NeuroNEXT Network

Standard Operating Procedure (SOP)

Investigator's Brochure Development and Approval

Version 4.0

SOP NN RA 207

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: Mar 8. 2024 08:12 CST* 08-Mar-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 12:20 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 14:57 EST* 22-Feb-2024
Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR INVESTIGATOR'S BROCHURE DEVELOPMENT AND APPROVAL

SOP: NN RA 207 Version No.: 4.0 Issue Date; 01Mar2024 Effective Date: 15Apr2024	INVESTIGATOR'S BROCHURE DEVELOPMENT AND APPROVAL	Supersedes Document : Version 3.0 Effective Date : 08Apr2023

Signature and Date:

Dixie Ecklund

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24-Feb-2024

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

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Date: Feb 22, 2024 13:53 EST

22-Feb-2024

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Joan Ohayon

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Date: Mar 11, 2024 11:19 EDT

11-Mar-2024

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

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1. POLICY

It is the policy of the NeuroNEXT Network that each multi-center study that is conducted within the Network and that involves an Investigational Product (IP) will have an Investigator's Brochure (IB) or equivalent IP information documentation. The purpose of the IB is to provide Clinical Study Site (CSS) investigators with information about the IP that includes, but is not limited to, the following:

- clinical and nonclinical data relevant to the use of the IP in human participants;
- a description of possible risks and adverse drug reactions to be anticipated;
- precautions or special monitoring to be completed as part of the study;
- information to facilitate understanding of the rationale for, and compliance with, protocol-specific instructions (e.g. dose, frequency and method of administration, safety monitoring procedures); and
- appropriate information on the clinical management of study participants during participation in the study.

The Protocol Principal Investigator (PPI)/ Sponsor is responsible for creating and updating the IB, and for ensuring that the IB meets, at the least, the minimum requirements for Good Clinical Practices (GCP) as set forth in the 2016 Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2).

The IB may include the following sections:

1. Signature Page
2. Table of Contents
3. Summary
4. Introduction
5. Physical, Chemical, and Pharmaceutical Properties and Formulation
6. Nonclinical Studies
    a. Nonclinical Pharmacology
    b. Pharmacokinetics and Product Metabolism in Animals
    c. Toxicology
7. Effects in Humans
    a. Pharmacokinetics and Product Metabolism in Humans
    b. Safety and Efficacy
    c. Marketing Experience
8. Summary of Data and Guidance for the Investigator

Where permissible by regulatory authorities, and as deemed appropriate by the PPI and the Protocol Steering Committee (PSC), the IP package insert, or other information sheet may be substituted for a full IB.

The IB will undergo appropriate review, approval, and sign-off prior to distribution to CSS. This will follow processes as outlined in SOP NN GA 103 – Document Development and Change Control. The IB will be reviewed annually, and additionally when a new risk is identified, or other new relevant information has become available.

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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 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 PPI and/or the Sponsor is/are responsible for creating and maintaining the IB for the study IP. The PPI is also responsible for fulfilling all regulatory requirements to maintain the IB, including working with the PSC, the CCC, and the DCC to ensure that the IB is updated appropriately and distributed to all participating CSS, the Single Institutional Review Board (SIRB), and other applicable parties.

The IB will be reviewed and approved by the PPI, Sponsor, and other signatories as appropriate. The PPI/Sponsor or their designee is responsible for submitting the IB to the FDA, as part of the Investigational New Drug (IND) application, as needed. After funding is secured, it is the responsibility of the protocol study team to submit the finalized, signed IB to the Single IRB (sIRB).

After funding is secured and the CSS selection process has occurred, it is the responsibility of the CCC Project Manager (PM) to distribute the finalized, signed IB to all CSS prior to initiation of the study, and throughout the study if updates are required.

It is the responsibility of the PPI/Sponsor, in collaboration with the PSC, to review the IB as needed, such as when a new risk or information becomes available.

The responsibility to conduct any or all of these activities may be delegated at the discretion of the Sponsor/PPI to the NeuroNEXT CCC and/or DCC, or to their subcontractors. Those individuals and entities 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 312.50	General Responsibility of Sponsors
ICH E6, 7.0	Investigator's Brochure

5. REFERENCES TO OTHER APPLICABLE SOPS

NN GA 103	Document Development and Change Control

6. ATTACHMENTS AND REFERENCES

NN RA 207-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

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CSS	Clinical Study Site(s)
DCC	Data Coordinating Center at The University of Iowa
GCP	Good Clinical Practice
IB	Investigator's Brochure
IND	Investigational New Drug application
IP	Investigational Product
PSC	Protocol Steering Committee
PM	Project Manager
PPI	Protocol Principal Investigator
SOP	Standard Operating Procedure

8. SPECIFIC PROCEDURES

A. Investigator's Brochure Development

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	PPI	Determine need for an Investigator's Brochure (IB).		
2.	PPI and/or Sponsor	Create the IB for the Investigational Product(s) (IP) being studied, as needed		NN GA 103
3.	PPI or designee	Secure the signatures and approval dates of PPI and other signatories, as appropriate.		
4.	PPI/ Sponsor or designee	Submit IB to FDA with IND application, as needed		
5.	Protocol Study Team	After funding is secured, submit the signed IB to the SIRB for review.		
6.	CCC PM	After funding is secured and CSS selection process has occurred, distribute the signed IB to all CSS prior to initiation of the study.		

B. Investigator's Brochure Maintenance

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	PPI / Sponsor or designee	Review the IB as needed, such as when new relevant information becomes available or risks are identified, to assess the need for updates.		

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#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
2.	PPI/ Sponsor, PSC, or designees	Update and finalize the IB according to the procedures described above and maintain version control as described in SOP NN GA 103.		NN GA 103
3.	PPI or designee,	Secure the signatures and approval dates of the PPI and other signatories, as appropriate.		
4.	Protocol Study Team	Submit the updated IB to the SIRB for review.		
5.	CCC PM	Distribute the updated IB to all CSS.		

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Attachment NN RA 207 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP) Investigator's Brochure Development and Approval SOP NN RA 207					
Version	**Description of Modification**	**Reason or Justification for Modification**	**Issue Date**	**Effective Date**	**Reviewer(s)**
1.0	New	N/A	13Apr2012	13May2012	N/A
2.0	Clarified that the PPI and/or the Sponsor is/are responsible for creating and maintaining the Investigator's Brochure for the study Investigational Product. Replaced references to 'Investigational Brochure' with 'Investigator's Brochure' in the title and throughout.	Updates for version 2.0.	21Sep2016	21Oct2016	N/A
3.0	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.	Updated for version 3.0	22Feb2023	08Apr2023	Catherine Gladden
3.0	Minor edits for clarity	Periodic Review	01Mar2024	15Apr2024	Preeti Paul

NN RA 207 Investigator's Brochure Development and Approval v4.0 2feb2024 clean

Final Audit Report 2024-03-11

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2024-03-08 - 2:12:33 PM GMT

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Signature Date: 2024-03-08 - 2:12:49 PM GMT - Time Source: server- IP address: 128.255.113.139

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

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