NCATS Prior Approval for Delayed-Onset Research with Human Subjects: A Guide for CTSI-CN Award Recipients

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A PARTNERSHIP WITH THE GEORGE WASHINGTON UNIVERSITY

CTSI-CN Support for NCATS Prior Approval

NCATS Prior Approval Informational Sessions

- Required for CTSI-CN Awardees
- Detailed overview and guidance about the process

NCATS Support Team – *members listed on slide 28*

- A tag team comprising regulatory and finance experts
- Free consultations as you go through the process

NCATS Forms Repository – *coming soon!*

- Example of successful applications from past awardees

Agenda

1. Definitions and Requirements (5 minutes)
2. Process and Logistics (5 minutes)
3. Required Documents and Forms (40 minutes)
4. Contacts and Links (5 minutes)
5. Questions and Answers (30 minutes)

1. Definitions and Requirements (1 of 5)

Delayed Onset Human Subjects Research: "[H]uman subjects research is anticipated within the period of the award but definite plans for involvement of human subjects cannot be described in the application…"[1]

HSS (Human Subjects System) module: located within ASSIST, designed to track plans and results with NIH-funded human subjects research

ASSIST (Application Submission System and Interface for Submission Tracking): grantee interface ancillary to NIH's eRA Commons, first established to facilitate submission of multi-project applications

Reference: 1. NIH Grants Policy Statement, section 4.1.15

1. Definitions and Requirements (2 of 5)

NCATS: National Center for Advancing Translational Sciences, the NIH center that funds CTSI-CN

CNH OGC: Children's National Hospital Office of Grants and Contracts – authorized to submit prior approval requests on behalf of CTSI-CN [both for Children's and for GWU]

GW OSP: GW's Office of Sponsored Projects

1. Definitions and Requirements (3 of 5)

HHS Definition of Human Subjects Research:

Per 45 CFR 46, a human subject is "a living individual about whom an investigator … conducting research:

- *Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information of biospecimens; or*
- *Obtains, uses studies, analyzes, or generates identifiable private information or identifiable biospecimens."*

Notes: (1) consult with IRB or RKS to determine if project is human subjects research; (2) only IRB can determine if an exemption applies; (3) exempt research is still considered human subjects research and still required NCATS prior approval

Reference: https://www.hhs.gov/ohrp/sites/default/files/revised-common-rule-reg-text-unofficial-2018-requirements.pdf

1. Definitions and Requirements (4 of 5)

NIH Definition of a Clinical Trial:

A study is a clinical trial if the answer to all four questions is yes:

- *Does the study involve human participants?*
- *Are the participants prospectively assigned to an intervention?*
- *Is the study designed to evaluate the effect of the intervention on the participants?*
- *Is the effect being evaluated a health-related biomedical or behavioral outcome?*

