NeuroNEXT Network

Standard Operating Procedure (SOP)

Quality Management

Version 4.0

SOP NN QA 802

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 7, 2024 14:29 CST* 07-Mar-2024
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NN QA 802
NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR QUALITY MANAGEMENT

SOP: NN QA 802 Version No: 4.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	QUALITY MANAGEMENT	Supersedes Document Version :3.0 Effective Date : 08Apr2023

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NN QA 802
NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR QUALITY MANAGEMENT

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1. POLICY

The NeuroNEXT Network Data Coordinating Center (DCC) and Clinical Coordinating Center (CCC) will oversee Quality Management (QM) activities for all NeuroNEXT clinical trials. These activities help to ensure that all study-related activities meet Quality Assurance (QA) and Quality Control (QC) standards that are founded in Good Clinical Practices (GCP) and first principles of sound scientific and statistical research.

The DCC and/or CCC perform the following QM activities for the Network:

- defining areas of quality oversight;
- developing a comprehensive NeuroNEXT Network Quality Management Plan;
- developing quality improvement strategies, methods, reports, and tools (as required for a study);
- participating in the development, periodic review, and revision of NeuroNEXT Network Standard Operating Procedures (SOPs);
- reviewing, approving, and overseeing the development of Clinical Study Site (CSS or 'Site') SOPs as applicable;
- evaluating adherence to Network SOPs;
- conducting comprehensive training and re-training (as needed) of all CCC, DCC, and CSS study personnel on the study protocol, procedures, GCP, AE/SAE reporting, outcome measures, investigational product (IP) management, data collection/data handling, and proper study conduct;
- developing appropriate monitoring procedures to evaluate program effectiveness, ensure data safety and integrity, and maintain compliance with GCP, FDA regulations, and NeuroNEXT protocol directives;
- conducting routine monitoring and study close-out visits to ensure the quality, integrity, and completeness of study data;
- managing and tracking the reporting and coding of Adverse Events and Serious Adverse Events;
- determining CSS performance goals and metrics, assessing CSS performance and progress toward recruitment and retention goals, and assisting CSS with developing Corrective Action and Preventative Action (CAPA) plans and resolving performance issues;
- evaluating reports to assess performance metrics and to identify performance issues, if applicable to a study;
- implementing data quality procedures for evaluating data collection, data management, information technology, and statistical analysis activities to ensure data quality;
- verifying that applicable NeuroNEXT electronic data systems are 21 CFR Part 11 compliant;
- performing periodic assessments of IP management processes at CSS;
- conducting routine internal reviews of the Site Regulatory Files to ensure completeness and compliance with applicable federal regulations.

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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 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

The CCC and DCC are responsible for overseeing QM activities for the NeuroNEXT Network, and for assessing adherence to Network SOPs and study protocols to assure quality performance.

4. APPLICABLE REGULATIONSAND GUIDELINES

21 CFR 11	Electronic Records; Electronic Signatures
21 CFR 50	Protection of Human Subjects
ICH E6, 2.13	The Principles of ICH GCP
ICH E6, 5.1	Quality Assurance and Quality Control
ICH E6, 5.19	Audit
ICH E6, 5.20	Noncompliance
FDA	Compliance Policy Guide 7151.02

5. REFERENCES TO OTHER APPLICABLE SOPS

This SOP applies to all NeuroNEXT Network SOPs.

6. ATTACHMENTS AND REFERENCES

NN QA 802 - A	Document History

7. TERMS AND ABBREVIATIONS

The following terms and abbreviations are used in this document:

CAPA	Corrective Action and Preventative Action
CCC	Clinical Coordinating Center at Massachusetts General Hospital
CFR	Code of Federal Regulations
CSS	Clinical Study Site(s)
DCC	Data Coordinating Center at The University of Iowa
FDA	Food and Drug Administration
GCP	Good Clinical Practices
ICH	International Conference for Harmonisation

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IP	Investigational Product
PPI	Protocol Principal Investigator
QA	Quality Assurance: refers to a scheduled program of auditing that may also include the creation and maintenance of SOPs, and objective reviews and quality improvement evaluations of targeted clinical trial areas and activities
QC	Quality Control: refers to day-to-day operational checks and activities that are undertaken to ensure that the quality requirements of the clinical trial are being met, and that SOPs are being followed
QM	Quality Management: refers to a system of oversight and review of QA processes and QC procedures
SAE	Serious Adverse Event
SOP	Standard Operating Procedure

8. SPECIFIC PROCEDURES

A. Quality Management Overview

#	*Who*	*Task*	*Attachment/ Reference*	*Related SOP*
1.	DCC and CCC Leadership, CCC QA	Define areas of quality oversight, goals, and metrics for the NeuroNEXT Network.		
2.	CCC QA	Develop and maintain a comprehensive Quality Management Plan for the NeuroNEXT Network that includes areas of Quality Management oversight described in the sections below, and that describes a plan for: • implementing corrective actions • resolving quality or performance issues • follow-up to ensure resolution.		
3.	DCC and CCC Leadership	Review and approve the comprehensive Quality Management Plan.		
4.	CCC, DCC	Create checklists, programs, reports, and other tools to assist with quality processes (as required or applicable to a study).		
5.	Site Support Team and Study Team	Evaluate reports to assess performance metrics and to identify performance issues.		

