

NeuroNEXT Network

Standard Operating Procedure (SOP) Adverse Events: Sponsor Responsibilities Version 1.0 SOP NN RA 205


Originators: NeuroNEXT CCC and DCC Personnel

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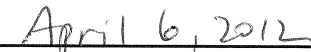

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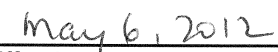

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Issue Date


Effective Date (30 calendar days after the Issue Date)

NN RA 205

NEURONEXT NETWORK STANDARD OPERATING POLICY AND PROCEDURE FOR ADVERSE EVENTS: SPONSOR RESPONSIBILITIES

SOP: RA 205 Version No.: 1.0 Effective Date:	ADVERSE EVENTS: SPONSOR RESPONSIBILITIES	Supersedes Document: NA Effective Date:
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1. POLICY

The NeuroNEXT Protocol Principal Investigator (PPI) will typically be the Investigational New Drug (IND) holder/Sponsor for NeuroNEXT protocols. The PPI, as the IND holder that is regulated by the US Food and Drug Administration (FDA), will be responsible for investigating and reporting to the FDA all AEs and SAEs that occur during the conduct of a clinical study within the period of time defined by federal regulations, and may delegate this responsibility to the study designated Independent Medical Monitor (IMM). The PPI will ensure that all participating investigators and their key study personnel are familiar with protocol-defined adverse events for investigational products under investigation, and that they are aware of the protocol-defined process by which Adverse Events (AE) and Serious Adverse Events (SAE) are to be elicited and documented throughout the study.

For studies not regulated by the FDA, the NeuroNEXT PPI will delegate responsibility of reviewing and reporting AEs and SAEs, as outlined in the study protocol, to the Independent Medical Monitor (IMM).

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 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 Sponsor/PPI, or their designee (i.e., IMM), is responsible for ensuring the collection and reporting all AEs as described in the study protocol. If the study is regulated by the FDA, these events are to be reported annually as described in 21 CFR 312.33.

The Sponsor/PPI, or their designee (i.e., IMM), is responsible for ensuring the collection, evaluation, and reporting all SAEs as described in the study protocol and other applicable study documents (e.g. Data and Safety Monitoring Plan). If the study is regulated by the FDA, the Sponsor/PPI is responsible for reporting these events in an expedited fashion if they meet the regulatory requirement for such reporting, as well as annually as described in 21 CFR 312.32 and 21 CFR 312.33, respectively.

The Sponsor/PPI, or designee (i.e., IMM), is responsible for ensuring that all participating investigators are aware of their responsibility to recognize and report all AEs and SAEs according to applicable regulations, guidelines, and the requirements of the protocol. All AEs and SAEs are to be reported using appropriate eCRFs and other forms, as required per protocol.

The PPI, or their designee (i.e., IMM), shall evaluate each reported Serious Adverse Event for the following:

- Serious / non-Serious: Does this event meet the regulatory definition of "Serious"?
- Expected / Unexpected: Is the event, including the severity and duration of the event, listed in the Investigators Brochure / Package Insert provided for this trial?
- Relationship to Study Drug/Intervention: Is there a possible causal relationship between the event and the investigational product?

The NeuroNEXT SOP NN RA 206 for Medical Monitoring and Safety Monitoring addresses the monitoring of serious adverse events and other medical events of interest in NeuroNEXT studies.

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/PPI, but the Sponsor/PPI has the ultimate responsibility and must therefore, supervise those delegated activities effectively.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32	IND Safety Reports
21 CFR 312.33	Annual Reports
21 CFR 312.50	General Responsibility of Sponsors
21 CFR 312.55	Informing Investigators
21 CFR 312.56	Review of Ongoing Investigations
21 CFR 312.64	Investigator Reports
ICH E6, 2.7	The Principles of ICH GCP
ICH E6, 4.3	Medical Care of Trial Subjects
ICH E6, 4.11	Safety Reporting
ICH E6, 5.3	Medical Expertise
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.16	Safety Information
ICH E6, 5.17	Adverse Drug Reaction Reporting
ICH E6, 6.8	Assessment of Safety

5. REFERENCES TO OTHER APPLICABLE SOPS

NN RA 201	Regulatory Authority Submission and FDA Contact
NN RA 206	Medical Monitoring and Safety Monitoring
NN SS 402	Roles and Responsibilities of Site PIs
NN PM 504	Investigational Site Staff Training
NN SM 602	Central Institutional Review Board Reporting

6. ATTACHMENTS AND REFERENCES

NN RA 205-A	Document History
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7. TERMS AND ABBREVIATIONS

The following terms and abbreviations are used in this document:

AE	Adverse Event
CCC	Clinical Coordinating Center at Massachusetts General Hospital
DCC	Data Coordinating Center at The University of Iowa
FDA	U.S. Food and Drug Administration
ICH	International Conference on Harmonisation

PPI	Protocol Principal Investigator
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
PWI	Protocol Work Instruction

8. SPECIFIC PROCEDURES

A. Adverse Events Reporting

#	Who	Task	Attachment/ References	Related SOP
1.	PPI / CCC / DCC or designee	Train all investigators and key study personnel on protocol-defined adverse events		NN SS 402 NN PM 504
2.	PPI / CCC / DCC or designee	Train all investigators and key study personnel on their role in identifying and reporting all AEs that occur throughout the study, as defined per protocol		NN SS 402 NN PM 504
3.	PPI / CCC / DCC or designee	Provide safety data to any safety oversight committees as defined per protocol		
4.	PPI / CCC / DCC or designee	Report cumulative safety data to FDA, if applicable, per 21 CFR 312.33		NN RA 201

B. Serious Adverse Event Reporting

#	Who	Task	Attachment/ References	Related SOP
2	PPI / CCC / DCC or designee	Train all investigators and key study personnel on their role in identifying and reporting all SAEs that occur throughout the study, as defined per protocol		NN SS 402 NN PM 504
3	PPI / CCC / DCC, IMM or designee	Evaluate each report of a SAE to determine if it meets the definition of "serious", "unexpected", and/or "possibly related to the study drug"		
4	PPI / CCC / DCC, IMM or designee	If study is being conducted under an IND, determine if SAE meets regulatory requirements for expedited reporting to FDA and submit report as appropriate		NN RA 201
5	PPI / CCC / DCC or designee	Provide safety data to any safety oversight committees as defined per protocol		NN SM 602
6	PPI / CCC / DCC or designee	Report cumulative safety data to FDA, if applicable, per 21 CFR 312.33		NN RA 201

Attachment NN RA 205 - A. Document History

NeuroNEXT Network Standard Operating Procedure (SOP)
Adverse Events: Sponsor Responsibilities
SOP NN RA 205

Version	Description of Modification	Reason or Justification for Modification	Completion Date	Issue Date	Effective Date
1.0	New	N/A			
2.0	<Provide a brief but complete summary of the modifications to the SOP>				