Reference: https://grants.nih.gov/policy/clinical-trials/definition.htm

1. Definitions and Requirements (5 of 5)

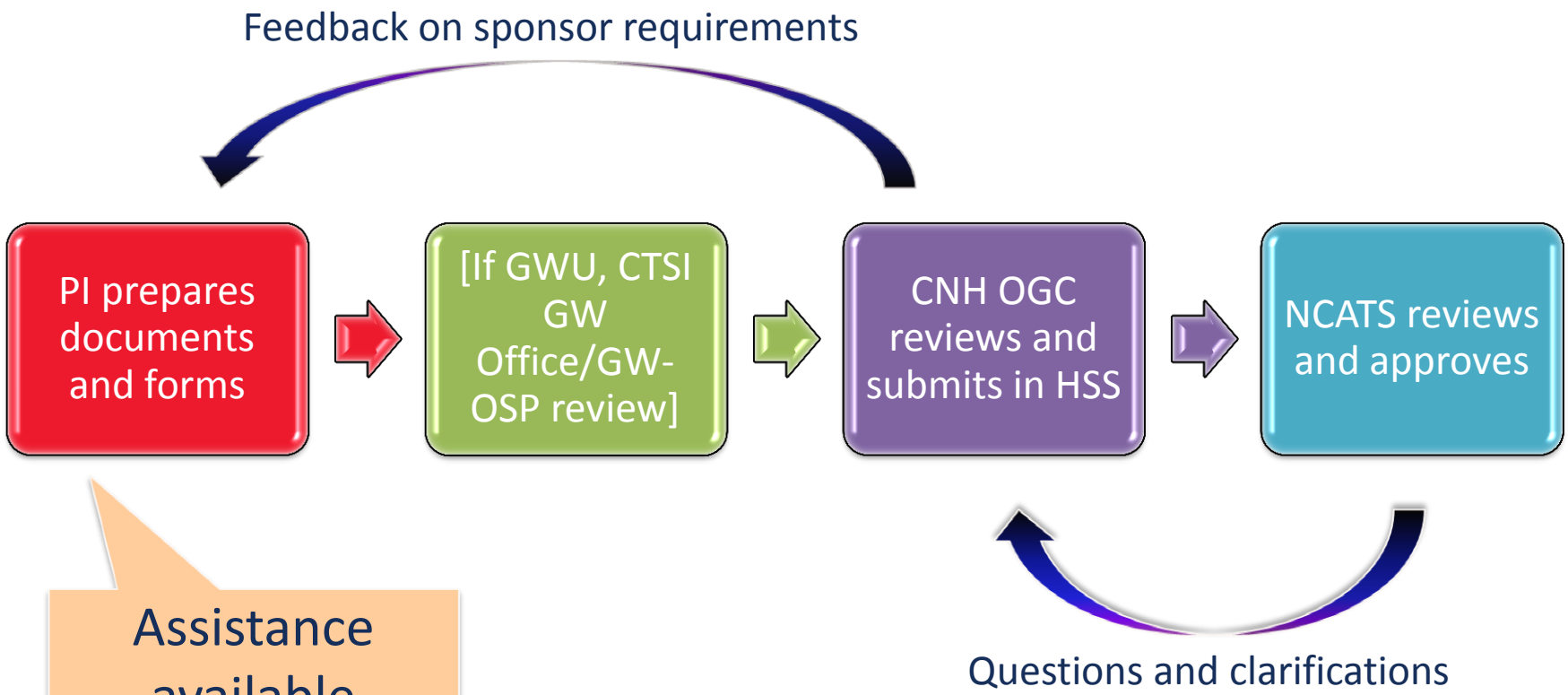
For human subjects project, must submit for prior approval: *"detailed information as required in the Research Plan of the application …"*

or, if a project is determined by the IRB to be exempt: *"identification of which exemptions(s) is/are applicable to the research, and a justification for the exemption ...."*

Note: Research involving use of vertebrate animals also requires prior approval, but the process is simpler and not described here.

Reference: NIH Grants Policy Statement, section 4.1.15

2. Process and Logistics (1 of 3)



2. Process and Logistics (2 of 3)

NCATS Support Team available to assist PI in preparing documents:

For GWU researchers:

- CTSI-CN Finance at GW – budget questions, document collection
- CTSI-CN Regulatory Knowledge & Support (RKS) Team – consultation and clarification
- GW IRB – protocol approval

For CNH researchers:

- CTSI-CN Finance at CNH for budgetary questions
- CTSI-CN RKS Team – consultation & clarification
- CNH OGC for questions about forms, required documents, etc.
- CNH IRB – protocol approval

2. Process and Logistics (3 of 3)

Timeframe:

Review by CNH OGC and submission in HSS: less than one week
[if there are not issues that need to be addressed]

Review by NCATS and feedback: usually less than two weeks

Most submissions require at least one round of NCATS feedback and clarification – but rarely more than one.

3. Required Documents and Forms (1 of 16)

Three documents or sets of documents are required:

A. Addendum form itself [includes both short-answers and instructions for other forms]

B. Additional documents as required by the addendum

C. HSS sections [virtually identical to the “Study Record” part of the “Human Subjects and Clinical Trial” application form]

Note: Addendum is described first because it is the starting point, but HSS sections require more work

3. Required Documents and Forms (2 of 16)

A. Addendum (currently using the 12/9/2019 version):

Section A.I: Fill-in-the-blank basic information, e.g.:

SECTION I. Complete each field.

