NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

Standard Operating Procedure (SOP)

Central Institutional Review Board (CIRB) Reliance Process for CIRB Pilot Study Sites

Version 1.0
SOP NEALS CIRB 101

Originators: NEALS NCRI Coordinating Center Personnel

Reviewed and Approved by:

M. Cudkowicz, MD, MSc (TREAT-ALS Principal Investigator)

P. Pearl O'Rourke, MD (Central IRB Director of Human Research Affairs)

M. Kearney, BA (NCRI Director of Research Operations)

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STANDARD OPERATING PROCEDURE FOR
CIRB RELIANCE PROCESS FOR CIRB PILOT STUDY SITES

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1. POLICY

A. Purpose and Applicability

This SOP applies to all entities participating in the NEALS CIRB Pilot Project Clinical Study Sites (CSS) that have executed a Central IRB (CIRB) Authorization Agreement (Reliance Agreement or RA) to rely on the Partners Human Research Committee (PHRC) for review of one or more NEALS clinical trials.

The PHRC is comprised of the IRBs of Massachusetts General Hospital and Brigham and Women's Hospital and is the CIRB for selected NEALS clinical trials. All NEALS clinical trials to be conducted within this pilot program, will be reviewed by the CIRB. The general eligibility requirements for a CSS to rely on the CIRB are addressed in the Reliance Agreement. These requirements pertain to overall qualifications of the CSS and include completion by the CSS of a satisfactory NEALS Clinical Study Site IRB Information Sheet. CSSs with an executed RA have been determined by the MGH Neurological Clinical Research Institute (NCRI) Coordinating Center (CC) and CIRB to meet the general requirements.

The purpose of this SOP is to set forth the process for a CSS to cede review to the CIRB of specific/individual NEALS clinical trial(s) as contemplated under its RA. The SOP describes the flow of protocol-specific information to and from the CSS to the CC/CIRB and the information, timelines and documentation required for the initial protocol review. It also sets forth the process and requirements for other review decisions for the life of the protocol.

B. Process for Ceding Review of a Trial

a. Initial Protocol Review

i. The Protocol Principal Investigator (PPI) of a NEALS clinical trial will submit the draft protocol for the trial to the CIRB via the NCRI CC-CIRB Liaison. This protocol will be designated by the CIRB as the 'parent' protocol.

ii. The CC will provide a copy of the grant or other funding award for the clinical trial to the CIRB.

iii. The CIRB will perform an initial assessment of the protocol to determine "IRB-readiness" (e.g., completeness of all parts of the submission) and will work with the PPI via the CC-CIRB Liaison as necessary to address any preliminary issues.

iv. The CIRB via the CC-CIRB Liaison will send the IRB-ready protocol to all participating CSSs via the CSS designee(s). The CSS designee(s) will initiate an analysis of the protocol at the CSS to identify and inform the CIRB of 1) substantive issues (if any) and 2) local research context issues raised by the protocol. The CSS designee(s) must either be an individual(s) who has knowledge of and experience with the CSS's local research context or involve such individuals at the CSS in the referenced analysis and determinations. Without limiting what is provided by the CSS, the CSS must, at minimum, provide complete information necessary to inform the CIRB of the CSS's local research context as relevant to the protocol.

The CIRB via the CC-CIRB Liaison may provide a questionnaire form for the CSS to complete to facilitate sharing of the following information with the CIRB:

1. Specific requirements of state or local laws, regulations, policies, standards or other factors applicable to the CSS or the trial that would affect the CSS's conduct of the specific trial including, as applicable;
    a. Identification of legally authorized representatives who can provide consent for individuals to participate in research;
    b. Requirements for enrollment of adults with impaired decision-making capacity;
    c. Requirements for wards of the state or other special populations (child or adult) to participate in research;
    d. Processes or requirements for enrollment of non-English-speaking participants;
    e. Other information about the local consent process, including practices regarding recruitment and compensation of participants;
    f. Requirements of confidentiality of specific types of health information;
    g. Special characteristics of the CSS or the community; and
    h. Other requirements or factors as applicable.

