

<b>Chapter 3: Study Position Responsibilities</b> .....	<b>2</b>
3.1 Chair’s Office Functions.....	2
3.1.1 Activities in Each Phase of the CITT .....	2
3.1.1.1 Start-Up Phase .....	2
3.1.1.2 Data Collection Phase .....	2
3.1.1.3 Study Close-Out Phase .....	2
3.1.2 Organization and Staffing.....	3
3.1.3 Responsibilities of the Chair.....	3
3.1.3.1 Chair of Committees of CITT Investigators .....	3
3.1.3.2 Publicity and Recruitment Efforts .....	3
3.1.3.3 Principal Spokesperson for CITT .....	3
3.1.3.4 Leading Ongoing Development and Implementation of the CITT MOP .....	3
3.1.3.5 Study Meetings and Communications .....	4
3.1.3.6 Coordinate Updates of Informed Consent Documents .....	4
3.1.3.7 CITT Publications.....	4
3.1.3.8 Training.....	4
3.1.3.9 Advertising and Communication.....	5
3.1.3.10 Subject Newsletter .....	5
3.1.3.11 CITT Personnel Newsletter.....	5
3.2 Data Coordinating Center (DCC) .....	5
3.2.1 Organization and Staffing.....	5
3.2.2 Responsibilities of the DCC.....	6
3.2.2.1 Committee Support .....	6
3.2.2.2 Documentation.....	6
3.2.2.3 Software Purchases .....	7
3.2.2.4 Randomization Planning and Implementation.....	7
3.2.2.5 Development of Study Forms .....	8
3.2.2.6 Dissemination of Study Forms.....	9
3.2.2.7 Establish Subject and Data Tracking Protocols .....	9
3.2.2.8 Data Processing, Entry and Editing .....	10
3.2.2.9 Development and Dissemination of Study Information .....	10
3.2.2.10 Development and Distribution of DCC Reports.....	11
3.2.2.11 Data and Safety Monitoring Committee (DSMC) Interactions .....	11
3.2.2.12 Study Meetings and Teleconferences .....	14
3.2.2.13 Data Security.....	15
3.3 Clinic Sites .....	15
3.3.1 Organization and Staffing.....	15
3.3.1.1 CITT Clinic Site Principal Investigator (PI).....	15
3.3.1.2 CITT Clinic Unmasked Examiner .....	15
3.3.1.3 CITT Clinic Masked Examiner.....	15
3.3.1.4 CITT Clinic Vision Therapist .....	15
3.3.1.5 CITT Clinic Site Coordinator .....	16
3.4 References.....	17

## Chapter 3: Study Position Responsibilities

### 3.1 Chair's Office Functions

The CITT Chair is responsible for the overall scientific conduct of the study and for maintaining communications among study members. The role of the Chair is to lead the CITT research team in conducting and successfully completing the clinical trial.

#### 3.1.1 Activities in Each Phase of the CITT

The activities of the Chair vary according to the phase of the study. The phases include: start-up (hiring, training and certification); data collection (enrollment, treatment, and follow-up); and study close-out (completion of follow-up and close-out of the trial).

##### 3.1.1.1 Start-Up Phase

In the *start-up phase* of the CITT, the Chair will play a major role in:

1. Leading publicity and recruitment efforts
2. Organizing and conducting a training meeting for CITT investigators and personnel in Philadelphia, PA
3. Training clinic site personnel in CITT procedures
4. Providing each clinic site with an initial supply of CITT stationery, envelopes, posters, birthday cards, and retention materials
5. Organizing and documenting monthly conference calls of the Executive Committee

##### 3.1.1.2 Data Collection Phase

During the *data collection phase*, responsibilities of the Chair include:

1. Leading publicity and recruitment efforts
2. Maintaining the CITT study organization as an effective collaborative group
3. Serving as a communication center for CITT Principal Investigators and other study personnel
4. Chairing meetings of CITT Executive and Full Investigative Group Committees
5. Coordinating study meetings for CITT investigators; preparing and distributing agendas prior to and minutes following the meetings
6. Providing updated information to the DCC for the Manual of Procedures
7. Supervising implementation of the MOP in collaboration with the Data Coordinating Center
8. Conducting site visits to each clinic site to monitor activities
9. Coordinating regular communications, including conference calls, among the CITT investigators to address issues and resolve questions in a timely manner
10. Maintaining routine communications with each clinic site PI

##### 3.1.1.3 Study Close-Out Phase

At the time of *study close-out*, the main work of the Chair will involve announcing the results of the study.