Name of Pilot Study Principal Investigator (PI) or KL2-Scholar *(Designated Study PI)*	Click here to enter text
Type of Proposed Research & Duration of Requested Support	☐ **Pilot Study** ☐ **KL2 Project** ___**Yrs** ___**Mo**
Name of KL2-Scholar Mentor *(if appropriate)*	Click here to enter text
Acknowledgement that Mentor/ Supervisor has reviewed and approves the submitted project	☐ **Yes**
Study Type *(as designated by institution and/or IRB)*	☐ **Exempt** **Exemption #** ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐ **No More Than Minimal Risk** ☐ **Greater Than Minimal Risk** ☐ **Clinical Trial**

3. Required Documents and Forms (3 of 16)

A. Addendum (currently using the 12/9/2019 version):

Section A.II: Short answers; four questions:

1. Provide a brief (< 500 words) summary of the specific aspects of the proposed study that will be supported by NCATS funds.
2. List a line item budget for each specific aspect to be supported with NCATS funds (list supplies, services, and personnel costs…
3. If the proposed research is considered an amendment or is a sub-study/ancillary study to an IRB-approved parent protocol, provide a summary of the parent protocol with an explanation of how the proposed study connects to it.
4. List names of Key Personnel involved in the study [limit the key personnel if possible – should only be key with respect to the work being funded]

3. Required Documents and Forms (4 of 16)

B. Additional Documents as Required by the Addendum:

First step: Identify relevant category: A (clinical trial) or B 1-4 (based on risk)

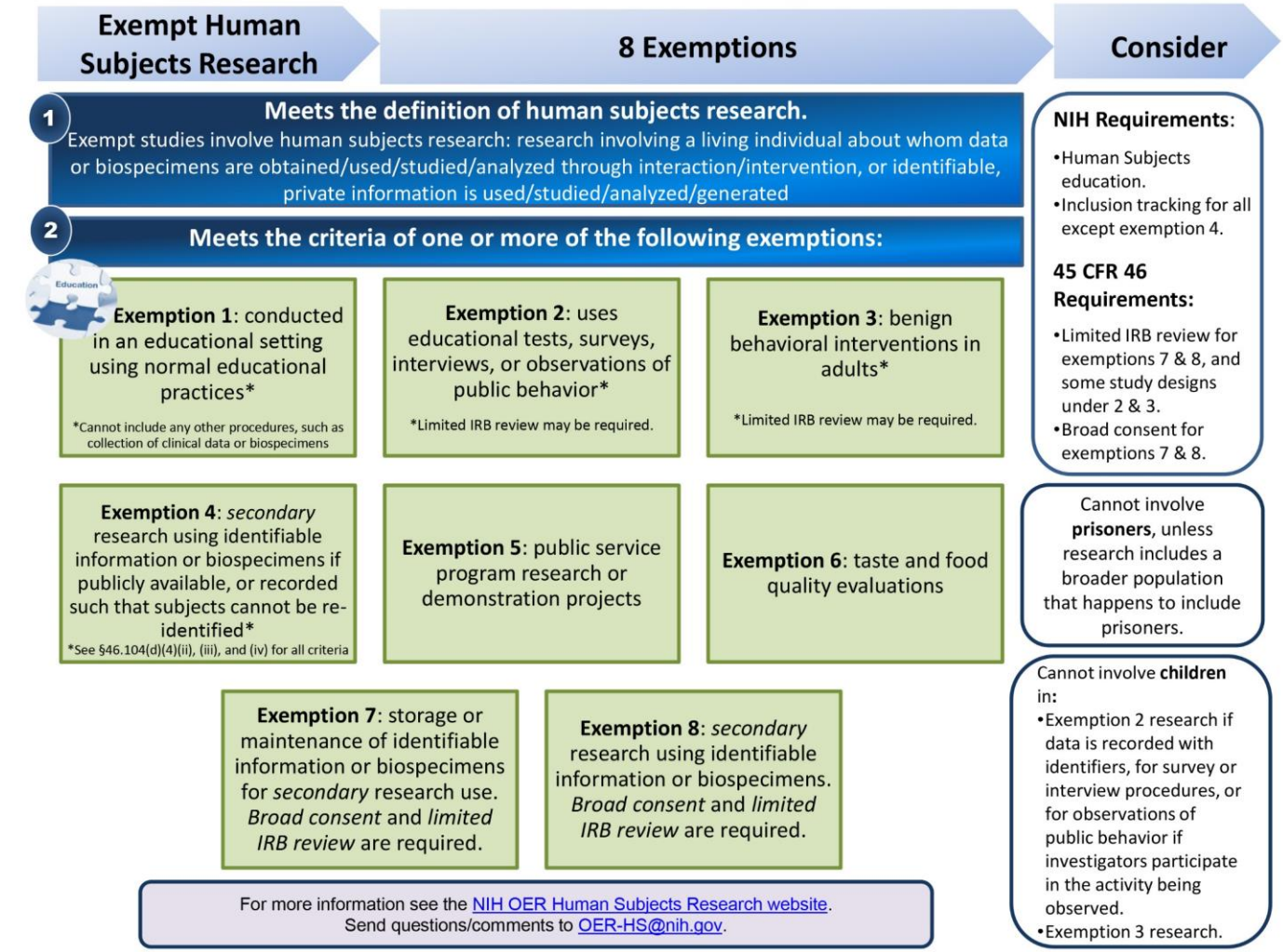
☐ **A.** Human Subjects Research that meets the NIH definition of a clinical trial

