. During protocol  
211 development, the Protocol Chair will work with Coordinating Center staff to develop the  
212 protocol. During the conduct of the study, in general, the Protocol Chair's principal role will be  
213 to lead in and encourage enrollment, respond to queries regarding the protocol received from the  
214 clinical sites, respond to protocol treatment deviations by clinical sites, and as needed, to  
215 consider modifications to the protocol. Other responsibilities include chairing the writing  
216 committee for the primary manuscript from the study and providing the initial public  
217 presentation of main outcomes. Quality control aspects will largely be the responsibility of the  
218 Operations Group, as they are generally cross-protocol issues.

219  
220 A Protocol Development Committee will be formed for each protocol. This will include the  
221 Protocol Chair, representatives of the Coordinating Center and, when appropriate, reading center  
222 or other resource sites, the Network Chair, and other selected investigators and coordinators.  
223 The activities of the Protocol Development Committees will be coordinated by the Coordinating  
224 Center.

225  
226 In general, an investigator should not serve as Protocol Chair for more than one major project at  
227 a time.

### 228 **E. Committees**

#### 229 **1. Executive Committee**

230 The standing members of the Executive Committee will include all members of the Operations  
231 Group (listed in a separate section), each Protocol Chair, an NEI representative, a Reading  
232 Center representative, a rotating site coordinator, and other Network investigators serving in  
233 relevant positions, such as the Protocol Development investigator member. Up to two additional  
234 rotating site investigators (not Protocol Chairs and not members of the Operations Group), may  
235 be selected to join the Executive Committee. The two site investigators and the site coordinator  
236 will be recommended by the Operations Group to the Executive Committee for approval.  
237  
238

239 In general, Protocol Chairs will serve on the Executive Committee while their respective  
240 protocol is active<sup>1</sup>. Protocol Chairs generally will rotate off of the Executive Committee the  
241 month after the final study visit of their respective protocol is completed, as recommended by the  
242 Operations Group and approved by the Executive Committee. Depending upon the size of the  
243 Executive Committee (i.e.; the number of Protocol Chairs), rotating site investigators may serve  
244 a one-year term renewable up to two years. If multiple Protocol Chairs are serving on the  
245 Executive Committee, then the rotating investigator members' one-year term will not be  
246 renewed. If there are not enough Protocol Chairs, the rotating members' one-year term may be  
247 renewed for an additional year. The site coordinator may serve a one-year term renewable up to  
248 two years. The size of the Executive Committee should not exceed 20 members.

249  
250 One of the Protocol Chairs or site investigators not serving as a member of the Operations Group  
251 will serve as the Chair of the Executive Committee for a one-year term. The Executive  
252 Committee Chair will be proposed by the Operations Group and approved by the Executive  
253 Committee. The Executive Committee Chair will be responsible for leading the monthly  
254 Executive Committee calls and will work closely with the Network Chair relating to Operations  
255 Group decisions or discussions that need to be discussed with the Executive Committee.  
256 Additional responsibilities may be added as needed.

257  
258 For issues requiring a vote, the Principal Investigator of the Coordinating Center will share a  
259 single vote with any co-investigators of the Coordinating Center.

260  
261 The Executive Committee has overall responsibility for providing scientific oversight of the  
262 activities of the project. This Committee also formulates all policy decisions related to the  
263 maintenance and conduct of the project.

264  
265 Responsibilities of the Executive Committee include:

- 266 • Primary responsibility for the scientific oversight of the Network
- 267 • Provide input on issues related to the Network, including issues brought to the Committee by  
268 the Operations Group
- 269 • Review monthly recruitment reports on active protocols across sites
- 270 • Develop and enforce Network policies
- 271 • Develop requirements for the participation of clinical sites and investigators and other site  
272 personnel
- 273 • Select and prioritize protocols to be developed following recommendation of the Operations  
274 Group and buy-in from investigators
- 275 • Select Network Chairs and Vice-Chair(s)
- 276 • Provide representatives to provide *ad hoc* review of the Coordinating Center and Network  
277 Chair's Office. External members of such a review may be included.
- 278 • Select Protocol Chairs following recommendation of the Operations Group

---

<sup>1</sup> A protocol is considered active until the final study visit has been completed.

- 279 • Review recommendations of the Operations Group of imaging needs and reading center(s)
- 280 for each protocol
- 281 • Review progress of imaging reading centers
- 282 • Review and approve final protocol and budget
- 283 • Consider and approve changes or modifications in protocol as may be necessary or desirable
- 284 • Advise and assist the Coordinating Center on operational matters
- 285 • Approve protocol dissemination plans including primary outcome manuscripts and
- 286 presentations
- 287 • Approve primary outcome and secondary outcome manuscripts
- 288 • Review and approve ancillary studies as recommended by the Operations Group
- 289 • Review and approve collaborations and funding, including unrestricted grants or gifts from
- 290 Industry or foundations
- 291 • Provide input to the Coordinating Center and Operations Center on Network budgets

292 The Executive Committee will convene by conference call once per month. Additional calls will  
 293 be held as needed. In general, two in-person Executive Committee meetings will be held each  
 294 year. Additional individuals (e.g., Protocol Chairs) may be asked to participate as indicated,  
 295 which may require pre-approval by the Executive Committee Chair.