### **3.1.2 Organization and Staffing**

The Chair's Office is at the Pennsylvania College of Optometry in Philadelphia, PA, under the direction of Mitchell Scheiman, OD. The College also serves as one of the clinic sites for the CITT. As detailed above, the Chair will be responsible for the overall direction of the CITT, as well as for the day-to-day operations of the Chair's office. The implementation of Chair operations requires the assistance of a CITT Site Coordinator who will provide generalized administrative and technical computer support to the Chair. The CITT Chair's Site Coordinator is Karen Pollack. Her responsibilities include scheduling meetings and conference calls, assisting in preparing and distributing minutes of the calls and meetings, and creating and distributing the CITT newsletter.

### **3.1.3 Responsibilities of the Chair**

#### ***3.1.3.1 Chair of Committees of CITT Investigators***

The Chair presides over meetings of the CITT Executive and Full Investigative Group Committees. The Chair's office is responsible for distribution of agendas prior to meetings and for maintaining a file of minutes of the CITT meetings.

#### ***3.1.3.2 Publicity and Recruitment Efforts***

The CITT Executive Committee will approve all publicity and press releases. The CITT Chair will be informed of all local presentations to the press and will be sent a copy of published material to keep on file.

The Chair will lead the recruitment effort for CITT. In order to assist the clinic sites with recruitment, the Chair's office will provide brochures, stationery, and items with the CITT logo. Sites with lagging recruitment will be contacted by the Chair to encourage efforts to increase enrollment.

#### ***3.1.3.3 Principal Spokesperson for CITT***

The Chair serves as the main spokesperson for the study. At the close-out of the study, he is responsible for announcing the results of the trial.

#### ***3.1.3.4 Leading Ongoing Development and Implementation of the CITT MOP***

The Manual of Procedures, created in a collaborated effort by the Study Chair, Executive Committee, NEI Representatives and the Data Coordinating Center, provides a detailed description of all aspects of the trial. The Study Chair is responsible for supervising proposed revisions. The Data Coordinating Center is responsible for coordinating and implementing all changes to this document throughout the trial. In collaboration with the Data Coordinating Center, the Chair will monitor implementation of this document by site visits and other types of protocol monitoring. The CITT MOP will be reviewed and approved by the DSMC prior to beginning recruitment. Major revisions of the MOP will be sent to the DSMC for review and approval. The Executive Committee will advise each clinical site of updates and revisions

through written and numbered memos. All revised pages of the Manual of Procedures will be distributed to each clinical site specifying the new version date. Distribution of MOP revisions to the CITT investigators will be coordinated by the Chair's office.

### ***3.1.3.5 Study Meetings and Communications***

The CITT Chair has a major role in coordinating study meetings and communications involving CITT investigators. Specific responsibilities include:

1. Planning, scheduling, and organizing the Executive Committee and the Full Investigative Group Committee meetings, in collaboration with the Data Coordinating Center
2. Participating in the Data and Safety Monitoring Committee meetings
3. Organizing the training and certification meeting to be held at the Pennsylvania College of Optometry during the first year of the study
4. Coordinating and documenting monthly conference calls of the Executive Committee to address procedural, logistic, policy or other issues
5. Making telephone calls as needed to clinic site staff, e.g., to encourage recruitment; documentation of these calls will be prepared and filed by the Chair
6. Making periodic site visits to each center

### ***3.1.3.6 Coordinate Updates of Informed Consent Documents***

Consent for participation in the trial requires completion of two separate consent forms. The first is for the eligibility examination and the second for enrollment into the study. Study Informed Consent document templates are included in Chapters 5 (Eligibility) and 6 (Enrollment). Each Clinic Site is required to obtain approval from its local Institutional Review Board (IRB) to use humans as experimental subjects. This requires filling out and filing forms every year. The DCC Project Coordinator will maintain a copy of each site's IRB approval documents, including the consent/assent forms. Two months before the anniversary date to renew this application, the DCC Project Coordinator will send out reminder notices to each clinic site. When approval is renewed, the clinic sites will forward copies of all documents to the Study Chair and to the DCC.