2. Based on the CSS's conduct of an investigator conflicts of interest analysis under the applicable policy as described in the NEALS Network Conflict of Interest and Financial Disclosure Requirements SOP, comments and information from the CSS (including information from the aforementioned questionnaire on state/local requirements) must be submitted in writing to the CIRB via the CC-CIRB Liaison as required by the STA.

v. Upon receipt of the comments/information from participating CSSs, the CIRB will review the protocol.

vi. While the protocol is under CIRB review, the CSS of the PPI will conduct relevant Local Ancillary Committee (AC) review as required by its policies. The PPI will provide evidence of such committee approval along with any relevant committee requirements that would affect the CSS's conduct of the trial to the CIRB via the CC-CIRB Liaison. Relevant committees may vary by protocol and may include: nursing, radiation safety, pharmacy, biomedical engineering, biosafety, Medicare or other cost/billing analysis, and contract review.

vii. The CIRB will work with the PPI via the CC-CIRB Liaison to address any modifications or other issues necessary to approve the protocol. If the protocol is approved by the CIRB, the approval will be approval of the parent protocol.

viii. The CIRB via the CC-CIRB Liaison will send the approved protocol and a model informed consent form (ICF) (which will include a model form of HIPAA authorization for use and disclosure of Protected Health Information) to all CSSs who submitted the information required in section B.a.iv above.

ix. Each CSS will then decide whether or not to participate in the protocol as approved. CSSs that decide to participate will:

1. Contact the CIRB via the CC-CIRB Liaison in writing regarding their decision to participate;
2. Coordinate relevant Local AC review as required by local policies;
3. Customize the approved study-wide model ICF in the areas permitted by the form to include/reflect information specific to the CSS. Attach or include any CSS form of HIPAA authorization if the CSS elects to use its own form/language in place of the model HIPAA form/language included in the study-wide ICF; and
4. Submit an application via the CC-CIRB liaison to be added as a study site, along with the customized model ICF and HIPAA authorization and evidence of approval from Local ACs (along with any relevant committee requirements that would affect the CSS's conduct of the trial), to the CIRB via the CC-CIRB Liaison.

ii. The CIRB will review the customized ICF including authorization language for consistency with the approved model ICF and will review the AC information and all other local information provided and, if all parts of the application are satisfactory, will approve each CSS as a site amendment to the parent protocol. The CIRB will provide an approved ICF for the CSS.

Note: The date for continuing review will be set by the review date of the parent protocol.

b. Continuing review

i. Dates for continuing review (expiration of CIRB approval) will be determined by date of parent protocol review;

ii. The CIRB via the CC-CIRB Liaison will notify each participating CSS regarding information required for continuing review. Each participating CSS will submit its responsive information for continuing review to the CC-CIRB Liaison;

iii. The CC-CIRB Liaison will submit a single continuing review application to the CIRB that includes continuing review information from all participating CSSs; and

iv. The CIRB will conduct continuing review and communicate results to participating CSSs via the CC-CIRB Liaison.

c. Amendments

i. The PPI will submit any study-wide protocol amendments to the CIRB via the CC-CIRB Liaison;

ii. The PI at each participating CSS may submit site-specific administrative amendments (e.g., study staff changes) and requests for protocol exceptions to the CIRB via the CC-CIRB Liaison. Any amendments proposed to the substantive content of the protocol must be coordinated with and submitted through the PPI; and

iii. The CIRB will review amendments and communicate regarding their approval status with the relevant CSS(s) via the CC-CIRB Liaison. Amendments requiring notification of all participating CSSs, as determined by the CIRB, will also be communicated via the CC-CIRB Liaison.

d. To report non-compliance, subject injuries, unanticipated problems, protocol deviations/violations, complaints, cessation/suspension/termination of protocol, and changes made without CIRB approval to eliminate apparent immediate hazards to subject/s, please see the Central IRB Reporting SOP

e. Study closure

i. The PPI will submit relevant material for study closure to the CIRB via the CC-CIRB Liaison.

