

# NeuroNEXT Network

## Standard Operating Procedure (SOP) Clinical Protocol Finalization and Maintenance Version 2.0 SOP NN PD 304

Originators: NeuroNEXT CCC and DCC Personnel

Reviewed and Approved by:

<b>Signature and Date:</b> <i>Christopher S. Coffey</i> <small>Electronically signed by: Christopher S. Coffey Reason: I approve this document Date: Mar 7, 2024 14:50 CST</small>	07-Mar-2024
<b>Name and Title:</b> Christopher S. Coffey, PhD (DCC Principal Investigator)	
<b>Signature and Date:</b> <i>Merit Cudkowicz</i> <small>Electronically signed by: Merit Cudkowicz Reason: I approve this document Date: Feb 22, 2024 16:59 CST</small>	22-Feb-2024
<b>Name and Title:</b> Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)	
<b>Signature and Date:</b> <i>Marianns Chase</i> <small>Electronically signed by: Marianne Chase Reason: I approve this document Date: Feb 22, 2024 15:14 EST</small>	22-Feb-2024
<b>Name and Title:</b> Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)	

**NN PD 304**

**NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR  
CLINICAL PROTOCOL FINALIZATION AND MAINTENANCE**

SOP: NN PD 304 Version No.: 2.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	<b>CLINICAL PROTOCOL FINALIZATION AND MAINTENANCE</b>	Supersedes Document : 1.0 Effective Date : 08Apr2023
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**Signature and Date:**  
*Dixie Ecklund*      Electronically signed by: Dixie Ecklund  
Reason: I approve this document  
Date: Feb 24, 2024 17:06 CST  
24-Feb-2024

**Name and Title:** Dixie J. Ecklund, RN MSN MBA (DCC Associate Director)

**Signature and Date:**  
*Stacey Grabert*      Electronically signed by: Stacey Grabert  
Reason: I approve this document  
Date: Feb 22, 2024 13:47 EST  
22-Feb-2024

**Name and Title:** Stacey Grabert, Pharm.D, MS, (CCC Director of Quality Assurance)

**Signature and Date:**  
*Joan Ohayon*      Electronically signed by: Joan Ohayon  
Reason: I approve this document  
Date: Mar 11, 2024 09:43 EDT  
11-Mar-2024

**Name and Title:** Joan Ohayon, RN, MSN, CRNP, MSCN (NINDS, NeuroNEXT Program Official)

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**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.

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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

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**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](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 Council 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		

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### 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
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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**Attachment NN PD 304 - A. Document History**

<b>NeuroNEXT Network Standard Operating Procedure (SOP) Protocol Development Finalization and Maintenance SOP NN PD 304</b>					
<b>Version</b>	<b>Description of Modification</b>	<b>Reason or Justification for Modification</b>	<b>Issue Date</b>	<b>Effective Date</b>	<b>Reviewer(s)</b>
1.0	New	N/A	22Feb2023	08Apr2023	Catherine Gladden
2.0	Minor edits for clarity	Periodic review	01Mar2024	15Apr2024	Preeti Paul








# NN PD 304 Clinical Protocol Finalization and Maintenance v2.0 2feb2024 clean

Final Audit Report

2024-03-11

Created:	2024-02-22
By:	Tania Leeder (tleeder@mgb.org)
Status:	Signed
Transaction ID:	CBJCHBCAABAA2VPKDRAH2jVomaJI34PMZVw3A5eaLv4
Number of Documents:	1
Document page count:	7
Number of supporting files:	0
Supporting files page count:	0

## "NN PD 304 Clinical Protocol Finalization and Maintenance v2.0 2feb2024 clean" History

-  Document created by Tania Leeder (tleeder@mgb.org)  
2024-02-22 - 6:24:04 PM GMT
-  Document emailed to christopher-coffey@uiowa.edu for signature  
2024-02-22 - 6:25:37 PM GMT
-  Document emailed to cudkowicz.merit@mgh.harvard.edu for signature  
2024-02-22 - 6:25:37 PM GMT
-  Document emailed to Marianne Chase (mchase@mgh.harvard.edu) for signature  
2024-02-22 - 6:25:37 PM GMT
-  Document emailed to dixie-ecklund@uiowa.edu for signature  
2024-02-22 - 6:25:37 PM GMT
-  Document emailed to Stacey Grabert (SGrabert@mgh.harvard.edu) for signature  
2024-02-22 - 6:25:37 PM GMT
-  Document emailed to ohayonj@ninds.nih.gov for signature  
2024-02-22 - 6:25:37 PM GMT



✔ Stacey Grabert (SGrabert@mgh.harvard.edu) authenticated with Adobe Acrobat Sign.

