

# NeuroNEXT Network

## Standard Operating Procedure (SOP)




### Site Initiation Visits and Site Training

Version 3.0

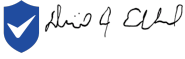
SOP NN SS 402

Originators: NeuroNEXT CCC and DCC Personnel

Reviewed and Approved by:

<p><b>Signature and Date:</b></p> <p>DocuSigned by Christopher Coffey</p> <p>   I approve this document 14-Feb-2023   12:33:32 PM PST</p> <p>14-Feb-2023</p> <p>C68AC8DD80334CF982AED1200765F147</p>
<p><b>Name and Title:</b> Christopher S. Coffey, PhD (DCC Principal Investigator)</p>
<p><b>Signature and Date:</b></p> <p>DocuSigned by Merit Cudkowicz</p> <p>   I approve this document 14-Feb-2023   11:54:02 AM EST</p> <p>14-Feb-2023</p> <p>9F8FE4180E504C6AB0A67B835E80C644</p>
<p><b>Name and Title:</b> Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)</p>
<p><b>Signature and Date:</b></p> <p>DocuSigned by Marianne Chase</p> <p>   I approve this document 14-Feb-2023   9:48:09 AM EST</p> <p>14-Feb-2023</p> <p>58FE690F6BCA4F2390E3DA15BCE3F578</p>
<p><b>Name and Title:</b> Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)</p>

**Signature and Date:**

DocuSigned by DIXIE ECKLUND  
 | I approve this document  
15-Feb-2023 | 10:50:21 AM PST  
7006AF622EFC40B6A067A08EC02591B6

15-Feb-2023

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

**Signature and Date:**

DocuSigned by Stacey Grabert  
 | I approve this document  
22-Feb-2023 | 11:27:01 AM EST  
60CC52B0747A44E6B2208D8D880698C0

22-Feb-2023

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

**Signature and Date:**

DocuSigned by Joan Ohayon  
 | I approve this document  
14-Feb-2023 | 9:34:39 AM PST  
72C6AAFD8CC4485582ACA0700072901A

14-Feb-2023

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

## **NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR SITE INITIATION VISITS AND SITE TRAINING**

### **1. POLICY**

The activities associated with the Initiation Visit for a NeuroNEXT Network study may be conducted at a kick-off meeting, during a visit by Clinical Coordinating Center (CCC) and/or Data Coordinating Center (DCC) personnel to the Clinical Study Site (CSS), and/or via teleconference or web-conferencing. During the Initiation Visit, the objectives and the methodology of the clinical study are reviewed with the site investigator and staff, and appropriate training of the site's research team is conducted in compliance with International Conference on Harmonisation/Good Clinical Practice guidelines.

The objectives of the Initiation Visit are to:

- verify that the site has completed study preparation procedures;
- verify that all regulatory documents are in place;
- verify that the site is eligible to receive the investigational product, if applicable;
- review the protocol, case report forms (CRFs) and other worksheets;
- review all regulatory requirements;
- provide the plan for study monitoring;
- provide the site with Study Team contact information;
- confirm the PPI/Sponsor's expectations for the conduct of the study.

An initiation visit checklist (if applicable), meeting agenda, or similar document that summarizes all the topics that must be reviewed with the investigator and his/her staff may be developed to assist during the Initiation Visit.

Before subjects may be enrolled in a study, relevant Investigators, Coordinators, and other study staff members (where necessary) must participate in training regarding the conduct of the trial. The CSS will be made aware of any training and certifications that must be completed before personnel will be permitted to enroll subjects.

If a CSS adds a new staff member at any time during the trial, the new staff member will be trained regarding the conduct of the trial, and will be required to complete all necessary training and certifications required for the trial, prior to that person's direct involvement in the trial.

### **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.

### **3. ROLES AND RESPONSIBILITIES**

The NeuroNEXT CCC and DCC are responsible for the following activities:

- Ensuring that all participating investigators understand and accept the obligations incurred in undertaking a clinical study
- Training the investigator and all other key site personnel in the use of the investigational product, if applicable, and the conduct of the clinical protocol
- Conducting the Initiation Visit and site training at the large-group Investigators Meeting, at clinical site(s), or via teleconference/webinar.

The CCC is responsible for providing the DCC with information about the site's study preparation, training activities and regulatory documents.

The responsibility to conduct any or all of these activities may be delegated at the discretion of the PPI/Sponsor to the NeuroNEXT CCC or DCC or to subcontractors of either. Those individuals and entities also take on responsibility for meeting regulatory requirements on behalf of the PPI/Sponsor, but the PPI/Sponsor has the ultimate responsibility and must therefore supervise those delegated activities effectively.