☐ **B.** Human Subjects Research that does not meet the NIH definition of a clinical trial (choose one of 4 sub-categories):

- ☐**B1**: Study deemed Greater than Minimal Risk by IRB OR the risk determination is not indicated in the IRB approval documentation OR involves pregnant women, human fetuses or neonates, prisoners, children, or individuals with impaired decision-making capacity
- ☐**B2**: Study deemed No More than Minimal Risk by the IRB and does not include populations listed under B1.
- ☐**B3**: Study meeting the criteria for Exemptions 1-3 or 5-8 under 45 CFR 46
- ☐**B4**: Study meeting the criteria for Exemption 4 (de-identified existing biospecimens) under 45 CFR 46

☐ **C.** Not Human Subject Research- No Prior Approval Required.

3. Required Documents and Forms (5 of 16)



3. Required Documents and Forms (6 of 16)

B. Additional Documents as Required by the Addendum:

	Clinical Trial	Non-Clinical Trial			
STUDY CATEGORY	A[1]	B1[2]	B2[3]	B3[4]	B4[5]
COMPLETE HSS SECTIONS (see below for details)	1-5	1, 2, 3.1 & 3.2	1, 2, 3.1 & 3.2	1, 2, 3.1[6] & 3.2	1, 3.1[6] & 3.2
NCATS-Required Documents					
Addendum	√	√	√	√	√
Certification of IRB-Approval	√	√	√		
Institutional Exemption Determination				√	√
Relevant biosketches not contained in the CTSA grant appl.	√	√	√		
Institutional letter attesting to completion of Human Subjects Training for PI and key personnel[7]	√	√	√	√	√
IRB-Approved Protocol	√	√			
IRB-Approved informed consent, verbal consent transcript, assent and parental permission documents, or documentation of IRB waiver (as applicable)	√	√			

3. Required Documents and Forms (7 of 16)

B. Additional Documents as Required by the Addendum:

Comments on specific items, as applicable:

- Certification of IRB Approval: if most recent approval does not include details on risk determination, include initial approval as well
- Biosketches of Key Personnel: use NIH format
- Confirmation of human subjects research training for key personnel
  - ✓ For GW: provide CITI certificate from https://humanresearch.gwu.edu/collaborative-irb-training-initiative-citi
  - ✓ For CNH: CNH OGC will provide
- IRB-approved Protocol: not required for all categories
- IRB-approved informed consent, etc.: not required for all categories

3. Required Documents and Forms (8 of 16)

C. HSS Sections:

Study category determines which HSS sections need to be completed (red)...