### ***3.1.3.7 CITT Publications***

Abstracts and manuscripts are reviewed and approved by the Executive Committee and the Data and Safety Monitoring Committee prior to submission to journals and professional meetings. In conjunction with the Executive Committee, the Chair is responsible for developing manuscripts for group review and ensuring that the CITT publications policies as detailed in Chapter 11 are followed.

### ***3.1.3.8 Training***

All clinic site staff will undergo training to prepare for CITT certification. This will include reading the relevant sections of the Manual of Procedures, performing assigned study tasks under supervision, completing forms or protocols on non-study subjects, and demonstrating study protocol competence. The Chair will organize and supervise a general training session for all CITT personnel in Philadelphia. Additional information on the certification process is provided in Chapter 10 of this manual.

### **3.1.3.9 Advertising and Communication**

We will place informational advertisements on two commercial websites ([www.3dvision.com](http://www.3dvision.com), [www.hometherapyinc.com](http://www.hometherapyinc.com)) and on several organization websites ([www.oep.org](http://www.oep.org), [www.covd.org](http://www.covd.org), [www.aoanet.org](http://www.aoanet.org), and [www.aaopt.org](http://www.aaopt.org)).

### **3.1.3.10 Subject Newsletter**

Each Clinic Site will distribute subject newsletters on a quarterly basis each year. This newsletter provides study-related information to give subjects a sense of the national perspective of the CITT, provide health information relevant to CITT subjects, and highlight achievements of both CITT professional and administrative personnel.

The newsletters are designed to maintain contact with subjects. The Study Chair's office will also send templates to each clinical site so they can personalize the newsletter for their subjects. A final copy of the newsletter will also be distributed to all CITT personnel.

### **3.1.3.11 CITT Personnel Newsletter**

There will also be a monthly newsletter distributed to all CITT personnel. This newsletter will provide updates about recruitment and retention, protocol modifications and other pertinent CITT information. The CITT Study Chair will prepare this newsletter with input from the DCC.

## **3.2 Data Coordinating Center (DCC)**

The Optometry Coordinating Center will serve as the Data Coordinating Center (DCC) for the CITT. It is accountable for many aspects of the study including form development, randomization, quality control of clinic site performance and data management and analysis. The DCC serves as the central location from which information on the study will flow. As with any clinical trial, the quality of the results are only as good as the quality of the data collected. The Data Coordinating Center must ensure that:

1. All protocols established by the Convergence Insufficiency Treatment Trial (CITT) Executive Committee and described in the Manual of Procedures are practiced by all persons involved in the study.
2. The CITT is implemented as designed by the CITT Executive Committee.
3. All data collected as part of the CITT are managed in an appropriate manner.
4. All analyses of CITT data are performed correctly and are reported accurately.

### **3.2.1 Organization and Staffing**

The Optometry Coordinating Center is located at The Ohio State University in the College of Optometry. The staff of the coordinating center who will serve in the CITT DCC includes the following:

Personnel	Role
Lynn Mitchell	Principal Investigator (PI), Assistant Director of the OCC
Tracy Kitts	Project Coordinator
Loraine Sinnott	Biostatistician
Melanie Bacher	Programmer
Linda Barrett	Data Entry Operator

The various responsibilities of the staff are displayed in Table 3-1 along with the person or persons responsible for each task.

In addition, Ms. Mitchell has enlisted the following consultants to assist in operation of the DCC:

Consultant	Area of expertise
Dr. Lisa Jones	Epidemiology
Dr. Melvin Moeschberger	Biostatistics
Dr. Karla Zadnik	Optometric Research
Dr. Gerald Beck	Clinical Trials/DCC

### 3.2.2 Responsibilities of the DCC

#### 3.2.2.1 Committee Support

For most committee meetings, the Data Coordinating Center will collaborate with the Study Chair's office to:

1. Determine optimal meeting dates
2. Communicate information about meetings to committee chair and meeting participants
3. Prepare meeting materials
4. Provide logistical support onsite
5. Duplicate and distribute materials prior to each meeting
6. Prepare and distribute minutes of the meetings
7. Follow-up on all action items after each meeting
8. Coordinate conference calls

#### 3.2.2.2 Documentation

The coordinating center supports the preparation, duplication, and dissemination of administrative and technical reports and manuscripts. These documents include:

1. Meeting minutes
2. Newsletters
3. Ancillary study protocols
4. Statistical reports
5. Bibliographies
6. Abstracts
7. Manuscripts for publication

**Table 3-1 Various Responsibilities of the Data Coordinating Center (DCC)**

Task	Person(s) responsible
Development of study forms	PI and Project Coordinator with Executive Committee
Dissemination of study forms	Project Coordinator
Development of randomization protocol	PI
Randomization planning and implementation	PI
Develop CITT database	PI, Project Coordinator and Programmer
Refine CITT and DCC Manual of Procedures	PI, Project Coordinator and Clinic Trial Experts
Subject tracking	Project Coordinator
Data entry and editing	Project Coordinator and Data Entry Operator
Maintain data security	PI, Project Coordinator, Programmer & Data Entry Operator
Conduct clinic site visits	PI or Project Coordinator
Develop CITT informational website	PI, Project Coordinator & Programmer
Develop training and certification materials	PI and Project Coordinator
Development and dissemination of recruitment updates and newsletters	Project Coordinator and Programmer
Generate and distribute DCC reports	PI and Project Coordinator
Lead monthly conference calls with site Coordinators <sup>1</sup>	PI and Project Coordinator
Participate in monthly conference calls with Executive Committee <sup>1</sup>	PI
Select random sample of data forms for audit <sup>1</sup>	Programmer
Perform data audits	All DCC staff
Development and implementation of data analysis procedures	PI and Biostatistician
Maintain certification and IRB information	Project Coordinator
Order supplies	Project Coordinator
Maintain roster of all CITT personnel	Project Coordinator

<sup>1</sup> During active enrollment only

### 3.2.2.3 Software Purchases

The coordinating center purchases and maintains the software necessary to run the CITT database.

### 3.2.2.4 Randomization Planning and Implementation

To ensure *approximately* the same number of subjects randomized to each of the four treatment groups for each site, randomization will also be performed separately for each site. It is also

common practice to randomize subjects within blocks defined as a multiple of the number of treatments to be assigned. This blocking factor (i.e. the block size), which is unknown to the investigators, is used to ensure that investigators cannot guess which treatment is to be assigned to the next subject enrolled and thus preferentially enroll subjects. In addition, it is also common to use more than one block size and to randomly select first a block size and then a given block of treatment assignments.

Ms. Mitchell, using the techniques described above, will create a list of group assignments for each site before recruitment is initiated. These lists will contain a random ordering of the four treatment groups. As recruitment proceeds at a given site, the corresponding list will be accessed sequentially by the randomization module to assign subjects. The list for each site will contain at least enough assignments for 41 subjects (i.e. 20% of the total number of subjects to be enrolled).

Similar to the pilot study, researchers will have the ability to randomize eligible subjects 24 hours a day 7 day a week using the new subject module of the CITT database. Data from the Eligibility Checklist is entered directly into the new subject module so that the software can determine eligibility and, if applicable, assign the subject to a treatment group. If, at the time of randomization, the internet site is unavailable, sites may page Ms. Mitchell to obtain group assignment. As with the website, the site will be required to convey the information of the Eligibility Checklist to Ms. Mitchell. She will determine eligibility status and if appropriate give the site the subject's group assignment.

### *3.2.2.5 Development of Study Forms*

All CITT study forms were developed during the pilot study period. This process began long before any data were collected and continued through the first few months of data collection. The forms were also used in a randomized clinical trial of Base-in Prism reading glasses performed by several members of the CITT study group. Each form contains the date of last revision in the upper right hand corner so that all clinic sites can be sure they have the most recent version of a form. To ensure continuity in the data collected, limited form changes will be considered during the study period especially after subjects have been recruited. Any requests for data form change must be submitted in writing to Ms. Mitchell and will then be reviewed by the entire CITT Executive Committee.

If a change is made to a study form after subject enrollment has begun, copies of the revised form will be sent to each clinic site to be replaced in each subject binder along with a numbered memorandum outlining the changes. In addition, an email update will be sent to all CITT personnel explaining the specific change made to the form. The CITT investigators website will, at all times, contain updated versions of each form.

Each CITT form will be self-contained, when possible. That is, their completion should not require reference to other forms or separate instruction manuals. To achieve this, the instructions necessary to complete each item will be contained on the backside of the form. In addition, individual items on each form will be self-explanatory.