#### **4. APPLICABLE REGULATIONS AND GUIDELINES**

21 CFR 312.50	Responsibilities of Sponsors
ICH E6, 2.0	The Principles of ICH GCP
ICH E6, 4.5	Compliance with Protocol
ICH E6, 5.3	Medical Expertise
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.7	Allocation of Responsibilities
ICH E6, 5.8	Compensation to Subjects and Investigators
ICH E6, 5.15	Record Access
ICH E6, 5.23	Multicenter Trials

#### **5. REFERENCES TO OTHER APPLICABLE SOPS**

NN RA 203	Site Regulatory File Maintenance
NN PM 501	Communication
NN PM 504	Investigational Site Staff Training
NN PM 505	Investigational Product Management
NN SM 602	Single Institutional Review Board Reporting
NN DM 1005	Data Collection and Data Handling

#### **6. ATTACHMENTS AND REFERENCES**

NN SS 402 – 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
CRF	Case Report Form
CSS	Clinical Study Site
DCC	Data Coordinating Center at The University of Iowa
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practices
ICH	International Council for Harmonisation
PPI	Protocol Principal Investigator
SIRB	Single Institutional Review Board

## 8. SPECIFIC PROCEDURES

### A. Initiation Visit Preparation

#	Who	Task	Attachment/ Reference	Related SOP
1.	CCC Project Manager/DCC Lead Coordinator	Schedule an Initiation Visit, allowing sufficient time for all activities, depending on the protocol. Review purpose of visit if necessary.		NN PM 501
2.	CCC Project Manager /DCC Lead Coordinator	Confirm the status of the study regarding SIRB review and approval, status of other regulatory reviews, and if applicable, FDA status.		NN SM 602
3.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	Prior to the visit, prepare by reviewing the protocol, CRFs and any other relevant documents. If needed, prepare slide presentations.		

### B. Investigative Site Training

#	Who	Task	Attachment/ Reference	Related SOP
1.	CSS Personnel	Participate in training regarding the conduct of the trial, and complete any required certifications before enrolling any study subjects.		
2.	CCC Project Manager and DCC Lead Coordinator	During the Site Initiation Visit meeting, ascertain the investigator's understanding of all elements of trial conduct through discussions and questions.		
3.	CCC Project Manager and DCC Lead Coordinator	Review the required elements of the investigator's study file and the importance of maintaining accurate and up-to-date records		NN RA 203
4.	CCC Project Manager and DCC Lead Coordinator	Confirm existence of all applicable and required documentation in the investigator's study file. <sup>1</sup>		NN RA 203
5.	CCC Project Manager and DCC Lead Coordinator	Review the clinical protocol, informed consent form and CRFs.		
6.	CCC Project Manager	Review procedures for obtaining and documenting informed consent, including required signatures and disposition of copies.		
7.	CCC Project Manager and DCC Lead Coordinator	Reinforce the need for strict adherence to the protocol.		
8.	DCC Lead Coordinator, DCC Monitor	Review instructions for completion of CRFs, including corrections and queries. Emphasize the need for timely and accurate completion of CRFs.		NN DM 1005

#	Who	Task	Attachment/ Reference	Related SOP
9.	DCC Lead Coordinator, DCC Monitor	Review the use of relevant logs and forms with all site personnel.		
10.	CCC Project Manager and DCC Lead Coordinator, DCC Monitor	If applicable, instruct relevant site personnel (including research pharmacist) on the pharmacologic aspects of the investigational product.		NN PM 505
11.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	If applicable, review investigational product allocation and randomization, as defined in the protocol.		NN PM 505
12.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	If applicable, review procedures for product accountability, storage, dispensing, reconciliation, as well as discrepancy investigation requirements and inventory recordkeeping.		
13.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	If applicable, verify receipt and records pertaining to investigational product already on site.		NN PM 505
14.	DCC Lead Coordinator and DCC Monitor	If applicable, confirm physical requirements (e.g., product inventory and storage, document and record storage).		NN PM 505
15.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	Review protocol requirements regarding the recognition, handling, recording and reporting of adverse events, including regulations and reporting timeframes.		NN SM 602
16.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	Review laboratory assessments and reporting procedures (with laboratory personnel if appropriate). Specifically address unusual or critical requirements.		
17.	CCC Project Manager and DCC Lead Coordinator	Confirm that enrollment of the first subject may not occur until all Initiation Visit procedures and regulatory requirements have been completed.		

Note:

<sup>1</sup>For example, protocol and Investigator Statement, SIRB-approved informed consent form, SIRB approval letter, and other regulatory authority approvals.

