NeuroNEXT Network

Standard Operating Procedure (SOP)

Case Report Form Development

Version 3.0

SOP NN DM 1003

Originators: NeuroNEXT CCC and DCC Personnel

Reviewed and Approved by:

Signature and Date: DocuSigned by Christopher Coffey Christopher Coffey | I approve this document 17-Feb-2023 | 3:49:15 PM PST C68AC8DD80334CF982AED1200765F147 17-Feb-2023
Name and Title: Christopher S. Coffey, PhD (DCC Principal Investigator)
Signature and Date: DocuSigned by Merit Cudkowicz Merit Cudkowicz | I approve this document 17-Feb-2023 | 9:29:50 AM EST 9F8FE4180E504C6AB0A67B835E80C644 17-Feb-2023
Name and Title: Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)
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17-Feb-2023 | 4:21:02 PM PST

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22-Feb-2023 | 11:07:55 AM EST

60CC52B0747A44E6B2208D8D880698C0

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NN DM 1003

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR CASE REPORT FORM DEVELOPMENT

1. POLICY

Case Report Forms (CRFs) are designed to capture all clinically-relevant data that are collected for an approved NeuroNEXT protocol (e.g. subject demographic data, results of physical, radiological and laboratory examinations, and analytical and clinical data).

Depending on the requirements of the protocol, a CRF development team consisting of the Protocol Principal Investigator (PPI) and representatives from the NeuroNEXT Clinical Coordinating Center (CCC) and the Data Coordinating Center (DCC) may be formed to design and develop CRFs for the protocol using standardized CRFs and common data elements (CDEs) when possible. After all CRFs for a protocol are finalized, they will be signed by the final reviewers, which may include the PPI, the DCC Data Management Lead, and other applicable DCC and CCC personnel.

A CRF may originate from the DCC, or the DCC may support CRF development and management by a third party. All CRFs are prepared using version control measures.

After the CRFs have been finalized, the DCC will begin development of the electronic CRFs (eCRFs) and the Electronic Data Capture system (EDC). The DCC will work with the PPIs to ensure that they are aware that delays in CRF development may result in delays in development of the EDC system and possible escalation of the costs associated with development and implementation. To limit the costs associated with development of the EDC, it is the policy of the DCC to limit changes to CRFs once the development process has begun.

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 DCC is responsible for supervising the implementation of this procedure. The DCC may delegate the responsibility for designing a CRF to a designated qualified individual.

The DCC is responsible for preparing the initial drafts of case report forms, in conjunction with the PPI and the Study Team.

The PPI, the DCC Data Management Lead, and other applicable CCC and DCC personnel are responsible for signature-approving all CRF templates.

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

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.30	Protocol Amendments
ICH E6 2.2, 2.4 – 2.6	The Principles of ICH GCP
ICH E6, 2.10, 2.11	The Principles of ICH GCP
ICH E6, 5.5	Trial Management, Data Handling, and Recordkeeping
ICH E6, 5.23	Multicenter Trials
ICH E6, 6.0	Clinical Trial Protocol and Protocol Amendment(s)

ICH E8	General Considerations for Clinical Trials (2022)

5. REFERENCES TO OTHER APPLICABLE SOPS

NN GA 103	Document Development and Change Control
NN RA 204	Informed Consent Form Preparation
NN CS 702	Application Development and Validation
NN DM 1001	Clinical Data Management
NN DM 1002	Data Management Plan Development
NN DM 1004	Specifications Development, Testing Plans, and Validation Documentation
NN DM 1005	Data Collection and Data Handling

6. ATTACHMENTS AND REFERENCES

NN DM 1003 – 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
CDE	Common Data Elements
Clinical Study Site (CSS)	Clinical site that conducts research for a NeuroNEXT protocol within or outside the Network
DCC	Data Coordinating Center at The University of Iowa
DM	Data Management Team at the DCC
IT	Information Technology Team at the DCC
Protocol Principal Investigator (PPI)	Principal Investigator of a NeuroNEXT protocol

8. SPECIFIC PROCEDURES

A. Case Report Form Development

#	*Who*	*Task*	*Attachment/ Reference*	*Related SOP*
1.	PPI, CCC, DCC	When applicable, convene a CRF Development team, consisting of the PPI and appropriate representatives from the CCC and DCC.		
2.	CRF Development Team	Review the protocol and identify specific data points that will be required for the planned statistical analyses. When possible, NINDS Common Data Elements (CDEs) are to be utilized within and across studies. Refer to the Data Management Plan, as appropriate.		NN DM 1001
3.	CRF Development Team	Determine the appropriate CRF format (paper-based, computer entry, electronic diary, or Internet-based).		

#	Who	Task	Attachment/ Reference	Related SOP
4.	DCC DM	Create draft CRFs, using standardized CRFs when possible.		
5.	DCC DM	Circulate the draft CRFs among the CRF Development team and other appropriate reviewers for review of content and format. All relevant parties should conduct a careful review to ensure that the proposed CRFs capture all necessary subject and protocol data.		NN GA 103 NN DM 1004
6.	DCC DM	Revise CRF drafts as needed.		NN GA 103
7.	CRF Development Team	Review the CRF to ensure that the CRF language is clear, consistent, and captures all desired data points, especially primary endpoints.		
8.	CRF Development Team	During the final review process, make and document minor revisions to the CRFs as directed by the final reviewers, including the Sponsor and/or CCC, as appropriate.		NN GA 103
9.	DCC DM	When final revisions are completed, forward all CRFs to the NINDS CDE team to review for compliance with CDE requirements.		
10.	DCC DM	Retain copies (in PDF format) of all CRFs that have been implemented for the protocol's data collection system.		NN GA 103
11.	DCC DM	Secure the signatures and approval dates of CRF Development team final reviewers in appropriate boxes on the Change Control Form or on a signature approval form.		NN GA 103
12.	DCC DM	When protocol amendments are finalized, revise CRFs, if applicable, to reflect changes to the protocol.		
13.	CCC or DCC DM	Implement, review, and approve any subsequent changes to the CRF as described in NN GA 103. Document all CRF revisions that occur after the initial finalization.		NN GA 103
14.	DCC DM	For all amendments, secure the signatures and approval dates of final reviewers in appropriate boxes on the Change Control Form or a signature approval form.		NN GA 103

