NeuroNEXT Network

Standard Operating Procedure (SOP)

Network Coordinating Center Capacity

Version 3.0

SOP NN GA 108

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: Feb 23, 2024 13:49 CST* 23-Feb-2024
Name and Title: Christopher S. Coffey, PhD (DCC Principal Investigator)
Signature and Date: Merit Cudkowicz *Electronically signed by: Merit Cudkowicz Reason: I approve this document Date: Feb 22, 2024 12:01 CST* 22-Feb-2024
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 12:59 EST* 22-Feb-2024
Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)

NN GA 108
NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR NETWORK COORDINATING CENTER CAPACITY

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

Signature and Date:

Dixie Ecklund

Electronically signed by: Dixie Ecklund
Reason: I approve this document
Date: Feb 24, 2024 17:03 CST

24-Feb-2024

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

Signature and Date:

Electronically signed by: Stacey Grabert
Reason: I approve this document
Date: Feb 22, 2024 13:58 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 09:41 EDT

11-Mar-2024

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

NN GA 108
NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR NETWORK COORDINATING CENTER CAPACITY

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

1. POLICY

The CCC and DCC, in collaboration with NINDS, will evaluate and determine the Network Coordinating Center capacity for evaluating proposals, assisting Protocol Principal Investigators (PPIs) with protocol design/development and grant applications, and implementing funded studies. The capacity for the Coordinating Centers to perform their designated activities will continue to be evaluated on an ongoing basis, and the number, size, and complexity of future studies that are funded under the Network may be adjusted as necessary.

The CCC and DCC will evaluate Network Coordinating Center capacity in relation to the following criteria:

A. Number of proposals in the grant application phase

Applicants may submit proposals to NINDS on a rolling basis. In consultation with the CCC and DCC, the NINDS may evaluate and "batch" concept proposals and release them to the CCC/DCC for development within agreed upon timeframes, as needed.

B. Size and scope of studies being conducted

Studies conducted within the Network may be Phase I gene-based studies or Phase II trials, which can vary quite substantially in size and scope. In some rare disease there may be the potential to conduct a Phase II/III study if the premise is supported by NINDS. Phase I gene-based studies, and Phase II/III studies would potentially be even more complex and require additional resources. For the purposes of determining Network Coordinating Center capacity and resource allocation requirements, proposed studies are classified according to their size and complexity. The following factors must be considered when evaluating size and scope of proposed studies:

- Study Phase (Phase 1, Phase II or Phase II/III)
- Number of subjects screened/enrolled
- Number of participating sites
- Length of study
- Intensity of visit schedule
- Complexity of intervention, including:
  - Drug distribution
  - Route of administration
  - Laboratory requirements
- Complexity related to outcome assessments, including:
  - Number of assessments
  - Requirements for EDC programming
  - Site training/certification
  - Study monitoring
- Complexity related to vendors, including:
  - Number of vendors

- Site training/certification requirements
- Requirements for data downloads
- Impact on study monitoring

- Safety considerations, including:
  - Known risks associated with intervention
  - FDA regulated or IND/IDE exempt
- Extent and complexity of secondary and exploratory outcomes, including:
  - Number of secondary and exploratory outcomes
  - Types of analysis required for these outcomes.

Metrics and other criteria that are used to classify proposed studies as “small” or “large” are presented in Attachment B.

C. Resources required from the CCC and DCC to conduct “small” and “large” studies:

The CCC and DCC infrastructure grants provide salary support for Network activities and some oversight of study-related activities. If a proposed study is characterized as “small” based on the criteria described in Attachment B and falls below a minimal threshold (e.g. traditional Phase II, non-interventional, surveillance /biomarker study with minimal data collection and no requirement for study monitoring), the CCC and DCC staff efforts may be assessed and reduced accordingly. If a proposed study is characterized as “large” based on the criteria described in Attachment B and falls above a maximum threshold for size or scope, the CCC and DCC staff efforts may be assessed and increased accordingly. Not including faculty and leadership effort, effort is allocated toward studies as described in the Attached Network Capacity Worksheet.

D. Studies conducted concurrently within the Network

Funding for study specific Network Coordinating Centers personnel is included in each study grant, as such the Network can sustain multiple concurrent funded studies. However, all pre-award activities (proposal development through receipt of funding award) are funded through infrastructure grants awarded separately to the Network Coordinating Centers.

