NeuroNEXT Network

Standard Operating Procedure (SOP)

Clinical Protocol Finalization and Maintenance

Version 1.0

SOP NN PD 304

Originators: NeuroNEXT CCC and DCC Personnel

Reviewed and Approved by:

Signature and Date: DocuSigned by Christopher Coffey Christopher Coffey | I approve this document 14-Feb-2023 | 12:35:25 PM PST C68AC8DD80334CF982AED1200765F147 14-Feb-2023
Name and Title: Christopher S. Coffey, PhD (DCC Principal Investigator)
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Name and Title: Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)
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NN PD 304

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR CLINICAL PROTOCOL FINALIZATION AND MAINTENANCE

1. POLICY

This policy is intended to provide guidance for NeuroNEXT Network personnel who participate in the finalization and maintenance of clinical study protocols. These procedures have been developed in collaboration with the NINDS and reflect ICH guidelines on protocol development.

It is the policy that once funding is awarded, each clinical study protocol will undergo refinement by the Protocol Steering Committee (PSC), Single Institutional Review Board (SIRB) and NINDS Data and Safety Monitoring Board (DSMB) as appropriate. The NeuroNEXT Network will incorporate all applicable regulatory requirements and guidance documents that are available to the Protocol Principal Investigator (PPI), Clinical Coordinating Center (CCC) and Data Coordinating Center (DCC), as well as counsel from appropriate individuals who are experts in the subject matter pertaining to the protocol.

2. SCOPE

This SOP has been developed to be in alignment with federal regulations and Good Clinical Practices (GCP) as set forth in the 2016 Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E (R2). The policies and procedures described in this SOP apply to the NeuroNEXT CCC and DCC within the context of their oversight and advisory roles for the NeuroNEXT Network, and to all NeuroNEXT investigators, staff, subcontractors, or other entities associated with the NeuroNEXT Network who manage, oversee, and conduct research regulated by FDA and/or applicable review committees.

3. ROLES AND RESPONSIBILITIES

Development of the clinical protocol occurs prior to grant submission.

Upon receipt of funding, and completion of site selection by NEC the Protocol Steering Committee (PSC) is formed. The PSC may include: the Protocol Principal Investigator (PPI), appropriate members of the PPI study team, appropriate members of the former PWG for this study, appropriate members of the CCC and DCC, a CCC Project Manager, appropriate subject matter experts, and a patient community advocate.

The PSC under the leadership of the PPI review the protocol version submitted with the grant application for updates that may be needed per grant review, etc. Once the PSC determines that the protocol is “final” the protocol will be shared with the DSMB for review when applicable (i.e. for protocols determined to require DSMB oversight). Feedback from the DSMB is reviewed by the PSC and updates made as indicated. The DSMB and PSC approved protocol is then submitted to the sIRB for review. The sIRB approved protocol is then distributed to the selected Clinical Study Sites (CSS).

Maintenance of the protocol document, including version control and revisions may be delegated by the PPI to the CCC. Substantive changes to the protocol or the analysis plan are reviewed and approved by the PSC.

All versions of the protocol that have been sIRB approved are also approved via sign off by the PPI as well as the Directors of the CCC and DCC.

The PPI is responsible for fulfilling all regulatory requirements to maintain the clinical protocol. The If the study is conducted under and IND, it is the responsibility of the PPI to submit all version of the protocol to FDA. It is also the responsibility of the PPI to update clinicaltrials.gov when any substantive amendments are made to the study protocol

The PPI is responsible for working with the PSC, CCC and DCC to ensure that the protocol is properly conducted and maintained throughout the duration of the study.

The responsibility to conduct any of these activities may be delegated at the discretion of the PPI, acting as the Sponsor, to the NeuroNEXT CCC and/or DCC or to their subcontractors. Those individuals and entities to whom activities have been delegated take on responsibility for meeting regulatory requirements on behalf of the Sponsor, but the Sponsor has the ultimate responsibility, and must therefore supervise those delegated activities effectively.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.20	Requirements for an IND
21 CFR 312.21	Phases of an Investigation
21 CFR 312.23	IND Content and Format
21 CFR 312.30	Protocol Amendments
21 CFR 312.62	Investigator Recordkeeping and Record Retention
21 CFR 314.126	Adequate and Well-Controlled Studies
ICH E6 2.2, 2.4 – 2.6	The Principles of ICH GCP
ICH E6, 2.10, 2.11	The Principles of ICH GCP
ICH E6, 4.5	Compliance with Protocol
ICH E6, 4.9	Records and Reports
ICH E6, 5.1	Quality Assurance and Quality Control
ICH E6, 5.4	Trial Design
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.23	Multicentre Trials
ICH E6, 6.0	Clinical Trial Protocol and Protocol Amendment(s)
ICH E8	General Considerations for Clinical Trials (December 1997)
ICH E9	Statistical Principles for Clinical Trials (September 1998)
ICH E10	Choice of Control Group and Related Issues in Clinical Trials (May 2001)