Information to be entered on any given form will be only what is available at that point in time. If additional information is required at a later date, this information will be collected on another form.

Each form contains a field for the identification of the examiner who has collected the data contained on the form. Examiners will be identified using a unique identification code created using their initials. If multiple examiners at the same clinic site share the same initials, the numbers 1, 2, 3 etc will be added to the end of their ID to distinguish them. This will allow for cross-referencing by the project coordinator to ensure that the examiner had the appropriate certification to collect such data.

### ***3.2.2.6 Dissemination of Study Forms***

Each clinic site will be provided separate CITT binders containing all relevant study forms. The binders are indexed by visit (eligibility, week 1 of training, week 12 masked exam). There is also a section in the binder for the subject's informed consent forms. Using the binders, all information about a subject is contained in one centralized location. The binders are such that forms can be removed for completion by the masked examiners or vision therapist, faxed to the DCC, and then returned to the binder.

At the beginning of data collection, each site will be provided with 25 binders representing their expected subject recruitment level during the study. Additional binders can be provided as needed to those clinic sites which exceed their recruitment quota.

### ***3.2.2.7 Establish Subject and Data Tracking Protocols***

Successful tracking in the CITT involves not only assuring that subjects are examined in the appropriate time frame but also that data forms move through the CITT system in a timely fashion. To assist in these endeavors, various data reports will be generated at the DCC on a weekly and/or monthly basis (Table 3-2). In addition, the CITT database contains a specialized subject scheduling module to assist site coordinators. This module:

1. Allows the site coordinator to produce a list of all study visits for any subject
2. Allows for daily updates on subject visit information (e.g. next scheduled visit for a subject, all subjects due for a study visit on that day, or all subjects who are overdue for a study visit)
3. Maintain study visits within acceptable time windows

**Table 3-2 Reports to be Generated by the Data Coordinating Center**

<b>Report</b>	<b>When</b>	<b>Sent to</b>	<b>Contents</b>
Missing eligibility	Weekly	Clinic site <sup>1</sup>	List of subjects who have been enrolled but for whom no eligibility forms have been received
Session schedule	Weekly	Clinic site <sup>1</sup>	List of subjects who are due or past due for a therapy session
Exam schedule	Weekly	Clinic site <sup>1</sup>	List of subjects who are due or past due for a masked exam
Missing form	Weekly	Clinic site <sup>1</sup>	List of subjects and specific forms which are missing or late
Recruitment update	Monthly <sup>2</sup>	All CITT personnel	Number of subjects enrolled to date, by site
Retention update	Weekly	All CITT personnel	Progress of all subjects in study
Visit out of window	As needed	Clinic site <sup>1</sup>	List of subjects who have been examined out of window and reminder of appropriate window for next masked examination
Edit	Monthly	All CITT personnel	Number of subject forms requiring at least one edit, by site
Outstanding edits	Monthly	Clinic site <sup>1</sup>	List of subjects with outstanding form edits
Study update	Monthly	Study Chair	Time between randomization and receipt of eligibility forms; Time between masked examinations, by treatment group; etc.
Form audit	Monthly <sup>3</sup>	All DCC personnel	Data from random sample of data forms for comparison with database
DCC internal check-up	Monthly	DCC personnel	Time between receipt of form and data entry; Number of mismatched records (from double data entry); etc.
Site recruitment	Monthly	Study Chair	List of sites which have not recruited the required 3 subjects in the past two months
Full Investigator Group (FIG) meeting	Annually	All CITT personnel	Recruitment and retention information, most edited fields, list of fields with excessive missing data, number of visits out of window, etc.

<sup>1</sup> Study Coordinator and PI only of appropriate site

<sup>2</sup> Only during recruitment phase of study

<sup>3</sup> Only during recruitment and active treatment phase of study

### **3.2.2.8 Data Processing, Entry and Editing**

Members of the DCC will be responsible for determining the optimum methods for data receipt, entry and editing. Protocols to achieve these goals can be found in Chapter 10.

### **3.2.2.9 Development and Dissemination of Study Information**

During the CITT pilot study, a website was developed by the DCC for the main purpose of advertising the study. A link to our site was placed on various binocular vision and vision therapy web pages. During the CITT pilot study, we received 3-5 requests for information per week from our web presence. Unfortunately, the majority of the cases did not produce eligible subjects because the individuals were not near one of the six clinic sites. Dr. Scheiman also contracted with members of the JAEB Center for Health Research in Tampa, Florida, to develop a website for CITT personnel. This site contained contact information for all persons associated with the CITT pilot study. As part of the CITT, these two websites will be combined to offer not only a location for persons across the U.S. to learn about our study, but also a place for personnel to access study protocols and forms.