### C. Documenting the Initiation Visit

#	Who	Task	Attachment/ Reference	Related SOP
1.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	Record date(s) of visit(s) by monitors and other designees on a site visit log, if applicable		
2.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	Complete an Initiation Visit Checklist during the visit, if applicable.		
3.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	Review the completed checklist (if applicable) or other documentation of the Initiation Visit with the Sponsor, if applicable.		
4.	CCC Project Manager, DCC Lead Coordinator, DCC Monitor	File the checklist or other documentation of the Initiation Visit in the appropriate section of the Trial Master File.		NN RA 203
5.	DCC Lead Coordinator, DCC Monitor	Send a post-visit letter summarizing the visit and listing pending items.		


**Certificate Of Completion**

Envelope Id: 1462D6899C2A40BBAE6B5EEF348F3884	Status: Completed
Subject: Complete with DocuSign: NN SS 402 Site Initiation Visits and Site Training v3.0.docx	
Source Envelope:	
Document Pages: 7	Signatures: 6
Certificate Pages: 6	Initials: 0
AutoNav: Enabled	Envelope Originator: Tania Leeder TLEEDER@PARTNERS.ORG
Envelopeld Stamping: Disabled	IP Address: 73.123.188.5
Time Zone: (UTC-05:00) Eastern Time (US & Canada)	

**Record Tracking**

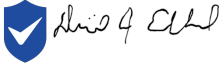
Status: Original 2/14/2023 9:45:05 AM	Holder: Tania Leeder TLEEDER@PARTNERS.ORG	Location: DocuSign
--	--	--------------------

**Signer Events**

Signer Events	Signature	Timestamp
Christopher Coffey christopher-coffey@uiowa.edu Security Level: Email, Account Authentication (Required)	  Signature Adoption: Pre-selected Style Signature ID: C68AC8DD-8033-4CF9-82AE-D1200765F147 Using IP Address: 128.255.113.139  With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:47:01 AM Viewed: 2/14/2023 3:33:15 PM Signed: 2/14/2023 3:33:35 PM

**Electronic Record and Signature Disclosure:**  
Accepted: 2/14/2023 3:33:15 PM  
ID: 9202c731-a09e-40ed-8ff2-ba31a402020e

DIXIE ECKLUND  
dixie-ecklund@uiowa.edu  
Security Level: Email, Account Authentication (Required), Login with SSO

DocuSigned by DIXIE ECKLUND  
 | I approve this document  
15-Feb-2023 | 10:50:21 AM PST  
7006AF622EFC40B6A067A08EC02591B6

Sent: 2/14/2023 9:47:02 AM  
Viewed: 2/15/2023 1:48:43 PM  
Signed: 2/15/2023 1:50:27 PM

Signature Adoption: Drawn on Device  
Signature ID:  
7006AF62-2EFC-40B6-A067-A08EC02591B6  
Using IP Address: 128.255.112.230

With Signing Authentication via DocuSign password  
With Signing Reasons (on each tab):  
I approve this document

**Electronic Record and Signature Disclosure:**  
Accepted: 2/15/2023 1:48:43 PM  
ID: 28dbe007-0f86-48ea-9876-edc61c01a441



**Signer Events****Signature****Timestamp**

Joan Ohayon  
 ohayonj@ninds.nih.gov  
 Security Level: Email, Account Authentication  
 (Required)

*Joan Ohayon*

Sent: 2/14/2023 9:47:04 AM  
 Viewed: 2/14/2023 12:34:13 PM  
 Signed: 2/14/2023 12:34:54 PM

Signature Adoption: Pre-selected Style  
 Signature ID:  
 72C6AAFD-8CC4-4855-82AC-A0700072901A  
 Using IP Address: 156.40.137.188

With Signing Authentication via DocuSign password  
 With Signing Reasons (on each tab):  
 I approve this document

**Electronic Record and Signature Disclosure:**  
 Accepted: 2/13/2023 2:03:22 PM  
 ID: 385a0a53-0f0c-4395-88f6-d5700c36e050

Marianne Chase  
 MCHASE@mgh.harvard.edu  
 Sr Director, Clinical Trial Operations  
 Insight OBO The Massachusetts General Hospital  
 Security Level: Email, Account Authentication  
 (Required), Logged in

*Marianne Chase*


Sent: 2/14/2023 9:47:02 AM  
 Viewed: 2/14/2023 9:47:40 AM  
 Signed: 2/14/2023 9:48:13 AM

Signature Adoption: Pre-selected Style  
 Signature ID:  
 58FE690F-6BCA-4F23-90E3-DA15BCE3F578  
 Using IP Address: 73.114.253.109

With Signing Authentication via DocuSign password  
 With Signing Reasons (on each tab):  
 I approve this document

**Electronic Record and Signature Disclosure:**  
 Not Offered via DocuSign

Merit Cudkowicz  
 cudkowicz.merit@mgh.harvard.edu  
 Chief of Neurology  
 Security Level: Email, Account Authentication  
 (Required)