B. Case Report Form Version Control

#	Who	Task	Attachment/ Reference	Related SOP
1.	DCC DM	Prior to finalization of the initial CRFs for a study, the CRF versions are documented by a version date (date change was made) and a version number. Preliminary version numbers should be restricted to values that are less than 1.0 (e.g. .10, .20, etc.).		NN GA 103 NN DM 1001
2.	DCC DM	Designate the final, approved versions of all initial CRFs for a study as version 1.0. The version date for all initial		NN GA 103

#	*Who*	*Task*	*Attachment/ Reference*	*Related SOP*
		CRFs for a study is the date that the CRFs were finalized and approved.		
3.	DCC DM	Minor changes do NOT require a signature approval. A minor change refers to any change to a CRF that does NOT require a modification to the database and that does not change validation programming (e.g. re-wording a question, correcting spelling errors, changing formats or fonts).		NN GA 103
4.	DCC DM	For a minor change, increment the CRF version number to a succeeding numerical value that does not change the current whole number (e.g. 1.0 to 1.1).		NN GA 103
5.	Study Team	Major changes to an approved CRF require a signature approval. A major change is any change to a CRF that results in changes to the database (e.g. adding a question that creates a field in the database, deleting a question that removes a field in the database) and/or changes to the validation programming.		NN GA 103
6.	DCC DM	For a major change to a CRF, increment the new version number to the next whole number (e.g. 1.2 to 2.0).		NN GA 103
7.	DCC DM	Create and maintain a change table to continually track changes to version numbers and version dates, and to specify reason(s) for any change(s) to CRFs.		NN GA 103
8.	DCC DM	Review changes with the Study Team.		
9.	DCC DM	Send a signature approval form to the appropriate signatories for approval of requested major changes.		NN GA 103
10.	DCC IT	The version number for CRFs (paper templates) does NOT necessarily match the eCRF version number. The eCRF version number is determined independently by the DCC IT Developers.		NN CS 702

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Status: Completed
Subject: Complete with DocuSign: NN DM 1003 Case Report Form Development v3.0.docx
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Signatures: 6
Envelope Originator:
Certificate Pages: 6
Initials: 0
Tania Leeder
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TLEEDER@PARTNERS.ORG
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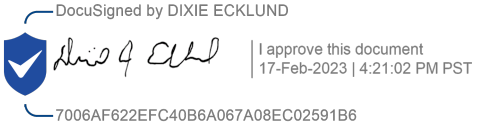
Electronic Record and Signature Disclosure: Accepted: 2/17/2023 6:49:04 PM ID: bf7c5a90-2c5c-467c-a20c-a568183fbfcc		
DIXIE ECKLUND dixie-ecklund@uiowa.edu Security Level: Email, Account Authentication (Required), Login with SSO	 Signature Adoption: Drawn on Device Signature ID: 7006AF62-2EFC-40B6-A067-A08EC02591B6 Using IP Address: 128.255.112.230 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/17/2023 8:33:05 AM Viewed: 2/17/2023 7:20:28 PM Signed: 2/17/2023 7:21:04 PM
Electronic Record and Signature Disclosure: Accepted: 2/17/2023 7:20:28 PM ID: d1ec393e-a45a-482c-85f6-789fd0120186		

Signer Events	Signature	Timestamp
Joan Ohayon ohayonj@ninds.nih.gov Security Level: Email, Account Authentication (Required)	 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	Sent: 2/17/2023 8:33:06 AM Resent: 2/21/2023 8:25:04 AM Viewed: 2/21/2023 9:35:00 AM Signed: 2/21/2023 9:35:17 AM
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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	 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	Sent: 2/17/2023 8:33:05 AM Viewed: 2/17/2023 1:24:45 PM Signed: 2/17/2023 1:25:25 PM
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Merit Cudkowicz cudkowicz.merit@mgh.harvard.edu Chief of Neurology Security Level: Email, Account Authentication (Required), Logged in	 DocuSigned by Merit Cudkowicz I approve this document 17-Feb-2023 | 9:29:50 AM EST 9F8FE4180E504C6AB0A67B835E80C644 Signature Adoption: Pre-selected Style Signature ID: 9F8FE418-0E50-4C6A-B0A6-7B835E80C644 Using IP Address: 68.239.56.73 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/17/2023 8:33:06 AM Viewed: 2/17/2023 9:29:41 AM Signed: 2/17/2023 9:29:53 AM
Electronic Record and Signature Disclosure: Accepted: 2/17/2023 9:29:41 AM ID: 705dee74-fe1b-45c9-b68b-8850760aa3d9		

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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: 2/17/2023 8:33:06 AM Resent: 2/21/2023 8:25:05 AM Viewed: 2/22/2023 11:07:39 AM Signed: 2/22/2023 11:07:58 AM
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Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	2/17/2023 8:33:07 AM
Certified Delivered	Security Checked	2/22/2023 11:07:39 AM
Signing Complete	Security Checked	2/22/2023 11:07:58 AM
Completed	Security Checked	2/22/2023 11:07:58 AM

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