As designed, the portion of the website applicable for site personnel will have password restricted access. Thus, members of the general population will not have access to these screens. The website will provide a central location for each site to track recruitment along with the ability to access the most current version of each report listed in Table 3-2. For those reports which are clinic-specific, such as the Missing Form report, only personnel at that site will be able to view the report. This new site will be developed and maintained by the CITT Programmer with assistance from the Project Coordinator. A link to the new and improved CITT website will be provided on the NEI-clinical trials website. This website will provide one central repository for CITT information.

### ***3.2.2.10 Development and Distribution of DCC Reports***

Quarterly, the DCC will distribute to all CITT PIs, DSMC members, NEI representatives and the Study Chair, a report detailing the internal operations of the DCC. This report will include all monthly reports plus information on:

1. Recruitment and retention status.

Quarterly, the DCC will produce and distribute to DSMC members and NEI representatives a slightly different look at recruitment and retention as it applies to treatment group assignment. This information will help evaluate each treatment arm's retention rate and would be the first indication of unequal losses to follow-up.

2. Summary statistics for major variables at eligibility to assess comparability between participants and non-participants.

Variables to be included in this report are age, sex, race, and the following data values obtained at the eligibility examination: CI Symptom Score, near point of convergence break, positive and negative fusional vergence break, accommodative amplitude, near and distance phoria, and spherical equivalent refractive error. This information will be used to evaluate the generalizability of the study by ensuring that eligible subjects who agree to participate are not clinically different from those eligible subjects who would not participate.

3. Characteristics of data flow at DCC.

Information reported will include the number of data forms processed during each month of the study and summary statistics for data flow variables.

4. Quality of data received at the DCC.

Summary statistics on the quality of data received at the DCC will also be reported. This will include information relative to data forms and also to fields within each data form. Although only composite information is planned for presentation in the quarterly report, it will be possible to report the information for any specific clinic site if irregularities are noticed by personnel of the DCC.

5. Any other information requested by a DSMC member or NEI personnel.

### ***3.2.2.11 Data and Safety Monitoring Committee (DSMC) Interactions***

The Data Coordinating Center will produce a draft copy of the agenda for both the open and closed session of the DSMC meeting. This agenda will be sent to the Study Chair, DSMC Chair and an NEI representative for comments and corrections.

Before each meeting of the Data and Safety Monitoring Committee (DSMC), formal interim analyses will be performed. Approximately 6 weeks before the scheduled meeting, a copy of the current database will be set aside for all analyses. This “frozen” database will contain information from the study as of the data saved and will not be updated. A copy of the frozen dataset will be archived along with all programming code utilized to generate the reports presented.

To allow time for final preparation of the DSMC report, all tables and text to be included must be given to the Project Coordinator 1-2 days before the scheduled mailing date. Reports will be mailed to all DSMC members at least 2 weeks before the meeting date. This will allow the members plenty of time to read through the report and contact the DCC if there are any questions. The reports will be sent via express mail. Approximately 4 days after sending, the Project Coordinator will contact each member to verify that the report was delivered.

Interim analyses require repeated significance testing on the same data, thus adjustments have to be made to the hypothesis testing procedure to maintain the overall type-1 error rate. The alpha spending function approach to group sequential testing will be used for the analyses<sup>2</sup>. In this method, the overall type-1 error probability is allocated over the course of the clinical trial.

**Table 3-3 Proposed Reporting and Meeting Schedule**

Study Month	Calendar Month	% of Total Enrollment <sup>a</sup>	% Completed 12-wk Exam	Monthly Updates	Quarterly Updates	Interim Analyses	Face-to-Face Meeting
10	7/05	6.7	0	X			
11	8/05	13.5	0	X			
12	9/05	20.2	0	X			
13	10/05	26.9	6.7	X	X		
14	11/05	33.7	13.5	X			
15	12/05	40.4	20.2	X			
16	1/06	47.1	26.9	X	X		
17	2/06	53.8	33.7	X			
18	3/06	60.6	40.4	X		X	X
19	4/06	67.3	47.1	X	X		
20	5/06	74.0	53.8	X			
21	6/06	80.8	60.6	X			
22	7/06	87.5	67.3	X	X		
23	8/06	94.2	74.0	X		X	
24	9/06	100.0	80.8	X			
25	10/06		87.5	X	X		
26	11/06		94.2	X			
27	12/06		100.0	X			
28	1/07				X		
29	2/07						
30	3/07						X