DocuSigned by Merit Cudkowicz  
  
 I approve this document  
 14-Feb-2023 | 11:54:02 AM EST  
 9F8FE4180E504C6AB0A67B835E80C644

Sent: 2/14/2023 9:47:03 AM  
 Viewed: 2/14/2023 11:53:48 AM  
 Signed: 2/14/2023 11:54:04 AM

Signature Adoption: Pre-selected Style  
 Signature ID:  
 9F8FE418-0E50-4C6A-B0A6-7B835E80C644  
 Using IP Address: 132.183.13.4

With Signing Authentication via DocuSign password  
 With Signing Reasons (on each tab):  
 I approve this document

**Electronic Record and Signature Disclosure:**  
 Accepted: 2/14/2023 11:53:48 AM  
 ID: 2733fd5b-81b2-4c0f-99f0-179283615ebc

Signer Events	Signature	Timestamp
Stacey Grabert sgrabert@mgh.harvard.edu Director QA Stacey Grabert Security Level: Email, Account Authentication (Required)	  Signature Adoption: Pre-selected Style Signature ID: 60CC52B0-747A-44E6-B220-8D8D880698C0 Using IP Address: 132.183.56.49  With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:47:03 AM Viewed: 2/22/2023 11:26:51 AM Signed: 2/22/2023 11:27:04 AM
<b>Electronic Record and Signature Disclosure:</b> Accepted: 7/20/2020 8:50:14 AM ID: 5ebadf74-e399-40fd-be82-9c7ca902061b		
In Person Signer Events	Signature	Timestamp
Editor Delivery Events	Status	Timestamp
Agent Delivery Events	Status	Timestamp
Intermediary Delivery Events	Status	Timestamp
Certified Delivery Events	Status	Timestamp
Carbon Copy Events	Status	Timestamp
Witness Events	Signature	Timestamp
Notary Events	Signature	Timestamp
Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	2/14/2023 9:47:04 AM
Certified Delivered	Security Checked	2/22/2023 11:26:51 AM
Signing Complete	Security Checked	2/22/2023 11:27:04 AM
Completed	Security Checked	2/22/2023 11:27:04 AM
Payment Events	Status	Timestamps
Electronic Record and Signature Disclosure		

## **ELECTRONIC RECORD AND SIGNATURE DISCLOSURE**

From time to time, Insight OBO The Massachusetts General Hospital (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

### **Getting paper copies**

At any time, you may request from us a paper copy of any record provided or made available electronically to you by us. You will have the ability to download and print documents we send to you through the DocuSign system during and immediately after the signing session and, if you elect to create a DocuSign account, you may access the documents for a limited period of time (usually 30 days) after such documents are first sent to you. After such time, if you wish for us to send you paper copies of any such documents from our office to you, you will be charged a \$0.00 per-page fee. You may request delivery of such paper copies from us by following the procedure described below.

### **Withdrawing your consent**

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

### **Consequences of changing your mind**

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

### **All notices and disclosures will be sent to you electronically**

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

### **How to contact Insight OBO The Massachusetts General Hospital:**

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:

To contact us by email send messages to: [jhenrique@mgh.harvard.edu](mailto:jhenrique@mgh.harvard.edu)

### **To advise Insight OBO The Massachusetts General Hospital of your new email address**

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at [jhenrique@mgh.harvard.edu](mailto:jhenrique@mgh.harvard.edu) and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

If you created a DocuSign account, you may update it with your new email address through your account preferences.

### **To request paper copies from Insight OBO The Massachusetts General Hospital**

To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to [jhenrique@mgh.harvard.edu](mailto:jhenrique@mgh.harvard.edu) and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

### **To withdraw your consent with Insight OBO The Massachusetts General Hospital**

To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

- i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;
- ii. send us an email to [jhenrique@mgh.harvard.edu](mailto:jhenrique@mgh.harvard.edu) and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

### **Required hardware and software**

The minimum system requirements for using the DocuSign system may change over time. The current system requirements are found here: <https://support.docusign.com/guides/signer-guide-signing-system-requirements>.

### **Acknowledging your access and consent to receive and sign documents electronically**

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please confirm that you have read this ERSD, and (i) that you are able to print on paper or electronically save this ERSD for your future reference and access; or (ii) that you are able to email this ERSD to an email address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format as described herein, then select the check-box next to ‘I agree to use electronic records and signatures’ before clicking ‘CONTINUE’ within the DocuSign system.

By selecting the check-box next to ‘I agree to use electronic records and signatures’, you confirm that:

- You can access and read this Electronic Record and Signature Disclosure; and
- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify Insight OBO The Massachusetts General Hospital as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by Insight OBO The Massachusetts General Hospital during the course of your relationship with Insight OBO The Massachusetts General Hospital.