296

## 297 **2. Steering Committees and Other Subcommittees**

298 Steering Committees and other subcommittees may be developed as needed for non-Network  
 299 areas where additional expertise is desired (e.g. genetics studies).

300

## 301 **3. Operations Group**

302 The Operations Group includes the current and past Network Chair(s), the Network Vice-  
 303 Chair(s), an NEI representative, and the Coordinating Center Principal Investigator and  
 304 Executive Director.

305 Specific functions of the Operations Group include:

306

### 307 **Develop and maintain a program of quality assurance in the study**

- 308 • Monitor the performance of all participating sites and central units
- 309 • Each site will be assigned to a team consisting of a Coordinating Center protocol monitor and
- 310 a Vice-Chair investigator who will be responsible for oversight of that site's performance,
- 311 including recruitment.
- 312 • Review quality assurance reports regarding Network performance, comprehensively on a
- 313 semiannual basis, and at any other times that issues arise
- 314 • Monitor adherence to protocols through review of collected data regarding performance and
- 315 site visits (accompanied by outside, independent, unconflicted consultants as needed)
- 316 • Review quality metrics across all sites and DRCRnet studies approximately twice per year at
- 317 in-person meetings

- 318
- Review site visit reports
- 319
- Report site performance to the Executive Committee as needed

320

321 **Protocol development**

- 322
- Review and approve study procedures of new protocols
- 323
- Conduct initial review of submitted protocol concepts from investigators and decide on
- 324
- degree of merit and public health importance for presentation to investigators at the
- 325
- semiannual Coordinator/Investigator meetings and recommendation to the Executive
- 326
- Committee
- 327
- Select a Protocol Development Committee, if indicated, for each protocol to be developed
- 328
- Address imaging issues for Network protocols
- 329
- Submit recommendations to Executive Committee

330

331 **Oversight of active protocols**

- 332
- Provide input on protocol close-out procedures

333

334 **Manuscripts**

- 335
- Conduct initial review of manuscript ideas (with Manuscript Investigator Position) submitted
- 336
- by investigators and decide on degree of merit for recommendation to the Coordinating
- 337
- Center
- 338
- Prioritize manuscripts to be written, including review of manuscript ideas solicited from
- 339
- investigators
- 340
- Select a writing committee for each manuscript

341

342 **Presentations**

- 343
- Plan for meeting presentations
- 344
- Review and approve abstracts prior to submission
- 345
- Review of posters and presentations

346

347 **Dissemination of study results**

- 348
- Develop plan for dissemination of study results as indicated

349

350 **New centers and investigators**

- 351
- Communicate with new centers, both before and after Network approval is granted

352

353

354 A weekly conference call of the Operations Group will be held. Additional calls will be held  
355 with some or all of the Operations Group as deemed necessary by the Network Chair and  
356 Coordinating Center Principal Investigator or Co-Investigator. In general, two in-person  
357 Operations Group meetings will be held each year to review quality control, site monitoring, and  
358 protocol ideas.

359

#### 360 **4. Data and Safety Monitoring Committee (DSMC)**

361 The responsibility for reviewing the ethical conduct of the study and for monitoring the data for  
362 evidence of adverse or beneficial treatment effects is assigned to the Data and Safety Monitoring  
363 Committee (DSMC). The Data and Safety Monitoring Committee is advisory to the  
364 Coordinating Center.

365

366 The members of the DSMC will be selected by the National Eye Institute, which will select one  
367 of the members to serve as the Chair. The members will include individuals with expertise in  
368 clinical trials, biostatistics, diabetic retinopathy, and diabetes as well as a layperson. The NEI  
369 Project Officer will be considered an ex-officio nonvoting member.

370

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

377

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

383

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

388

389 DSMC financial disclosures will be reviewed by two individuals with experience in financial  
390 disclosures and financial conflicts who are independent of the Operations Center and  
391 Coordinating Center investigators. These two individuals will provide advice to the Network  
392 Chair and PI of the Coordinating Center or designate regarding financial conflicts and  
393 management of financial conflicts following Network policies. It is anticipated that this external  
394 advice usually or always will be followed. This external advice will be documented along with  
395 any rationale if and when the advice is not followed.

396

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

398

399  
400  
401  
402  
403  
404  
405  
406  
407  
408  
409  
410  
411  
412  
413  
414  
415  
416  
417  
418  
419  
420  
421  
422  
423  
424  
425  
426  
427  
428  
429  
430  
431  
432  
433  
434  
435  
436  
437  
438  
439  
440  
441  
442  
443  
444

### DRCR.net Organizational Structure

