

# NeuroNEXT Network

## Standard Operating Procedure (SOP)

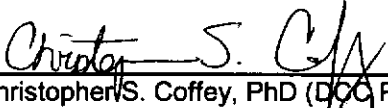
### Quality Management


Version 2.0

SOP NN QA 802

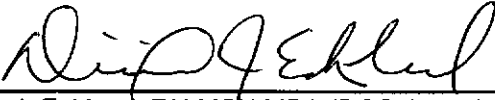
Originators: NeuroNEXT CCC and DCC Personnel

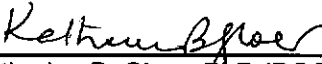
Reviewed and Approved by:

  
Christopher S. Coffey, PhD (DCC Principal Investigator)

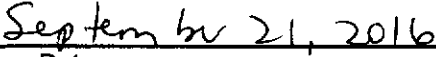
  
Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)

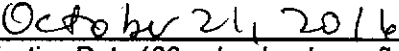
  
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Issue Date

  
Effective Date (30 calendar days after the Issue Date)

## NN QA 802

# NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR QUALITY MANAGEMENT

|  |                    |  |
|--|--------------------|--|
| SOP: NN QA 802<br>Version No: 2.0<br>Effective Date: 21Oct2016 | QUALITY MANAGEMENT | Supersedes<br>Document: Version 1.0<br>Effective Date: 13May2012 |
|--|--------------------|--|

### 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;
- evaluating adherence to Network SOPs;
- conducting comprehensive training and re-training (as needed) of all CCC, DCC, and Clinical Study Site (CSS) study personnel on the study protocol, procedures, GCP, AE/SAE reporting, outcome measures, 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 investigational product (IP) management processes at CSS;

- conducting routine internal reviews of the Site Regulatory Files to ensure completeness and compliance with applicable federal regulations.

## 2. SCOPE

This SOP has been developed to be in alignment with federal regulations and Good Clinical Practices (GCP) as set forth in the 1996 ICH E6 Consolidated Guidance. 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/or the 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 REGULATIONS AND 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 on Harmonisation   |
| PPI  | Protocol Principal Investigator   |
| QA   | Quality Assurance: refers to a scheduled program of systematic monitoring that includes 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/<br>Reference | Related SOP |
|----|--|--|--------------------------|-------------|
| 1. | DCC and CCC Leadership,<br>DCC QM Lead | Define areas of quality oversight, goals, and metrics for the NeuroNEXT Network.   |                          |             |
| 2. | CCC and DCC QM Lead                    | 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: <ul style="list-style-type: none"> <li>• implementing corrective actions</li> <li>• resolving quality or performance issues</li> <li>• follow-up to ensure resolution.</li> </ul> |                          |             |
| 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/<br>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<br>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<br>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<br>NN GA 103 |

### D. Areas of Quality Oversight

| #  | Who                              | Task  | Attachment/Reference | Related SOP  |
|----|----------------------------------|---|----------------------|--|
| 1. | CCC and DCC                      | <p><b>Training</b></p> <p>Conduct and document training for study personnel that includes, but is not limited to, the following areas:</p> <ul style="list-style-type: none"> <li>• Study protocol, procedures, and proper study conduct</li> <li>• GCP</li> <li>• Investigational product management</li> <li>• Outcome measures</li> <li>• AE/SAE reporting</li> <li>• Data Collection and Data Handling</li> </ul> <p>Perform periodic checks of training records to ensure completeness and compliance with SOPs.</p> |                      | NN SS 402<br>NN SS 403<br>NN SS 404<br>NN PM 504<br>NN PM 505<br>NN SM 602<br>NN DM 1005 |
| 2. | CCC and DCC                      | <p><b>CSS Monitoring</b></p> <p>Conduct scheduled interim monitoring and final study close-out monitoring.</p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• CCC: perform reviews and closeout of the Site Regulatory Files.</li> </ul>   |                      | NN SS 403<br>NN SS 405   |
| 3. | DCC                              | <p><b>Safety Reporting and Management</b></p> <p>Manage and track the reporting and coding of Adverse Events and Serious Adverse Events for each NeuroNEXT study.</p>   |                      | NN RA 206  |
| 4. | Site Support Team and Study Team | <p><b>Site Performance</b></p> <p>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.</p>   |                      | NN SS 404<br>NN SS 406   |

| #   | Who  | Task  | Attachment/<br>Reference | Related SOP  |
|-----|--|---|--------------------------|--|
| 5.  | NeuroNEXT Recruitment and Retention Committee, CCC, DCC, PPI | <p><b>Recruitment and Retention</b></p> <p>Collaborate to develop a Recruitment and Retention Plan for each NeuroNEXT study that may include:</p> <ul style="list-style-type: none"> <li>metrics and goals for CSS enrollments</li> <li>methods and reports for tracking recruitment and retention</li> <li>incentives for CSS to reach their goals.</li> </ul>   |                          | NN SM 603  |
| 6.  | Study Team   | <p><b>Reports</b></p> <p>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.</p>  |                          |  |
| 7.  | DCC  | <p><b>NeuroNEXT Network User Access</b></p> <p>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.</p>               |                          | NN CS 704  |
| 8.  | DCC QM Lead or designee                                      | <p><b>Data Systems and Data Management</b></p> <p>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.</p> |                          | NN CS 701<br>NN CS 702<br>NN CS 703<br>NN CS 704<br>NN CS 705<br>NN CS 706<br>NN DM 1004<br>NN DM 1005 |
| 9.  | DCC QM Lead or designee                                      | <p><b>Biostatistics</b></p> <p>Perform periodic, random evaluations of Biostatistics reports for compliance with Network SOPs and to check for adequate documentation.</p>  |                          |  |
| 10. | Study Team and IP distributor                                | <p><b>Investigational Product (IP) Management</b></p> <p>Perform periodic assessments of investigational product management processes at CSS to determine if standardization or quality improvements are needed or desirable.</p>   |                          | NN PM 505  |
| 11. | CCC and/or Sponsor   | <p><b>Site Regulatory Files</b></p> <ul style="list-style-type: none"> <li>CCC: Perform QC checks of regulatory documents and reports to be submitted to FDA or other applicable regulatory authorities.</li> <li>Sponsor and/or CCC: Perform periodic scheduled internal reviews of the Site Regulatory Files for each NeuroNEXT study.</li> </ul>               |                          | NN RA 201  |

**Attachment NN QA 802 - A. Document History**

| <b>NeuroNEXT Network Standard Operating Procedure (SOP)</b><br><b>Quality Management</b><br><b>SOP NN QA 802</b> |   |   |                   |                       |
|--|---|---|-------------------|-----------------------|
| <b>Version</b>   | <b>Description of Modification</b>  | <b>Reason or Justification for Modification</b> | <b>Issue Date</b> | <b>Effective Date</b> |
| 1.0  | New   | N/A   | 13Apr2012         | 13May2012             |
| 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             |
|  |   |   |                   |                       |
|  |   |   |                   |                       |