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.

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

3. ROLES AND RESPONSIBILITIES

The CCC and DCC leadership team will communicate with NINDS leadership on an ongoing basis regarding the pipeline of proposal submissions, applications and funded projects to review network capacity issues that may arise. These communications may also be used by the External Oversight Board (EOB) convened by NINDS to oversee this project.

The EOB and NEC may evaluate the Network capacity proposals presented by the CCC, DCC, and NINDS leadership teams and offer strategies as to align goals between the FOA and the funding capabilities.

4. APPLICABLE REGULATIONS AND GUIDELINES

FDA	FDAAA 801 - Food and Drug Administration Amendments Act of 2007

5. REFERENCES TO OTHER APPLICABLE SOPS

NN GA 105	Vendor Selection and Agreements
NN SS 401	Site Selection and Qualification
NN SS 402	Site Initiation Visits and Site Training
NN SS 403	Routine Monitoring Visits
NN SS 404	Site Performance Monitoring
NN SS 405	Study Closeout Visits
NN PM 502	Clinical Trial Budget Development
NN PM 504	Investigational Site Staff Training
NN PM 505	Investigational Product Management
NN PM 506	Site Invoicing and Payments
NN SM 601	Central Institutional Review Board (CIRB) Reliance Process
NN SM 603	Subject Eligibility and Enrollment
NN BIO 902	Statistical Analysis Plan Development
NN DM 1003	Case Report Form Development

6. ATTACHMENTS AND REFERENCES

NN GA 108 – A	Document History
NN GA 108 – B	Definitions of “Small” and “Large” NeuroNEXT Studies

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
EOB	External Oversight Board
FTE	Full-time Equivalent
GCP	Good Clinical Practice
NEC	NeuroNEXT Executive Committee
NIH	National Institutes of Health
PPI	Protocol Principal Investigator
SOP	Standard Operating Procedure

8. SPECIFIC PROCEDURES

A. Network Capacity Evaluation

#	*Who*	*Task*	*Attachment/ Reference*	*Related SOP*
1.	CCC and DCC	Assess overall Network Coordinating Center capacity and present potential strategies for optimization of Network efficiency to NINDS, the NEC, and the EOB for review.		
2.	CCC and DCC	Provide NEC members with periodic updates on Network Coordinating Center capacity to facilitate new proposal reviews.		
3.	CCC and DCC	Evaluate each new proposal to determine the appropriate study “size” based on criteria defined above and in Attachments B-D. After sample size and overall study design has been determined, communicate the determination to the NEC.		
4.	CCC and DCC PIs	Evaluate the CCC/DCC recommendation of study size based on criteria listed above and in Attachments B-D. Communicate to applicable NeuroNEXT PPIs any requirements for additional funding that are to be included in study-specific grant applications.		
5.	NINDS	May review CCC/DCC proposals for optimization of Network efficiency with regard to Network Coordinating Center capacity.		
6.	NINDS	“Batch” new proposals that are submitted to the Network as needed based upon Network Coordinating Center capacity.		
7.	EOB	May review proposals for optimization of Network efficiency and provide guidance on alignment of Network goals and funding capabilities.		

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

Attachment NN GA 108 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP) Network Coordinating Center Capacity SOP NN GA 108					
Version	**Description of Modification**	**Reason or Justification for Modification**	**Issue Date**	**Effective Date**	**Reviewer(s)**
1.0	New	N/A	21Sep2016	21Oct2016	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.	Updates for v2.0	22Feb2023	08Apr2023	Catherine Gladden
3.0	Minor edits for clarity	Periodic review	01Mar2024	15Apr2024	Preeti Paul

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

Attachment NN GA 108 – B. Definitions of "Small" and "Large" NeuroNEXT Studies

Network Capacity Worksheet

PI Name: [insert PPI name]

Date: [insert date form completed]

The CCC and DCC will evaluate the "network capacity" with relation to:

- Number of proposals in the application phase
- Size and scope of studies being conducted

The following must be considered when evaluating size and scope of studies:

