NeuroNEXT Network

Standard Operating Procedure (SOP)

Investigational Product Management

Version 3.0

SOP NN PM 505

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 7, 2024 14:55 CST* 07-Mar-2024
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Signature and Date: Merit Cudkowicz *Electronically signed by: Merit Cudkowicz Reason: I approve this document Date: Feb 22. 2024 17:08 CST* 22-Feb-2024
Name and Title: Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)
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Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR INVESTIGATIONAL PRODUCT MANAGEMENT

SOP: NN PM 505 Version No.: 3.0 Issue Date: 01Mar2024 Effective Date: 15Apr2024	INVESTIGATIONAL PRODUCT MANAGEMENT	Supersedes Document Version : 2.0 Effective Date : 08Apr2023

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Dixie Ecklund

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24-Feb-2024

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22-Feb-2024

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

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Joan Ohayon

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11-Mar-2024

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

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR INVESTIGATIONAL PRODUCT MANAGEMENT

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1. POLICY

For all NeuroNEXT Network studies that involve distribution of an Investigational Product (IP) (including drugs, biologics, and devices), no IP will be released to a Clinical Study Site (CSS) prior to Single Institutional Review Board (SIRB) approval of the study and certification from the Clinical Coordinating Center (CCC) that the CSS has been activated for study participation. Once the IP has been released to a CSS, IP inventories will be monitored, and all IP will be accounted for throughout the course of the study. The IP will be handled according to applicable regulations and Protocol Principal Investigator (PPI), SIRB, and funding agency requirements, as well as CSS institutional policies and the Delegation of Responsibilities log for each study.

The IP will be stored in a secure environment according to institutional policies, and state and federal regulations as applicable. with Access will be limited to key study personnel. The IP will be maintained according to the environmental storage requirements detailed in the protocol, the Investigational Brochure, or other instructions supplied by the IP provider. Only individuals authorized by the study protocol, institutional guidelines, and state law are permitted to dispense IP to study participants. Procedures for destruction of any unused IP must comply with study protocol, institutional requirements, and applicable Occupational Safety and Health Administration (OSHA) and biohazard materials policies, if appropriate, and only with the express written authorization of the Sponsor or other supplier.

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 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 CCC is responsible for ensuring that all necessary approvals have been obtained for the study before any IP is distributed to investigators.

The CSS is responsible for requesting re-stocking of the IP via the on-line interactive web response system created by the DCC, or using a comparable system or process, to ensure that the CSS maintains adequate IP inventory. In certain cases, the DCC and Central Pharmacy may work together to establish minimum/maximum par levels of IP in an effort to automate the re-stocking process. The DCC and/or the Central Pharmacy is responsible for ensuring that investigator requests for IP are processed expeditiously to ensure that CSS have adequate supplies on-hand at all times.

Each CSS investigator is responsible for tracking the disposition of all IP during the course of the study, from the time of receipt to the time of final disposition (e.g. return to the supplier, on-site destruction). This includes a complete accountability/reconciliation of all IP to the participant level.

The DCC Monitors (if contractually agreed upon) are responsible for evaluating the adequacy of IP accountability during routine monitoring.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.6	Labeling of an Investigational New Drug

21 CFR 312.7	Promotion and Charging for Investigational Drugs
21 CFR 312.40	General Requirements for Use of an Investigational New Drug in a Clinical Investigation
21 CFR 312.59	Disposition of Unused Supply of Investigational Drug
21 CFR 312.61	Control of the Investigational Drug
21 CFR 312.69	Handling of Controlled Substances
21 CFR 312.110	Import and Export Requirements
21 CFR 312.160	Drugs for Investigational Use in Laboratory Research Animals or In Vitro Tests
ICH E6, 2.12	The Principles of ICH GCP
ICH E6, 4.6	Investigational Product
ICH E6, 4.7	Randomization Procedures and Unblinding
ICH E6, 5.13	Manufacturing, Packaging, Labeling and Coding Investigational Product(s)
ICH E6, 5.14	Supplying and Handling Investigational Product(s)

5. REFERENCES TO OTHER APPLICABLE SOPS

NN RA 203	Site Regulatory Binder Maintenance
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 Close-out Visits

6. ATTACHMENTS AND REFERENCES

NN PM 505 – 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
CSS	Clinical Study Site(s)
DCC	Data Coordinating Center at The University of Iowa
FDA	U.S. Food and Drug Administration
ICH	International Council for Harmonisation
IP	Investigational Product(s)
OSHA	Occupational Safety and Health Administration
PPI	Protocol Principal Investigator

SRF	Site Regulatory File
SIRB	Single Institutional Review Board

8. SPECIFIC PROCEDURES

A. Labeling and Release of Investigational Product

#	*Who*	*Task*	*Attachment*	*Related SOP*
1.	CCC	In collaboration with the PPI or designee, authorize shipment of IP to a Central Investigational Product Distribution Facility (e.g. Central Pharmacy or Manufacturing facility subcontractor) if needed, after contracts are finalized with the Supplier.		
2.	CCC, in collaboration with PPI or designee	In collaboration with the PPI or designee, work with the Central Investigational Product Distribution Facility to finalize product labeling and packaging requirements.		
3.	CCC	Authorize Central Investigational Product Distribution Facility to ship product to CSS when training is completed and applicable regulatory and protocol specific requirements have been fulfilled.		NN SS 401 NN SS 402 NN RA 203
4.	CCC or DCC	Instruct CSS to maintain records containing signed receipts for delivery of IP in their Site Regulatory File (SRF), and provide a copy to the CCC.		NN SS 402