…and where CNH OGC will insert additional documents in the HSS (blue)

	Clinical Trial	Non-Clinical Trial			
STUDY CATEGORY	A[1]	B1[2]	B2[3]	B3[4]	B4[5]
COMPLETE HSS SECTIONS (see below for details)	1-5	1, 2, 3.1 & 3.2	1, 2, 3.1 & 3.2	1, 2, 3.1[6] & 3.2	1, 3.1[6] & 3.2

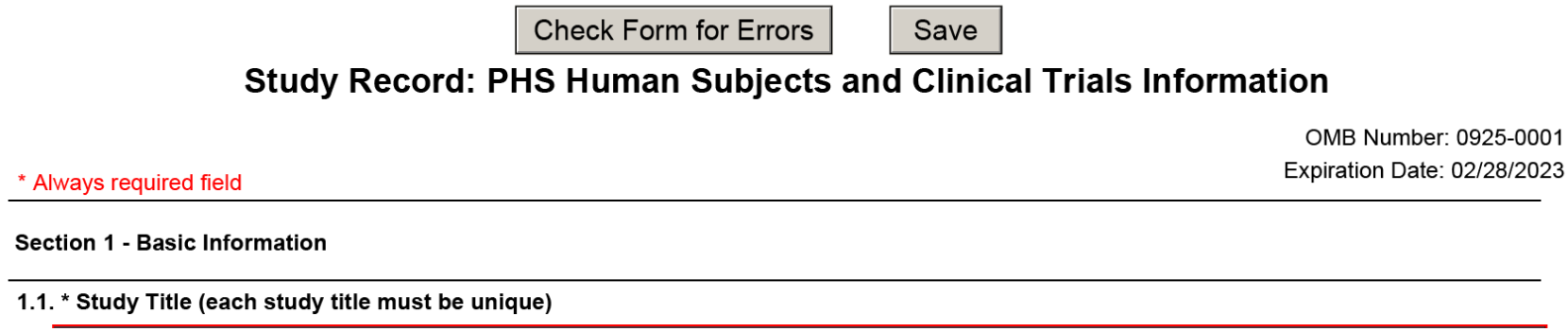
[snip]

Specified NCATS Required Document PDFs should be combined and attached in HSS Sections	*5.1*	*2.7 (Study Timeline attachment box must be used to attach the Study Timeline plus the NCATS-specified documents.)*	*3.1[6] (Protections of Human Subjects attachment box must be used to attach justification for exemption statement.)*

3. Required Documents and Forms (9 of 16)

C. HSS Sections:

Because only CNH OGC has access to the this grant in HSS, we use the "Study Record" form to collect data/files from the PI. For this form, follow the application instructions at https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/general/g.500-phs-human-subjects-and-clinical-trials-information.htm


Check Form for Errors Save

Study Record: PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001
Expiration Date: 02/28/2023

* Always required field

Section 1 - Basic Information

1.1. * Study Title (each study title must be unique)

3. Required Documents and Forms (10 of 16)

C. HSS Sections: Section 1: Basic Information

Note: Identify exemption(s) only as determined by an IRB.

1.1. * Study Title (each study title must be unique)

1.2. * Is this Study Exempt from Federal Regulations? ☐ Yes ☐ No

1.3. Exemption Number ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8

1.4. * Clinical Trial Questionnaire

If the answers to all four questions below are yes, this study meets the definition of a Clinical Trial.

