NeuroNEXT Network

Standard Operating Procedure (SOP)

Site Regulatory File Maintenance

Version 4.0

SOP NN RA 203

Originators: NeuroNEXT CCC and DCC Personnel

Reviewed and Approved by:

Signature and Date: Christopher S. Coffey *Electronically signed by: Christopher S. Coffey* *Reason: I approve this document* *Date: Mar 8, 2024 08:09 CST* 08-Mar-2024
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)
Signature and Date: Marianne Chase *Electronically signed by: Marianne Chase* *Reason: I approve this document* *Date: Feb 22, 2024 14:50 EST* 22-Feb-2024
Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)

NN RA 203

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR SITE REGULATORY FILE MAINTENANCE

SOP: NN RA 203 Version No.: 4.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	SITE REGULATORY FILE MAINTENANCE	Supersedes Document : Version 3.0 Effective Date : 08Apr2023

Signature and Date:

Dixie Ecklund

Electronically signed by: Dixie Ecklund
Reason: I approve this document
Date: Feb 24, 2024 17:15 CST

24-Feb-2024

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

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Electronically signed by: Stacey Grabert
Reason: I approve this document
Date: Feb 22, 2024 13:56 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 11:16 EDT

11-Mar-2024

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

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR SITE REGULATORY FILE MAINTENANCE

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1. POLICY

The NeuroNEXT Protocol Principal Investigator (PPI), acting as the regulatory Sponsor of a study, shall ensure that each Clinical Study Site (CSS) participating in a trial, maintains an organized, easily accessible, and complete Site Regulatory File (SRF) as required by regulation. The CSS will be informed that the SRF for each trial shall be available for monitoring and audits, whether internal or by a third party, and for FDA inspection.

Each SRF should contain essential documents applicable to the project. Essential documents are documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. Essential documents are outlined in the International Council on Harmonization Integrated Addendum to E6(R1): Guideline for Good Clinical Practice E6(2), Section 8: Essential Documents for the Conduct of a Clinical Trial.

The SRF shall be stored in a secure manner (under lock and key, accessed by authorized personnel only). All SRF contents will be maintained on site for a minimum of two (2) years after the conclusion of the study or two (2) years after FDA marketing approval. After that, the original files may be archived to a secure location that ensures that the files are available within 24 hours as required by regulatory authorities. Record retention guidelines are defined in *MGB Guidelines on Retention of Research Data, Materials, and Records*, as MGB IRB is the IRB of record for NeuroNEXT.

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 E6(R2). The policies and procedures described in this SOP apply to the NeuroNEXT Clinical Coordinating Center (CCC) and Data Coordinating Center (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

The Sponsor and all participating CSS investigators are responsible for ensuring that complete and accurate regulatory documents are collected maintained and retained throughout the course of a clinical investigation. Each CSS-Investigator is responsible for maintenance of SRF at their individual site, as per FDA Form 1572 and/or Investigator of Record Agreement (IoRA)

The Sponsor is responsible for verifying that all CSS files are complete, accurate, and securely maintained by the participating investigators.

The Sponsor is responsible for terminating the participation of, and discontinuing shipments of investigational product to, any participating CSS investigator who has failed to maintain, or make available, required records or reports of the study, as required by applicable regulations.

The responsibility to conduct any or all of these activities may be delegated at the discretion of the Sponsor to the NeuroNEXT CCC and/or DCC, or to their subcontractors. Those individuals and entities take on the 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 312.57	Recordkeeping and Record Retention
21 CFR 312.62	Investigator Recordkeeping and Record Retention

21 CFR 312.68	Inspection of Investigator's Records and Reports
ICH E6, 2.10, 2.11	The Principles of ICH GCP
ICH E6, 4.9	Records and Reports
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.15	Record Access
ICH E6, 8.0	Essential Documents for the Conduct of a Clinical Trial

5. REFERENCES TO OTHER APPLICABLE SOPS

NN SS 401	Site Selection and Qualification
NN SS 402	Site Initiation Visits and Site Training
NN SS 403	Routine Monitoring Visits
NN SS 405	Study Closeout Visits
NN SS 406	Suspension or Early Termination of a Study or a Clinical Site

6. ATTACHMENTS AND REFERENCES

NN RA 203-A	Document History

7. TERMS AND ABBREVIATIONS

The following terms and abbreviations are used in this document:

CCC	Clinical Coordinating Center at Massachusetts General Hospital
CFR	Code of Federal Regulations
CSS	Clinical Study Site
DCC	Data Coordinating Center at The University of Iowa
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Council for Harmonisation
IoRA	Investigator of Record Agreement
PPI	Protocol Principal Investigator
SRF	Site Regulatory File

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8. SPECIFIC PROCEDURES

A. Creating the SRF

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	CSS	Establish the SRF as appropriate after project approval is secured and site qualification is completed.		NN SS 401
2.	CSS	Organize project and site regulatory files.		NN SS 402
3.	Sponsor / CCC or DCC designee	Review with the CSS investigator and other key personnel the requirements and procedures to create and maintain the site's regulatory file through the duration of the study and after its completion.		NN SS 402
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B. Maintaining the SRF

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	CSS	Periodically review file contents to ensure they are being kept up to date.		
2.	Sponsor / CCC or DCC designee	Examine study files at sites during routine monitoring visits.		NN SS 403
3.	Sponsor / CCC or DCC designee	Report gaps, missing items, and discrepancies to CSS investigator.		NN SS 403
4.	Sponsor / CCC or DCC designee	Report records retention noncompliance to the Sponsor.		NN SS 403
5.	Sponsor / CCC or DCC designee	At the study closeout visit, confirm that all required documents and records are in the site's regulatory file.		NN SS 405 NN SS 406
6.	Sponsor / CCC or DCC designee	Arrange for archive storage when appropriate, after written approval from Sponsor.		