- Phase of study (Phase I gene-based; Phase II; or Phase II/III)
- Number of subjects screened/enrolled
- # of participating sites
- Length of study
- Intensity of visit schedule
- Complexity of intervention, including:
    - Drug distribution
    - Route of administration
    - Laboratory requirements
- Complexity of outcome assessments, including:
    - Number of assessments
    - Requirements for EDC programming
    - Site training/certification
    - Study monitoring
- Complexity of vendors, including:
    - Number of vendors
    - Requirements for data downloads
    - Site training/certification
    - Study monitoring

- Safety considerations, including:
  - Known risks associated with intervention
  - FDA regulated or IND/IDE exempt
- Extent and complexity of secondary and exploratory outcomes, including:
  - Number of secondary and exploratory outcomes
  - Types of analysis required for these outcomes

For the purposes of the Network, we will define “small and “large” studies based on these criteria.

“Small” study				**“Large” study**		
Phase of Study	Phase II			Phase of Study	Phase I or Phase II/III	
Sample Size	<=100			Sample Size	>100	
# of sites	<=15			# of sites	>15	
Length of Study	2 years or less			Length of Study	Greater than 2 years	
Visit schedule	<= 12 visits			Visit schedule	>12 visits	
Complexity of intervention • Route of administration • Drug distribution • Laboratory requirements	Simple			Complexity of intervention • Route of administration • Drug distribution • Laboratory requirements	Complex	
Complexity of outcome assessments • # of assessments	Simple			Complexity of outcome assessments • # of assessments	Complex	•

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

"Small" study				**"Large" study**		
• Training/Cert requirements • Requirement for EDC programming • Monitoring impact				• Training/Cert requirements • Requirement for EDC programming • Monitoring impact		
Vendor Complexity • # of vendors • Training/Cert requirements • Frequency of data downloads • Monitoring impact	Simple			Vendor Complexity • # of vendors • Training/Cert requirements • Frequency of data downloads • Monitoring impact	Complex	•
Safety Considerations • Known risks • FDA regulated or exempt	Minimal risk	•		Safety Considerations • Known risks • FDA regulated or exempt	More than minimal risk	•
Extent of secondary and exploratory outcomes • Number • Type of analysis	Minimal			Extent of secondary and exploratory outcomes • Number • Type of analysis	Extensive	•
Total checked =				Total checked =		

The CCC and DCC pre-award team will make an initial review of criteria which will be confirmed by the CCC and DCC PIs. If a study is evaluated as meeting > 5 of 10 of the criteria within the "small" study category, it will be considered a small study. Alternatively, if it meets ≥ 5 of the 10 criteria within the "large" study category, it will be considered a large study. Additional adjustments may be made to the budget as needed.

- Resources required from the CCC and DCC to conduct “small” and “large” studies:

  The CCC and DCC infrastructure grants provide salary support for network as well as some oversight of study-related activities. If there is a study that is characterized as a “small” study, based on the criteria above, which falls below a minimal threshold (e.g. Phase II, non-interventional, surveillance /biomarker study with minimal data collection and no requirement for study monitoring), the CCC and DCC staff efforts may be assessed and reduced accordingly. If a proposed study is characterized as “large” based on the criteria described in Attachment B and falls above a maximum threshold for size or scope, the CCC and DCC staff efforts may be assessed and increased accordingly. Not including faculty and leadership effort, current funding results in effort allocated towards studies as below:

DCC	Small Study effort	Large Study effort	CCC	Small Study effort	Large Study effort
DCC IT	0.35 FTE	0.5 FTE	CCC Project Manager	0.50 FTE	1.0 FTE
DCC Data Management	0.5 FTE	0.5 FTE	CCC Assistant Project Manager	0.50 FTE	1.0 FTE
DCC Biostat	0.4 FTE	0.5 FTE	CCC Grant Administrator	0.25 FTE	0.25 FTE
DCC Protocol Coordinator/Study Monitor	0.5 FTE	1.0 FTE	CCC Administrative Assistant	0.25 FTE	0.25 FTE
			Quality Assurance	0.25 FTE	0.50 FTE
Total FTE	1.75 FTE	2.5 FTE		1.75 FTE	3.0 FTE

Length of grant and recruitment:

Total participants =
Number of participating sites =
Startup =
Recruitment =
Follow up=
Close out=
Screen failure rate
Length of Participants" active" on the study=

SOP: NN GA 108 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	NETWORK COORDINATING CENTER CAPACITY	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

Study Design and Outcomes

Study Title
Objectives
Primary aim of the trial:
Secondary aims:
Hypothesis:
Design and Outcomes

NN GA 108 Network Coordinating Center Capacity v3.0 clean

Final Audit Report 2024-03-11

Created:	2024-02-22
By:	Tania Leeder (tleeder@mgb.org)
Status:	Signed
Transaction ID:	CBJCHBCAABAAkpItv7pb6v0quibPG6WYFLfFZKMJsTw-
Number of Documents:	1
Document page count:	12
Number of supporting files:	0
Supporting files page count:	0

"NN GA 108 Network Coordinating Center Capacity v3.0 clean" History

Document created by Tania Leeder (tleeder@mgb.org)
2024-02-22 - 5:54:41 PM GMT

Document emailed to christopher-coffey@uiowa.edu for signature
2024-02-22 - 5:56:27 PM GMT

Document emailed to cudkowicz.merit@mgh.harvard.edu for signature
2024-02-22 - 5:56:27 PM GMT

Document emailed to Marianne Chase (mchase@mgh.harvard.edu) for signature
2024-02-22 - 5:56:28 PM GMT

Document emailed to dixie-ecklund@uiowa.edu for signature
2024-02-22 - 5:56:28 PM GMT

Document emailed to Stacey Grabert (SGrabert@mgh.harvard.edu) for signature
2024-02-22 - 5:56:28 PM GMT

Document emailed to ohayonj@ninds.nih.gov for signature
2024-02-22 - 5:56:28 PM GMT

Email viewed by Marianne Chase (mchase@mgh.harvard.edu)
2024-02-22 - 5:57:13 PM GMT

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

Challenge: The user opened the agreement.

2024-02-22 - 5:57:32 PM GMT

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

2024-02-22 - 5:59:21 PM GMT

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

Challenge: The user opened the agreement.

2024-02-22 - 5:59:47 PM GMT

Document e-signed by Marianne Chase (mchase@mgh.harvard.edu)

Signing reason: I approve this document

Signature Date: 2024-02-22 - 5:59:51 PM GMT - Time Source: server

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

Challenge: The user opened the agreement.

2024-02-22 - 6:00:29 PM GMT

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

2024-02-22 - 6:01:05 PM GMT

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

Signing reason: I approve this document

Signature Date: 2024-02-22 - 6:01:07 PM GMT - Time Source: server

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

Challenge: The user opened the agreement.

2024-02-22 - 6:58:11 PM GMT

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

Signing reason: I approve this document

Signature Date: 2024-02-22 - 6:58:20 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 - 7:04:44 PM GMT

Document emailed to ecklundd@uiowa.edu for signature

2024-02-23 - 7:04:45 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 - 7:04:59 PM GMT

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

2024-02-23 - 7:05:00 PM GMT

Email viewed by cscoffey@iowa.uiowa.edu

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

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

Challenge: The user opened the agreement.

2024-02-23 - 7:49:27 PM GMT

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

2024-02-23 - 7:49:44 PM GMT

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

Signing reason: I approve this document

Signature Date: 2024-02-23 - 7:49:46 PM GMT - Time Source: server

Email viewed by ecklundd@uiowa.edu

2024-02-24 - 11:03:18 PM GMT

ecklundd@uiowa.edu authenticated with Adobe Acrobat Sign.

Challenge: The user opened the agreement.

2024-02-24 - 11:03:35 PM GMT

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

2024-02-24 - 11:03:49 PM GMT

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

Signing reason: I approve this document

Signature Date: 2024-02-24 - 11:03:52 PM GMT - Time Source: server

Email viewed by ohayonj@ninds.nih.gov

2024-03-11 - 1:40:55 PM GMT- IP address: 104.47.65.254

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

Challenge: The user opened the agreement.

2024-03-11 - 1:41:04 PM GMT

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

2024-03-11 - 1:41:19 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 - 1:41:21 PM GMT - Time Source: server- IP address: 72.83.187.43

Agreement completed.

2024-03-11 - 1:41:21 PM GMT