B. Investigational Product Receipt, Storage and Dispensing to Participants

#	*Who*	*Task*	*Attachment*	*Related SOP*
1.	CCC or DCC	Instruct the CSS Investigator or designee at each site to perform an inventory upon receiving investigational product.		NN SS 402
2.	CCC or DCC	Instruct the investigator or designee to inform the appropriate party if there is missing or damaged IP or other discrepancies (e.g. temperature discursion during shipping).		NN SS 402
3.	CCC or DCC	If there is an urgent need to replace any missing or otherwise discrepant shipment contents, instruct the investigator to contact the appropriate party immediately.		NN SS 402
4.	CCC or DCC	Instruct the CSS to keep all records of drug delivery in the Site Regulatory File (SRF) for review by the Monitor during routine monitoring visits.		NN SS 402

#	*Who*	*Task*	*Attachment*	*Related SOP*
5.	DCC Monitor	Verify proper use (including distribution by protocol-specified randomization schema) of the IP by the CSS during study.		NN SS 403
6.	DCC Monitor	Verify that the IP is stored in an environmentally appropriate and secure location at the CSS, with access restricted to authorized personnel and with appropriate monitoring equipment.		NN SS 403
7.	DCC Monitor	Verify that IP is dispensed or otherwise provided only to participants enrolled in the clinical study.		NN SS 403
8.	DCC Monitor	Verify that the use of the IP occurs under the direct supervision of the investigator or other approved designee(s).		NN SS 403
9.	DCC Monitor	Verify that the product blind is not broken except in the case of an emergency or according to a protocol-defined situation.		NN SS 403
10.	DCC Monitor	If the blind is broken, verify that the PPI and CCC were notified and that the justification is noted in the CSS files.		NN SS 403
11.	DCC Monitor	Document in a “Note to File” for CCC files, the circumstances under which the blind was broken, and any actions taken, if necessary.		NN SS 403
12.	DCC Monitor	Verify that each CSS has accurate and complete records that show receipt and disposition of all IP.		NN SS 403
13.	DCC Monitor	Verify and reconcile the IP records during periodic monitoring visits.		NN SS 403
14.	DCC and CCC	Document inadequate record-keeping practices, discuss them with the investigator, and report them to the Sponsor.		NN SS 404
15.	CCC and DCC in collaboration with PPI	If a pattern of inadequate inventory management and documentation exists, consider terminating CSS participation in the study.		NN SS 404

C. Investigational Product Accountability and Reconciliation

#	*Who*	*Task*	*Attachment*	*Related SOP*
1.	DCC	Instruct the CSS that at study conclusion or termination, they must account for all supplies of IP; cross-reference		NN SS 403 NN SS 405

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#	*Who*	*Task*	*Attachment*	*Related SOP*
		all forms, and follow approved procedure for returning or destroying IP.[1]		
2.	DCC	Verify and reconcile all investigational product records.		
3.	DCC Monitor	Verify that the CSS has documented and explained any discrepancies in the beginning and ending inventory.		NN SS 405
4.	DCC Monitor	Collect copies of all IP inventory documentation, and provide them to the CCC, where they will be stored with the Trial Master File.		NN SS 405
5.	CSS	Maintain original investigational product inventory documentation in theSite Regulatory File.		NN SS 405 NN RA 203
6.	DCC	Instruct CSS to keep IP accountability records for a minimum of seven (7) years, or two (2) years after a marketing application is approved for the product, whichever is longer. CSS should contact the DCC to obtain written permission to destroy records before proceeding with destruction of documentation.		NN SS 405

Note:

[1]The CSS must have written authorization from the Sponsor or Sponsor designee (e.g. CCC Project Manager, PPI) to destroy the IP at the CSS.

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Attachment NN PM 505 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP) Investigational Product Management SOP NN PM 505					
Version	**Description of Modification**	**Reason or Justification for Modification**	**Issue Date**	**Effective Date**	**Reviewer(s)**
1.0	New	N/A	06Apr2012	06May2012	N/A
1.0	Reviewed – no changes (2016)	N/A	06Apr2012	06May2012	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)”. Additional minor updates throughout.	Updated for version 2.0	22Feb2023	08Apr2023	Catherine Gladden
3.0	Minor edits for clarity	Periodic review	01Mar2024	15Apr2024	Preeti Paul

NN PM 505 Investigational Product Management v3.0 clean

Final Audit Report 2024-03-11

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Document page count:	8
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2024-02-23 - 7:00:11 PM GMT

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Tania Leeder (tleeder@mgb.org) added alternate signer ecklundd@uiowa.edu. The original signer dixie-ecklund@uiowa.edu can still sign.

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2024-02-24 - 11:09:56 PM GMT

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2024-03-07 - 8:55:11 PM GMT- IP address: 128.255.113.139

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ohayonj@ninds.nih.gov authenticated with Adobe Acrobat Sign.
Challenge: The user opened the agreement.
2024-03-11 - 1:46:50 PM GMT

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Document e-signed by Joan Ohayon (ohayonj@ninds.nih.gov)
Signing reason: I approve this document
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Agreement completed.
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