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Attachment NN RA 203 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP) Site Regulatory File Maintenance SOP NN RA 203					
Version	**Description of Modification**	**Reason or Justification for Modification**	**Issue Date**	**Effective Date**	**Reviewer(s)**
1.0	New	N/A	22Mar2012	21Apr2012	N/A
2.0	Minor correction to replace 'data' with 'regulatory documents' in Section 3 and edits to SOP listing.	Updates for version 2.0	21Sep2016	21Oct2016	N/A
3.0	Updated "1996 ICH E6 Consolidated Guidance" to "2016 Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)". Updated signature block to accommodate for electronic signatures. Additional minor updates throughout.	Updated for version 3.0	22Feb2023	08Apr2023	Catherin Gladden
4.0	Updates to SOP references, minor updates throughout, added reference to essential documents, MGB IRB Policy record retention and requirement of	Periodic review	01Mar2024	15Apr2024	Preeti Paul

	permission in writing from PPI to destroy documentation.				

NN RA 203 Site Regulatory File Maintenance v4.0 2feb2024 clean

Final Audit Report 2024-03-11

Created:	2024-02-22
By:	Tania Leeder (tleeder@mgb.org)
Status:	Signed
Transaction ID:	CBJCHBCAABAAhap8j7IDTtuAyLXnr42eVTsGKFmUVmW5
Number of Documents:	1
Document page count:	8
Number of supporting files:	0
Supporting files page count:	0

"NN RA 203 Site Regulatory File Maintenance v4.0 2feb2024 clean" History

Document created by Tania Leeder (tleeder@mgb.org)
2024-02-22 - 6:02:21 PM GMT

Document emailed to christopher-coffey@uiowa.edu for signature
2024-02-22 - 6:03:54 PM GMT

Document emailed to cudkowicz.merit@mgh.harvard.edu for signature
2024-02-22 - 6:03:54 PM GMT

Document emailed to Marianne Chase (mchase@mgh.harvard.edu) for signature
2024-02-22 - 6:03:54 PM GMT

Document emailed to dixie-ecklund@uiowa.edu for signature
2024-02-22 - 6:03:54 PM GMT

Document emailed to Stacey Grabert (SGrabert@mgh.harvard.edu) for signature
2024-02-22 - 6:03:54 PM GMT

Document emailed to ohayonj@ninds.nih.gov for signature
2024-02-22 - 6:03:55 PM GMT

Email viewed by cudkowicz.merit@mgh.harvard.edu
2024-02-22 - 6:07:16 PM GMT

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

Challenge: The user opened the agreement.

2024-02-22 - 6:08:03 PM GMT

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

2024-02-22 - 6:08:39 PM GMT

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

Signing reason: I approve this document

Signature Date: 2024-02-22 - 6:08:41 PM GMT - Time Source: server

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

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2024-02-22 - 6:56:30 PM GMT

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Signing reason: I approve this document

Signature Date: 2024-02-22 - 6:56:40 PM GMT - Time Source: server

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

Challenge: The user opened the agreement.

2024-02-22 - 7:50:11 PM GMT

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Signature Date: 2024-02-22 - 7:50:54 PM GMT - Time Source: server

Email viewed by christopher-coffey@uiowa.edu

2024-02-22 - 7:55:15 PM GMT

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

2024-02-23 - 6:56:24 PM GMT

Document emailed to ecklundd@uiowa.edu for signature

2024-02-23 - 6:56:24 PM GMT

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

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2024-02-23 - 7:14:12 PM GMT

Email viewed by ecklundd@uiowa.edu

2024-02-24 - 11:15:12 PM GMT

ecklundd@uiowa.edu authenticated with Adobe Acrobat Sign.

Challenge: The user opened the agreement.

2024-02-24 - 11:15:24 PM GMT

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

2024-02-24 - 11:15:36 PM GMT

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

Signing reason: I approve this document

Signature Date: 2024-02-24 - 11:15:39 PM GMT - Time Source: server

Email viewed by cscoffey@iowa.uiowa.edu

2024-03-08 - 9:19:54 AM GMT- IP address: 172.226.137.0

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

Challenge: The user opened the agreement.

2024-03-08 - 2:09:27 PM GMT

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

2024-03-08 - 2:09:46 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: 2024-03-08 - 2:09:49 PM GMT - Time Source: server- IP address: 128.255.113.139

Email viewed by ohayonj@ninds.nih.gov

2024-03-11 - 3:15:51 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 - 3:15:59 PM GMT

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

2024-03-11 - 3:16:13 PM GMT- IP address: 72.83.187.43

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

Signing reason: I approve this document

Signature Date: 2024-03-11 - 3:16:15 PM GMT - Time Source: server- IP address: 72.83.187.43

Agreement completed.

2024-03-11 - 3:16:15 PM GMT