<sup>a</sup>Assuming 14 subjects enrolled each month (~1.5 per month per enrollment site)

### **A. Proposed Reporting Schedule**

It is the responsibility of the Data Coordinating Center to inform members of the DSMC and NEI representatives of study progress. Table 3-3 displays the proposed reporting and meeting schedule. For quarterly updates and interim analyses, a working database will be frozen one-month prior to the proposed due date to allow for data processing and report preparation.

### **B. Monthly Update Reports**

Monthly updates will include information on:

1. Overall recruitment and retention status.  
Information on recruitment and retention will be summarized both graphically and tabular. The figures will be continually updated and available on the CITT website so that site personnel may also review this information. Information for the tables will be updated monthly using specialized queries to the CITT database.
2. Summary statistics including sample distributions for major variables at eligibility to assess comparability between four treatment arms.  
Variables to be included in this report are age, sex, race, and the following data values obtained at the eligibility examination: CI Symptom Score, near point of convergence break, and positive fusional vergence break.
3. Any reported adverse events.  
Each documented adverse event will be reported. If a specific event occurs more than once, the rate of occurrence will also be calculated and presented.
4. Any other information requested by a DSMC member or NEI personnel.

### **C. Quarterly Update Reports**

Quarterly updates will include all monthly reports plus information on:

1. Recruitment and retention status.  
Quarterly, the DCC will produce and distribute to DSMC members and NEI representatives a slightly different look at recruitment and retention as it applies to treatment group assignment. This information will help evaluate each treatment arm's retention rate and would be the first indication of unequal losses to follow-up.
2. Summary statistics for major variables at eligibility to assess comparability between participants and non-participants.  
Variables to be included in this report are age, sex, race, and the following data values obtained at the eligibility examination: CI Symptom Score, near point of convergence break, positive and negative fusional vergence break, accommodative amplitude, near and distance phoria, and spherical equivalent refractive error. This information will be used to evaluate the generalizability of the study by ensuring that eligible subject who agree to participate are not clinically different from those eligible subjects who would not participate.
3. Characteristics of data flow at DCC.  
Information reported will include the number of data forms processed during each month of the study and summary statistics for data flow variables.
4. Quality of data received at the DCC.

Summary statistics on the quality of data received at the DCC will also be reported. This will include information relative to data forms and also to fields within each data form. Although only composite information is planned for presentation in the quarterly report, it will be possible to report the information for any specific clinic site if irregularities are noticed by personnel of the DCC.

5. Any other information requested by a DSMC member or NEI personnel.

#### **D. Interim Analyses and Face-to-Face Meetings**

Along with the information listed below, all information from either monthly or quarterly reports along with the following will be presented.

1. Summary statistics for the primary (CI Symptom Score) and secondary (near point of convergence break and positive fusional vergence break) outcome measures at the eligibility exam and each subsequent masked examination (4-, 8-, and 12-weeks). In addition, results from the preliminary comparison of treatment groups.
2. Descriptive data examining the effectiveness of the designed masking protocols. This will include information from the subject and the masked examiner on the perceived treatment assignment and the confidence of this response.

The following information will also be presented during face-to-face meetings:

1. Descriptive statistics on the retention of subjects in the long-term follow-up phase of the study (6- and 12-month follow-up examinations).
2. Quality of data received at the DCC  
Summary statistics will be repeated for each clinic site. This will allow readers to assess the quality of data received from each enrollment site to identify sites potentially in need of a site visit.
3. Information on any protocol violations will be presented during these meetings.

#### ***3.2.2.12 Study Meetings and Teleconferences***

Monthly during study enrollment and during active treatment, all Site Coordinators along with the DCC Project Coordinator and DCC Principal Investigator will participate in a conference call. This call will be used to discuss problems and solutions introduced by Site Coordinators, share innovative ideas for subject recruitment or tracking, and other issues raised by either personnel at one of the sites or at the Data Coordinating Center. If issues arise during years 3 or 4 which require discussion among all Site Coordinators, a conference call will be scheduled. The need to schedule such a call can be initiated by either the DCC or any Site Coordinator.