2. SCOPE

The policies and procedures described in this SOP apply to the NCRI CC within the context of their oversight and advisory roles for the NEALS CIRB Pilot Project, and to all CIRB CSS, CIRB Pilot investigators, staff, subcontractors, or other entities associated with the NEALS CIRB Pilot Project who manage, oversee, conduct, or are otherwise engaged in research in the CIRB Pilot Project.

3. ROLES AND RESPONSIBILITIES

Roles and responsibilities for the CC and CIRB as they relate to CIRB Reliance are detailed in section 8.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.114

21 CFR 56.114

5. REFERENCES TO OTHER APPLICABLE SOPS

NEALS Network Central IRB Reporting SOP

NEALS Network Conflict of Interest and Financial Disclosure Requirements SOP

6. ATTACHMENTS

NEALS CIRB Clinical Study Site IRB Information Sheet

NEALS Institutional Letter Agreeing to Participate

7. TERMS AND ABBREVIATIONS

The following terms and abbreviations are used in this document:

AC	Ancillary Committee
CC	NCRI Coordinating Center at Massachusetts General Hospital
CC-CIRB Liaison	NCRI Coordinating Center Central Institutional Review Board Liaison
CFR	Code of Federal Regulations
CIRB	Central Institutional Review Board
CSS	Clinical Study Site that conducts research for a particular NEALS protocol
CSS PI	Principal Investigator who is responsible for implementing and conducting a specific NEALS protocol at a Clinical Study Site
FCOI	Financial Conflict of Interest
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed consent form
PHRC	Partners Human Research Committee

PPI	Protocol Principal Investigator of a NEALS protocol
RA	Reliance Agreement/NEALS CIRB IRB Authorization Agreement

8. SPECIFIC PROCEDURES

#	Who	Task	Attachment/ Reference	Related SOP
1.	CSS Institutional Official	Sign CIRB Reliance Agreement and submit to CC	Reliance Agreement	
2.	CSS Investigators (PI and Co-Investigators)	Sign Investigator Commitment Statement at Exhibit A of the Reliance Agreement and submit to CC	Reliance Agreement	
3.	CSS PI/appropriate Institutional Representative	Facilitate completion of Clinical Study Site IRB Information Sheet by appropriate Institutional Representative/s and submit to CC	Reliance Agreement	
4.	PPI	Submit draft protocols to CC-CIRB Liaison and coordinate relevant Local Ancillary Committee reviews	Reliance Agreement	
5.	CC-CIRB Liaison	Submit draft protocols to CIRB		
6.	CIRB	Review draft protocol for readiness for CIRB review	COI SOP Reliance Agreement	COI SOP
7.	CIRB	Send IRB-ready draft protocol to CC-CIRB Liaison for submission to interested CSSs for local comments		
8.	CSS PI and Local Institutional Designee*	Review draft protocol and submit local comments to CC-CIRB Liaison		
9.	CC-CIRB Liaison	Submit local comments to CIRB		
10.	CIRB	Review final parent protocol and ICF. CIRB review may include required modifications or deferral. CIRB will work with CSS PPI through CC-CIRB Liaison to secure IRB approval. CIRB will communicate approval status to CSS PPI via the CC-CIRB Liaison.	Reliance Agreement	
11.	CC-CIRB Liaison	Submit final approved protocol and template ICF to all interested CSSs for final decision to participate		
12.	CSS PI	Communicate final decision to participate to CC-CIRB Liaison		
13.	CSS PI	Coordinate protocol submission to Local Ancillary Committees for review and approval as applicable	Reliance Agreement	

