

NeuroNEXT Network




Standard Operating Procedure (SOP)

Working with an External Biostatistician

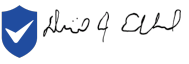
Version 2.0

SOP NN BIO 901

Originators: NeuroNEXT CCC and DCC Personnel

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<p>Name and Title: Christopher S. Coffey, PhD (DCC Principal Investigator)</p>
<p>Signature and Date:</p> <p>DocuSigned by Merit Cudkowicz</p> <p> I approve this document 17-Feb-2023 8:27:15 AM EST</p> <p>17-Feb-2023</p> <p>9F8FE4180E504C6AB0A67B835E80C644</p>
<p>Name and Title: Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)</p>
<p>Signature and Date:</p> <p>DocuSigned by Marianne Chase</p> <p> I approve this document 17-Feb-2023 1:34:52 PM EST</p> <p>17-Feb-2023</p> <p>58FE690F6BCA4F2390E3DA15BCE3F578</p>
<p>Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)</p>

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Name and Title: Stacey Grabert, Pharm.D, MS, (CCC Director of Quality Assurance)

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

NN BIO 901

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR WORKING WITH AN EXTERNAL BIOSTATISTICIAN

1. POLICY

This SOP describes NeuroNEXT Network procedures for engaging and working with an external Biostatistician.

It is expected that the NeuroNEXT Data Coordinating Center (DCC) will perform all biostatistics functions and activities for most NeuroNEXT Network clinical trials, and that the DCC will serve as the primary biostatistical resource for these trials.

For **all** NeuroNEXT clinical trials, the DCC will perform the following:

- all un-blinded statistical work for the trial;
- all statistical program development and implementation; and
- all data management activities.

For certain specific trials, it is possible that the Protocol Principal Investigator (PPI) may make a special request to the National Institute of Neurological Disorders and Stroke (NINDS) to allow a Biostatistician who is external to the DCC to work on biostatistics projects for the trial. The PPI must provide compelling rationale for using a statistician outside of the NeuroNEXT DCC, and the rationale must be pre-approved by NINDS.

If an external Biostatistician is approved by NINDS to work on a NeuroNEXT trial, NINDS has established the following parameters that limit the scope of activities that the external Biostatistician may perform. The external Biostatistician:

- will be blinded to safety data and interim analysis results during the course of the trial;
- may only receive raw blinded data or datasets during the course of the trial if and when permitted or required by NINDS and the DCC PI;
- may, for certain trials, be included as a blinded participant on the Protocol Steering Committee (PSC) or other relevant NeuroNEXT committees and may serve as a statistical advisor to these committees;
- may participate in the development of the Statistical Analysis Plan, in collaboration with DCC Biostatisticians;
- may take a lead role in the final study analysis in collaboration with DCC Biostatisticians (if agreed upon by NINDS and the DCC).

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 DCC within the context of their oversight and advisory roles for the NeuroNEXT Network, and to all NeuroNEXT investigators, staff, subcontractors, External Biostatisticians (if applicable), 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 NINDS is responsible for the following activities relevant to the use of external Biostatisticians for a NeuroNEXT trial:

- reviewing a request by a PPI for the use of an external Biostatistician;
- assessing the need for an external Biostatistician for the trial;
- establishing conditions for the use of an external Biostatistician; and
- communicating pre-approval of a successful request to the PPI and the DCC.

If pre-approved by NINDS to serve as a blinded Biostatistician for a NeuroNEXT clinical trial, and in collaboration with DCC Biostatisticians, an external Biostatistician may participate in the development of the Statistical Analysis Plan (SAP) and in the final study analysis. External Biostatisticians are responsible for collaborating with DCC Biostatisticians according to the procedures described in this SOP, and are not permitted to engage in any statistical work for a trial without written pre-approval by NINDS.

4. APPLICABLE REGULATIONS AND GUIDELINES

ICH E6, 4.5	Compliance with Protocol
ICH E6, 4.9	Records and Reports
ICH E6, 5.1	Quality Assurance and Quality Control
ICH E6, 5.4	Trial Design
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.23	Multicenter Trials
ICH E6, 6.0	Clinical Trial Protocol and Protocol Amendment(s)
ICH E8	General Considerations for Clinical Trials (December 1997)
ICH E9	Statistical Principles for Clinical Trials (September 1998)
ICH E10	Choice of Control Group and Related Issues in Clinical Trials (May 2001)

5. REFERENCES TO OTHER APPLICABLE SOPS

NN PM 501	Communication
NN BIO 902	Statistical Analysis Plan Development
NN BIO 906	Report Writing

6. ATTACHMENTS AND REFERENCES

NN BIO 901 - 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
DCC	Data Coordinating Center at The University of Iowa
External Biostatistician	A Biostatistician who is not a member of the DCC Biostatistics Team. An External Biostatistician may act as a Study Biostatistician for a study.

Independent Biostatisticians	Unblinded DCC Biostatisticians for a NeuroNEXT trial. Typically, at least two Independent Biostatisticians will be assigned to each study.
NINDS	National Institute of Neurological Disorders and Stroke
Protocol Principal Investigator (PPI)	Principal Investigator of a NeuroNEXT protocol
PSC	Protocol Steering Committee
SAP	Statistical Analysis Plan
Study Biostatistician	Blinded Biostatistician for a study.

8. SPECIFIC PROCEDURES

A. Requesting the Use of an External Biostatistician

#	Who	Task	Attachment/Reference	Related SOP
1.	PPI	Review the criteria for the use of an external Biostatistician.		
2.	PPI	Complete the NeuroNEXT Clinical Study Concept Form indicating the use and justification of an external Biostatistician and submit to the appropriate NINDS NeuroNEXT Program Director for approval.		

B. Establishing Conditions for the Use of an External Biostatistician

#	Who	Task	Attachment/Reference	Related SOP
1.	NINDS	Review the request from the PPI.		
2.	NINDS	Assess the need for an external Biostatistician.		
3.	NINDS and DCC	Establish conditions for the use of an external Biostatistician.		
4.	NINDS	Communicate pre-approval of a successful request to the PPI and the DCC.		NN PM 501

C. Collaboration between the DCC and an External Biostatistician

#	Who	Task	Attachment/Reference	Related SOP
1.	DCC Biostatisticians	If approved by NINDS and DCC Leadership, collaborate with an external Biostatistician in the design of the study, preparation for ESC submission, and preparation of the grant application.		
2.	DCC Biostatisticians	If directed to do so by NINDS and DCC Leadership, collaborate with a blinded external Biostatistician on the SAP, the final study analysis and Report, and manuscripts for publication.		

#	Who	Task	Attachment/ Reference	Related SOP
3.	DCC Biostatisticians	Follow NINDS guidelines for collaborating with an external Biostatistician in the NeuroNEXT Network with regard to providing raw blinded data or datasets to the external Biostatistician during the course of the trial (refer to the Policy section of this SOP).		
4.	External Biostatistician	Collaborate with the DCC in the development of the SAP.		
5.	External Biostatistician	If requested to do so by NINDS and the DCC, participate on the PSC or other applicable committees and serve as a statistical resource for members of these committees.		
6.	External Biostatistician	Collaborate with the DCC Biostatisticians for the final study analysis and Report.		
7.	External Biostatistician	Participate in the development of manuscripts that describe the final study results.		

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Marianne Chase
 MCHASE@mgh.harvard.edu
 Sr Director, Clinical Trial Operations
 Insight OBO The Massachusetts General Hospital
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 cudkowicz.merit@mgh.harvard.edu
 Chief of Neurology
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