NeuroNEXT Network

Standard Operating Procedure (SOP)

Trial Master File Maintenance and Auditing

Version 3.0

SOP NN RA 202

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 08:08 CST* 08-Mar-2024
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Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR TRIAL MASTER FILE MAINTENANCE AND AUDITING

SOP: NN RA 202 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	TRIAL MASTER FILE MAINTENANCE AND AUDITING	Supersedes Document : Version 2.0 Effective Date : 08Apr2023

Signature and Date:

Dixie Ecklund

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Date: Feb 24, 2024 17:15 CST

24-Feb-2024

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Reason: I approve this document
Date: Feb 22, 2024 13:57 EST

22-Feb-2024

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Joan Ohayon

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Date: Mar 11, 2024 11:16 EDT

11-Mar-2024

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NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR TRIAL MASTER FILE MAINTENANCE AND AUDITING

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1. POLICY

The NeuroNEXT Protocol Principal Investigator (PPI), acting as the regulatory Sponsor of a study, shall maintain an organized, easily accessible, legible, accurate, and complete Trial Master File (TMF) as required by regulation. The TMF shall be available for audits, whether internal or by a third party, and for FDA inspection.

The TMF 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 TMF shall be stored in a secure manner (under lock and key or electronically, accessed by authorized personnel only). All physical (paper) TMF 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.

These procedures define the organization of the TMF for the overall project, as well as each individual Clinical Study Site (CSS) and the retention policies for these documents and records.

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 and non-NeuroNEXT Clinical Study Site (CSS) 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 Clinical Study Site (CSS) investigators are responsible for ensuring that complete and accurate data are collected, documented, maintained and retained throughout the course of a clinical investigation.

The Sponsor is responsible for verifying that all CSS files are complete, accurate, and securely maintained by the participating CSS 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 as outlined in SOP NN SS 406: Suspension or Early Termination of a Study or Clinical Site

SOP: NN RA 202 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	TRIAL MASTER FILE MAINTENANCE AND AUDITING	Supersedes Document : Version 2.0 Effective Date : 08Apr2023

The responsibility to conduct any 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 312.58	Inspection of Sponsor'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	Records Access
ICH E6, 8.0	Essential Documents for the Conduct of a Clinical Trial

5. REFERENCES TO OTHER APPLICABLE SOPS

NN RA 201	Regulatory Authority Submissions and FDA Contact
NN RA 203	Site Regulatory File Maintenance
NN SS 401	Site Selection and Qualification
NN SS 403	Routine Monitoring Visits
NN SS 404	Site Performance Monitoring
NN SS 405	Study Close Out Visits
NN SS 406	Suspension or Early Termination of a Study or Clinical Site

6. ATTACHMENTS AND REFERENCES

NN RA 202-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
CSS	Clinical Study Site
DCC	Data Coordinating Center at The University of Iowa
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Council for Harmonisation
PPI	Protocol Principal Investigator

SOP: NN RA 202 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	TRIAL MASTER FILE MAINTENANCE AND AUDITING	Supersedes Document : Version 2.0 Effective Date : 08Apr2023

TMF Trial Master File

8. SPECIFIC PROCEDURES

A. Creating the TMF

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	Sponsor / CCC or DCC designee	Establish the TMF as appropriate after project funding and/or regulatory approval is secured (as needed) and site qualification is completed.[1]		NN RA 201 SS NN 401
2.	Sponsor / CCC or DCC designee	Organize project and site regulatory files.[1]		NN RA 203
3.	Sponsor / CCC or DCC designee	Arrange for secure storage of all study-related files.		
4.	Sponsor / CCC or DCC designee	Identify personnel with authorized access to the TMF, and create study specific TMF plan where this is documented.		

Note:
[1]As an investigative site is qualified, establish a separate Site Regulatory File for each participating site.
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B. Maintaining and Auditing the TMF

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	Sponsor / CCC or DCC designee	Periodically review/audit TMF contents to ensure they are being kept up to date.		NN SS 403 NN SS 404
2.	Sponsor / CCC or DCC designee	Provide study team with findings of TMF review/audit and document resolution of each finding, prior to finalization of TMF		NN SS 403 NN SS 404
3.	Sponsor / CCC or DCC designee	Add to the TMF as documents and records become available.		
4.	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 RA 203

SOP: NN RA 202 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	TRIAL MASTER FILE MAINTENANCE AND AUDITING	Supersedes Document : Version 2.0 Effective Date : 08Apr2023

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
5.	Sponsor / CCC or DCC designee	Arrange for archive storage of TMF and site regulatory files when appropriate.		NN RA 203

SOP: NN RA 202 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	TRIAL MASTER FILE MAINTENANCE AND AUDITING	Supersedes Document : Version 2.0 Effective Date : 08Apr2023

Attachment NN RA 202 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP) Trial Master File Maintenance SOP NN RA 202					
Version	**Description of Modification**	**Reason or Justification for Modification**	**Issue Date**	**Effective Date**	**Reviewer(s)**
1.0	New	N/A	22Mar2012	21Apr2012	N/A
1.0	Reviewed – no changes (2016)	N/A	22Mar2012	21Apr2012	N/A
2.0	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	Catherine Gladden
3.0	Changes to SOP references, added reference to essential documents, MGB IRB Policy on record retention and requirement of permission in writing from PPI to destroy documentation.	Periodic review	01Mar2024	15Apr2024	Preeti Paul

NN RA 202 Trial Master File Maintenance and Auditing v3.0 2feb2024 clean

Final Audit Report 2024-03-11

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

"NN RA 202 Trial Master File Maintenance and Auditing v3.0 2fe b2024 clean" History

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Document emailed to christopher-coffey@uiowa.edu for signature
2024-02-22 - 6:01:41 PM GMT

Document emailed to cudkowicz.merit@mgh.harvard.edu for signature
2024-02-22 - 6:01:42 PM GMT

Document emailed to Marianne Chase (mchase@mgh.harvard.edu) for signature
2024-02-22 - 6:01:42 PM GMT

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2024-02-22 - 6:01:42 PM GMT

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2024-02-22 - 6:01:42 PM GMT

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2024-02-22 - 6:03:30 PM GMT

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

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2024-02-22 - 6:04:03 PM GMT

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2024-02-22 - 6:04:22 PM GMT

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2024-02-23 - 6:56:52 PM GMT

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

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2024-02-24 - 11:14:42 PM GMT

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2024-02-24 - 11:14:53 PM GMT

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2024-02-24 - 11:15:05 PM GMT

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Signature Date: 2024-02-24 - 11:15:08 PM GMT - Time Source: server

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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 - 2:08:39 PM GMT

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2024-03-08 - 2:08:57 PM GMT- IP address: 128.255.113.139

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Signing reason: I approve this document

Signature Date: 2024-03-08 - 2:09:00 PM GMT - Time Source: server- IP address: 128.255.113.139

Email viewed by ohayonj@ninds.nih.gov

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

Challenge: The user opened the agreement.

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2024-03-11 - 3:16:49 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 - 3:16:51 PM GMT - Time Source: server- IP address: 72.83.187.43

Agreement completed.

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