Additionally, during enrollment and active treatment, the clinic site Principal Investigator and Vision Therapist will participate in monthly conference calls. These calls will be led by the Study Chair, and DCC Principal Investigator. Topics to be discussed during these calls include recruitment progress, issues surrounding the administration of any of the four treatment arms, and potential protocol or form changes.

### **3.2.2.13 Data Security**

As the central repository of information for the CITT, the DCC has particular responsibilities towards the security of the data. This includes, but is not limited to, protecting the data from hazards such as disasters and unauthorized access. Methods to ensure data security include housing the files in locked cabinets, making the CITT database password protected, and creating dataset back-ups stored in off-site locations (see Chapter 10, Section 12).

## **3.3 Clinic Sites**

### **3.3.1 Organization and Staffing**

The organization of CITT clinic sites varies from one location to another.

#### **3.3.1.1 CITT Clinic Site Principal Investigator (PI)**

The clinic site Principal Investigator (PI) is the individual responsible for the overall conduct of the study at his/her clinic site. This includes recruitment and retention of subjects, maintaining masking, and monitoring the activities of all personnel who take part in the recruitment, data collection, treatment activities, and follow-up care of CITT subjects. The PI will serve as the unmasked examiner and will be responsible for performing the eligibility examinations, determining eligibility, educating the subject about CITT, and administering the informed consent protocol (when the Site Coordinator does not) with each CITT subject. He/she is also responsible for ensuring that the CITT MOP is understood and strictly adhered to by all investigators and is responsible for the validity of all data collected at the CITT Clinic Site. The Principal Investigator must be certified to perform the Vision Therapist and Site Coordinator procedures. The clerical and correspondence tasks are also the responsibility of the PI, but each clinic will have a Site Coordinator to handle these day-to-day responsibilities.

#### **3.3.1.2 CITT Clinic Unmasked Examiner**

The unmasked examiner and will be responsible for the eligibility examination, determining eligibility, educating the subject about the CITT, and implementing the informed consent protocol with each CITT subject.

#### **3.3.1.3 CITT Clinic Masked Examiner**

The masked examiner will be a licensed optometrist or ophthalmologist. The masked examinations will be performed after completion of 4, 8 and 12 weeks of treatment and also at the 6- and 12-month follow-up examinations. At least two people should be certified at each CITT clinic site for this role to ensure adequate coverage to meet scheduling needs.

### ***3.3.1.4 CITT Clinic Vision Therapist***

All treatment activities will be the responsibility of the therapist. This individual may be an optometrist, ophthalmologist, vision therapist, or orthoptist. The therapist will administer the various treatment regimens and is responsible for carefully following the protocols for Home-based Pencil Push-up, Home-based Pencil Push-ups with Computer VT/Orthoptics, Office-based VT/Orthoptics, and Office-based Placebo VT/Orthoptics. The therapist plays an important role in maintaining masking by reminding subjects never to discuss the treatment with a masked examiner. Any questions about the treatment will be asked of the therapist or PI. The therapist also plays an important role in maintaining subject compliance and retention because of his/her frequent contact with the subject. At least two people should be certified to act in this position at each site.

### ***3.3.1.5 CITT Clinic Site Coordinator***

The CITT Site Coordinator is responsible for the daily operation of the CITT clinic site including performing clerical work and correspondence tasks, educating subjects about the CITT, scheduling, editing forms for quality of data entry, randomizing subjects, sending data to the Data Coordinating Center, answering edit queries, following protocols for subject retention, and communicating with the Clinic PI and other CITT personnel.

The CITT Site Coordinator plays a critical role in the CITT by insuring timely scheduling of subject visits (within appropriate windows), maintaining the subject database, assuring that quality data are sent to the Data Coordinating Center in a timely fashion, and emphasizing and maintaining masking.

### 3.4 References

1. Ellenberg SS, Fleming TR, DeMets DL. *Data Monitoring Committees in Clinical Trials: A Practical Perspective*. John Wiley and Sons, New York, New York. 2003.
2. DeMets DL, Lan KKG. Interim analysis: The alpha spending function approach. *Statistics in Medicine*. 1994; 13: 1341-1352.