5. REFERENCES TO OTHER APPLICABLE SOPS

NN GA 102	Document Development and Change Control
NN RA 201	Regulatory Authority Submissions and FDA Contact
NN PD 301	Proposal Feasibility and Protocol Synopsis Development
NN PD 303	Protocol Development and Maintenance

6. ATTACHMENTS AND REFERENCES

NN PD 301-A	Document History

NINDS Protocol Template for Definitive/Efficacy (Phase III) Trials available at http://www.ninds.nih.gov/research/clinical_research/toolkit/protocoltemplate.htm

7. TERMS AND ABBREVIATIONS

The following terms and abbreviations are used in this document:

CCC	Clinical Coordinating Center at Massachusetts General Hospital
DCC	Data Coordinating Center at The University of Iowa

ESC	Extramural Science Committee
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IDE	Investigational Device Exemption
IND	Investigational New Drug application
PPI	Protocol Principal Investigator
PSC	Protocol Steering Committee
PWG	Protocol Working Group

8. SPECIFIC PROCEDURES

A. Clinical Protocol Finalization

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	PPI	Work with appropriate PWG members to address comments from grant review;		
2.	PPI/designee, CCC, DCC	Submit “final” protocol to DSMB and sIRB for review and approval		
3.	PPI	Submit protocol amendments to FDA, if conducted under an IND		
4.	PPI/designee, CCC, DCC	Provide final sIRB approved protocol amendment to participating CSS		

B. Clinical Protocol Maintenance

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	PPI/Designee, CCC, DCC	Determine if protocol amendments and other materials to be submitted to the applicable regulatory authorities may require revision.	21 CFR 312 ICH E6	NN RA 201
2.	PPI/Designee, CCC, DCC	Create a protocol amendment, using track changes on a copy of the currently approved protocol. At a minimum, track changes should indicate the user and what has been added to or removed from the currently approved protocol. Retain all versions of tracked changes. Create a change document that lists all the pertinent changes in the protocol amendment.		NN GA 102
3.	PPI/Designee, CCC, DCC	Review, approve, and document the amended protocol by the same method used when the original protocol was reviewed and approved.		NN GA 102 NN RA 202
4.	PPI/Designee, CCC, DCC	Secure the signatures and approval dates of reviewers as appropriate.		NN GA 102

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
5.	PPI/Designee, CCC, DCC	If changes to a protocol result in necessary changes to the CRFs, follow the procedures outlined in NN GA 102, NN DM 1002, and NN DM 1003 to make associated changes to the CRFs.		NN GA 102 NN DM 1002 NN DM 1003
6.	PPI/Designee, CCC, DCC	If changes to a protocol result in necessary changes to the informed consent form, follow the procedures in NN GA 102, NN RA 204, NN RA 205, and NN SM 601 to make associated changes to the informed consent form.		NN GA 102 NN RA 204 NN RA 205 NN SM 601
7.	PPI/Designee, CCC, DCC	Determine if the amendment is an Informational Amendment or a Protocol Amendment and determine submission requirements. Once the amendment and all other materials are approved by the study team and PSC, submit the documents to all necessary regulatory authorities and review committees.		
8.	PPI/Designee, CCC, DCC	Collect the approval documentation for applicable sites. Collect documentation that states what items were approved, if this documentation is not already included. File the approval documents with other regulatory material for each site in the TMF.		NN RA 203

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Joan Ohayon ohayonj@ninds.nih.gov Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 72C6AAFD-8CC4-4855-82AC-A0700072901A Using IP Address: 156.40.137.188 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:42:44 AM Viewed: 2/14/2023 12:36:42 PM Signed: 2/14/2023 12:37:11 PM
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Marianne Chase MCHASE@mgh.harvard.edu Sr Director, Clinical Trial Operations Insight OBO The Massachusetts General Hospital Security Level: Email, Account Authentication (Required), Logged in	 Signature Adoption: Pre-selected Style Signature ID: 58FE690F-6BCA-4F23-90E3-DA15BCE3F578 Using IP Address: 73.114.253.109 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:42:43 AM Viewed: 2/14/2023 9:43:53 AM Signed: 2/14/2023 9:44:21 AM
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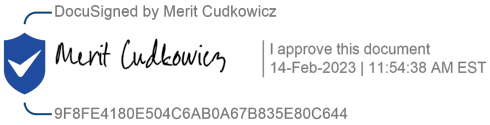
Merit Cudkowicz cudkowicz.merit@mgh.harvard.edu Chief of Neurology Security Level: Email, Account Authentication (Required), Logged in	 DocuSigned by Merit Cudkowicz I approve this document 14-Feb-2023 | 11:54:38 AM EST 9F8FE4180E504C6AB0A67B835E80C644 Signature Adoption: Pre-selected Style Signature ID: 9F8FE418-0E50-4C6A-B0A6-7B835E80C644 Using IP Address: 132.183.13.4 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:42:43 AM Viewed: 2/14/2023 11:54:28 AM Signed: 2/14/2023 11:54:40 AM
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