B. Network Standard Operating Procedures

#	Who	Task	Attachment/ Reference	Related SOP
1.	DCC and CCC SOP Development Committee	Collaborate to develop SOPs for the NeuroNEXT Network according to procedures described in SOP NN GA 101.		NN GA 101
2.	DCC and CCC SOP Development Committee	Review, revise, approve, and re-version NeuroNEXT Network SOPs as needed.		NN GA 101 NN GA 103

C. Clinical Study Site Standard Operating Procedures

#	Who	Task	Attachment/ Reference	Related SOP
1.	Site SOP Team	Collaborate to develop SOPs that apply to all NeuroNEXT Network CSS.		NN GA 101 NN GA 103
2.	Site SOP Development Committee	Finalize Site SOPs, and submit to DCC, CCC for approval and signatures.		NN GA 101
3.	Site SOP Development Committee	Review, revise, approve, and re-version NeuroNEXT Network Site SOPs as needed.		NN GA 101 NN GA 103

D. Areas of Quality Oversight

#	Who	Task	Attachment/ Reference	Related SOP
1.	CCC and DCC	**Training** Conduct and document training for study personnel that includes, but is not limited to, the following areas: • Study protocol, procedures, and proper study conduct • GCP • Investigational product management • Outcome measures • AE/SAE reporting • Data Collection and Data Handling Perform periodic checks of training records to ensure completeness and compliance with SOPs.		NN SS 402 NN SS 403 NN SS 404 NN PM 504 NN PM 505 NN SM 602 NN DM 1005

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#	*Who*	*Task*	*Attachment/ Reference*	*Related SOP*
2.	DCC	**CSS Monitoring** Conduct scheduled interim monitoring and final study close-out monitoring. • DCC: perform comparisons of study data listings with source documents as detailed in the study Monitoring Plan, and as described in SOPs NN SS 403 and NN SS 405.		NN SS 403 NN SS 405
3.	DCC	**Safety Reporting and Management** Manage and track the reporting and coding of Adverse Events and Serious Adverse Events for each NeuroNEXT study.		NN RA 206
4.	Study Team	**Site Performance** Create CSS performance goals and metrics, identify performance issues, and assist CSS in developing CAPA plans and resolving performance issues, or determine criteria for CSS termination, as described in SOPs NN SS 404 and NN SS 406.		NN SS 404 NN SS 406
5.	NeuroNEXT Recruitment and Retention Committee, CCC, DCC, PPI	**Recruitment and Retention** Collaborate to develop a Recruitment and Retention Plan for each NeuroNEXT study that may include: • metrics and goals for CSS enrollments • methods and reports for tracking recruitment and retention • incentives for CSS to reach their goals.		NN SM 603
6.	Study Team	**Reports** Generate and review reports, as appropriate and applicable to a study, to evaluate program effectiveness, assess implementation of quality measures and compliance with data quality objectives, and to identify areas for improvement.		
7.	DCC	**NeuroNEXT Network User Access** Perform periodic reviews of CCC, DCC, and CSS User Access records to ensure that current NeuroNEXT personnel are assigned appropriate database and website access rights and roles, and that NeuroNEXT personnel who have left the Network no longer have NeuroNEXT User Access rights or roles.		NN CS 704

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#	*Who*	*Task*	*Attachment/ Reference*	*Related SOP*
8.	DCC QM Lead or designee	**Data Systems and Data Management** Conduct periodic random reviews of Data Management processes and NeuroNEXT data system development documentation to assess compliance with NeuroNEXT SOPs, 21 CFR Part 11, and other federal regulations governing data quality, security, and electronic systems, and to check for adequate documentation.		NN CS 701 NN CS 702 NN CS 703 NN CS 704 NN CS 705 NN CS 706 NN DM 1004 NN DM 1005
9.	DCC QM Lead or designee	**Biostatistics** Perform periodic, random evaluations of Biostatistics reports for compliance with Network SOPs and to check for adequate documentation.		
10.	Study Team and IP distributor	**Investigational Product (IP) Management** Perform periodic assessments of investigational product management processes at CSS to determine if standardization or quality improvements are needed or desirable.		NN PM 505
11.	CCC and/or Sponsor	**Site Regulatory Files** • CCC: Perform QC checks of regulatory documents and reports to be submitted to FDA or other applicable regulatory authorities. • Sponsor and/or CCC: Perform periodic scheduled internal reviews of the Site Regulatory Files for each NeuroNEXT study.		NN RA 201

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Attachment NN QA 802 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP) Quality Management SOP NN QA 802					
Version	**Description of Modification**	**Reason or Justification for Modification**	**Issue Date**	**Effective Date**	**Reviewer(s)**
1.0	New	N/A	13Apr2012	13May2012	N/A
2.0	Removed references to Project Work Instructions (PWIs) and revised/condensed the Policy section. Modified frequency of SOP reviews to be as-needed. Combined areas of Network and Study-specific quality oversight into one section of the Specific Procedures. Added an item for safety reporting and management, clarified that the CCC performs reviews an closeout of the Site Regulatory Files, and made other minor revisions to the Specific Procedures.	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.	Updates for version 3.0	22Feb2023	08Apr2024	Catherine Gladden
4.0	Added CCC and DCC to oversight in section 3. Revised definition of QA in section 7.	Periodic Review	01Mar2024	15Apr2024	Preeti Paul

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Final Audit Report 2024-03-07

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