NeuroNEXT Network

Standard Operating Procedure (SOP)
Investigational Product Management
Version 1.0
SOP NN PM 505

Originators: NeuroNEXT CCC and DCC Personnel

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April 4, 2012

Issue Date

May 6, 2012

Effective Date (30 calendar days after the Issue Date)
NN PM 505
NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR INVESTIGATIONAL PRODUCT MANAGEMENT

SOP: NN PM 505
Version No.: 1.0
Effective Date: N/A

INVESTIGATIONAL PRODUCT MANAGEMENT

Supercedes
Document: N/A
Effective Date: NA

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 Central Institutional Review Board (CIRB) 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), CIRB, 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, with access 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 subjects. 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 1996 ICH E6 Consolidated Guidance. 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 subject level.

The DCC Monitors (or subcontractor Monitors) 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

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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 Conference on Harmonisation
   IP Investigational Product(s)
   OSHA Occupational Safety and Health Administration
   PPI Protocol Principal Investigator
   SRF Site Regulatory File
8. SPECIFIC PROCEDURES

A. Labeling and Release of Investigational Product

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<tr>
<th>#</th>
<th>Who</th>
<th>Task</th>
<th>Attachment</th>
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<tbody>
<tr>
<td>1.</td>
<td>CCC</td>
<td>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.</td>
<td>NN SS 401</td>
<td>NN SS 402</td>
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<td>2.</td>
<td>CCC, in collaboration with PPI or designee</td>
<td>In collaboration with the PPI or designee, work with the Central Investigational Product Distribution Facility to finalize product labeling and packaging requirements.</td>
<td>NN RA 203</td>
<td>NN SS 402</td>
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<td>3.</td>
<td>CCC</td>
<td>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.</td>
<td>NN SS 402</td>
<td>NN SS 402</td>
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<td>4.</td>
<td>CCC or DCC</td>
<td>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.</td>
<td>NN SS 402</td>
<td>NN SS 402</td>
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B. Investigational Product Receipt, Storage and Dispensing to Subjects

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| 1. | CCC or DCC                | Instruct the Site Investigator or designee to perform an inventory upon receiving IP. 
| 2. | CCC                       | Instruct the investigator or designee to inform the appropriate party if there is missing or damaged IP or other discrepancies (e.g. temperature excursion during shipping). | NN SS 402 | NN SS 402   |
| 3. | DCC Monitor               | 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 | 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 | NN SS 402   |
| 5. | DCC Monitor               | Verify proper use (including distribution by protocol-specified randomization schema) of the IP by the CSS during study. | NN SS 403 | 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 | NN SS 403   |
| 7. | DCC Monitor               | Verify that IP is dispensed or otherwise provided only to subjects enrolled in the clinical study. | NN SS 403 | 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 | NN SS 403   |
### C. Investigational Product Accountability and Reconciliation

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<tr>
<td>1.</td>
<td>DCC</td>
<td>Instruct the CSS that at study conclusion or termination, they must account for all supplies of IP; cross-reference all forms, and follow approved procedure for returning or destroying IP.</td>
<td>NN SS 403</td>
<td>NN SS 405</td>
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<td>2.</td>
<td>DCC</td>
<td>Verify and reconcile all investigational product records</td>
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<td>3.</td>
<td>DCC Monitor</td>
<td>Verify that the CSS has documented and explained any discrepancies in the beginning and ending inventory.</td>
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<td>NN SS 405</td>
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<td>4.</td>
<td>DCC Monitor</td>
<td>Collect copies of all IP inventory documentation, and provide them to the CCC, where they will be stored with the Trial Master File.</td>
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<td>NN SS 405</td>
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<td>5.</td>
<td>CSS</td>
<td>Maintain original investigational product inventory documentation in their Regulatory Master File.</td>
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<td>NN SS 405</td>
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<td>6.</td>
<td>DCC</td>
<td>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.</td>
<td></td>
<td>NN SS 405</td>
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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.
<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Issue Date</th>
<th>Modification Completion Date</th>
<th>Reason or Justification for Modification</th>
<th>Description of Modification</th>
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<tr>
<td>N/A</td>
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<td>1.0</td>
<td>2.0</td>
<td>Provide a brief but complete summary of the modifications to the SOP</td>
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SOP NN Pm 505
Investigational Product Management
NeuroNEXT Network Standard Operating Procedure (SOP)

Attachment NN Pm 505 - A. Document History