14.	CSS PI	Submit Protocol-specific Local Site Context IRB Form to CC	Reliance Agreement	
15.	CC-CIRB Liaison	Communicate all CSS decisions to participate to CIRB		
16.	CC-CIRB Liaison	Submit each additional CSS protocol and site-specific ICF to CIRB as 'child' amendments for approval		
17.	CIRB	Review each CSS 'child' amendment and ICF and communicate approval status to relevant CSSs via the CC-CIRB Liaison		
18.	CC-CIRB Liaison	Communicate CIRB approval status to relevant CSSs		
19.	CSS PI/Designee	Report non-compliance, subject injuries, unanticipated problems, protocol deviations/violations, complaints, cessation of research activities, changes made without CIRB approval to eliminate apparent immediate hazards to subject/s to CC-CIRB Liaison	CIRB Reporting SOP Reliance Agreement	CIRB Reporting SOP
20.	CC-CIRB Liaison	Submit CSS reports of non-compliance, subject injuries, unanticipated problems, protocol deviations/violations, complaints, cessation of research activities, changes made without CIRB approval to eliminate apparent immediate hazards to subject/s to CIRB	CIRB Reporting SOP	CIRB Reporting SOP
21.	CIRB, CC	Communicate all reportable events to CSS that may affect subject safety or the conduct of the clinical trial at all sites	CIRB Reporting SOP Reliance Agreement	CIRB Reporting SOP
22.	CSS PI	Submit continuing review applications to CC-CIRB Liaison	Reliance Agreement	
23.	CC-CIRB Liaison	Submit continuing review applications to CIRB	Reliance Agreement	
24.	CIRB	Review continuing review applications for all CSS. Communicate approval status to participating CSSs via CC-CIRB Liaison.	Reliance Agreement	
25.	CC-CIRB Liaison	Communicate CIRB approval status of continuing review applications to participating CSSs		
26.	PPI	Submit study-wide protocol amendments to the CIRB via the CC-CIRB Liaison	Reliance Agreement	
27.	CC-CIRB Liaison	Submit study-wide protocol amendments to the CIRB	Reliance Agreement	
28.	CIRB	Review study-wide protocol amendments and communicate approval status to participating CSSs via CC-CIRB Liaison	Reliance Agreement	

29.	CC-CIRB Liaison	Communicate CIRB approval status of study-wide amendments to participating CSSs	
30.	CSS PI	Submit site-specific administrative amendments (e.g., study staff changes) and requests for protocol exceptions to the CIRB via the CC-CIRB Liaison	Reliance Agreement
31.	CC-CIRB Liaison	Submit site-specific administrative amendments and requests for protocol exceptions to the CIRB	Reliance Agreement
32.	CIRB	Review site-specific administrative amendments and requests for protocol exceptions and communicate approval status to relevant CSS(s) via the CC-CIRB Liaison	Reliance Agreement
33.	CC-CIRB Liaison	Communicate CIRB approval status of site-specific administrative amendments and requests for protocol exceptions to participating CSSs	
34.	PPI	Coordinate and submit substantive content amendments to the protocol as requested by CSS to the CIRB via the CC-CIRB Liaison	Reliance Agreement
35.	CC-CIRB Liaison	Submit substantive content amendments to the protocol to the CIRB	Reliance Agreement
36.	CIRB	Review substantive content amendments and communicate approval status to relevant CSS(s) via the CC-CIRB Liaison.	Reliance Agreement
37.	CC-CIRB Liaison	Communicate CIRB approval status of substantive content amendments to the protocol to the CSSs [Amendments requiring notification of all participating CSSs, as determined by the CIRB, will also be communicated via the CC-CIRB Liaison]	
38.	PPI	Submit relevant material for study closure to the CIRB via the CC-CIRB Liaison	
39.	CIRB	Review relevant material for study closure and communicate approval status to the PPI via the CC-CIRB Liaison	
40.	CC-CIRB Liaison	Communicate approval status of study closure material to the PPI	

*Institutional Representative may be a site/local IRB member.