Challenge: The user opened the agreement.

2024-02-22 - 6:47:09 PM GMT

📄 Document e-signed by Stacey Grabert (SGrabert@mgh.harvard.edu)

Signing reason: I approve this document

Signature Date: 2024-02-22 - 6:47:24 PM GMT - Time Source: server

📧 Email viewed by christopher-coffey@uiowa.edu

2024-02-22 - 7:55:47 PM GMT

✔ Marianne Chase (mchase@mgh.harvard.edu) authenticated with Adobe Acrobat Sign.

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2024-02-22 - 8:14:04 PM GMT

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Signature Date: 2024-02-22 - 8:14:20 PM GMT - Time Source: server

📧 Email viewed by cudkowicz.merit@mgh.harvard.edu

2024-02-22 - 10:59:27 PM GMT

✔ cudkowicz.merit@mgh.harvard.edu authenticated with Adobe Acrobat Sign.

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2024-02-22 - 10:59:43 PM GMT

📄 Signer cudkowicz.merit@mgh.harvard.edu entered name at signing as Merit Cudkowicz

2024-02-22 - 10:59:54 PM GMT

📄 Document e-signed by Merit Cudkowicz (cudkowicz.merit@mgh.harvard.edu)

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Signature Date: 2024-02-22 - 10:59:56 PM GMT - Time Source: server

📧 Tania Leeder (tleeder@mgb.org) added alternate signer ecklundd@uiowa.edu. The original signer dixie-ecklund@uiowa.edu can still sign.

2024-02-23 - 7:02:18 PM GMT

📧 Document emailed to ecklundd@uiowa.edu for signature

2024-02-23 - 7:02:19 PM GMT

📧 Tania Leeder (tleeder@mgb.org) added alternate signer cscoffey@iowa.uiowa.edu. The original signer christopher-coffey@uiowa.edu can still sign.


2024-02-23 - 7:02:29 PM GMT

📧 Document emailed to cscoffey@iowa.uiowa.edu for signature

2024-02-23 - 7:02:30 PM GMT

 Email viewed by cscoffey@iowa.uiowa.edu

2024-02-23 - 7:14:13 PM GMT

 Email viewed by ecklundd@uiowa.edu

2024-02-24 - 11:05:51 PM GMT

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Challenge: The user opened the agreement.

2024-02-24 - 11:06:03 PM GMT


 Signer ecklundd@uiowa.edu entered name at signing as Dixie Ecklund

2024-02-24 - 11:06:18 PM GMT

 Document e-signed by Dixie Ecklund (ecklundd@uiowa.edu)

Signing reason: I approve this document

Signature Date: 2024-02-24 - 11:06:20 PM GMT - Time Source: server

 Email viewed by cscoffey@iowa.uiowa.edu

2024-03-07 - 8:49:44 PM GMT- IP address: 128.255.113.139

 cscoffey@iowa.uiowa.edu authenticated with Adobe Acrobat Sign.

Challenge: The user opened the agreement.

2024-03-07 - 8:49:58 PM GMT


 Signer cscoffey@iowa.uiowa.edu entered name at signing as Christopher S. Coffey

2024-03-07 - 8:50:13 PM GMT- IP address: 128.255.113.139

 Document e-signed by Christopher S. Coffey (cscoffey@iowa.uiowa.edu)

Signing reason: I approve this document

Signature Date: 2024-03-07 - 8:50:16 PM GMT - Time Source: server- IP address: 128.255.113.139

 Email viewed by ohayonj@ninds.nih.gov

2024-03-11 - 1:43:24 PM GMT- IP address: 104.47.64.254

 ohayonj@ninds.nih.gov authenticated with Adobe Acrobat Sign.

Challenge: The user opened the agreement.

2024-03-11 - 1:43:33 PM GMT

 Signer ohayonj@ninds.nih.gov entered name at signing as Joan Ohayon

2024-03-11 - 1:43:46 PM GMT- IP address: 72.83.187.43

 Document e-signed by Joan Ohayon (ohayonj@ninds.nih.gov)

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Signature Date: 2024-03-11 - 1:43:48 PM GMT - Time Source: server- IP address: 72.83.187.43

 Agreement completed.

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