1.4.a. Does the study involve human participants?	☒ Yes ☐ No
1.4.b. Are the participants prospectively assigned to an intervention?	☐ Yes ☐ No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	☐ Yes ☐ No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	☐ Yes ☐ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g., NCT87654321) for this trial, if applicable

3. Required Documents and Forms (11 of 16)

C. HSS Sections: Section 2: Study Population Characteristics

2.1. Conditions or Focus of Study

x

Add New Condition

2.2. Eligibility Criteria

2.3. Age Limits **Minimum Age** **Maximum Age**

2.3.a. Inclusion of Individuals Across the Lifespan Add Attachment Delete Attachment View Attachment

2.4. Inclusion of Women and Minorities Add Attachment Delete Attachment View Attachment

2.5. Recruitment and Retention Plan Add Attachment Delete Attachment View Attachment

2.6. Recruitment Status

2.7. Study Timeline Add Attachment Delete Attachment View Attachment

2.8. Enrollment of First Participant

2.9. Inclusion Enrollment Report(s)

3. Required Documents and Forms (12 of 16)

C. HSS Sections: Section 2 details: 2.9 Inclusion Enrollment Reports

Provide demographic data on planned enrollment (pictured below) and/or cumulative/actual enrollment (similar table not pictured).

Planned

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More than One Race	0	0	0	0	0
Total	0	0	0	0	0

3. Required Documents and Forms (13 of 16)

C. HSS Sections: Section 3: Protection and Monitoring Plans

3.1. Protection of Human Subjects | Add Attachment | Delete Attachment | View Attachment

3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?

☐ Yes ☐ No ☐ N/A

If yes, describe the single IRB plan | Add Attachment | Delete Attachment | View Attachment

Required only if clinical trial

3.3. Data and Safety Monitoring Plan | Add Attachment | Delete Attachment | View Attachment

3.4. Will a Data and Safety Monitoring Board be appointed for this study?

☐ Yes ☐ No

3.5. Overall Structure of the Study Team | Add Attachment | Delete Attachment | View Attachment

3. Required Documents and Forms (14 of 16)

C. HSS Sections: Section 4: Protocol Synopsis (showing 4.1)

Required only if clinical trial

4.1. Study Design

4.1.a. Detailed Description

4.1.b. Primary Purpose

4.1.c. Interventions

x	Intervention Type	
	Name	
	Description	

Add New Intervention

4.1.d. Study Phase

Is this an NIH-defined Phase III clinical trial? Yes No

4.1.e. Intervention Model

4.1.f. Masking Yes No

Participant Care Provider Investigator Outcomes Assessor

4.1.g. Allocation

3. Required Documents and Forms (15 of 16)

C. HSS Sections: Section 4: Protocol Synopsis (showing 4.2 – 4.7)

Required only if clinical trial

4.2. Outcome Measures

x Name	
Type	
Time Frame	
Brief Description	

Add New Outcome

4.3. Statistical Design and Power Add Attachment | Delete Attachment | View Attachment

4.4. Subject Participation Duration

4.5. Will the study use an FDA-regulated intervention? ☐ Yes ☐ No

4.5.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/Investigational Device Exemption (IDE) status

Add Attachment | Delete Attachment | View Attachment

4.6. Is this an applicable clinical trial under FDAAA? ☐ Yes ☐ No

4.7. Dissemination Plan Add Attachment | Delete Attachment | View Attachment

3. Required Documents and Forms (16 of 16)

C. HSS Sections: Sections 5 and 6 (required only if clinical trial)

Section 5 is where we upload the attachments required by the Addendum (IRB approval, biosketches, etc.) for clinical trials only. No other questions.

Section 5 - Other Clinical Trial-related Attachments

5.1. Other Clinical Trial-related Attachments [Add Attachments]

Section 6: Clinical Trial Milestone Plan

6.1. Study Primary Completion Date	○ Anticipated ○ Actual
6.2. Study Final Completion Date	○ Anticipated ○ Actual
6.3. Enrollment and randomization	
Enrollment of the first subject (Study Start Date)	○ Anticipated ○ Actual
25% of planned enrollment recruited by	○ Anticipated ○ Actual
50% of planned enrollment recruited by	○ Anticipated ○ Actual
75% of planned enrollment recruited by	○ Anticipated ○ Actual
100% of planned enrollment recruited by	○ Anticipated ○ Actual
6.4. Completion of primary endpoint data analyses	○ Anticipated ○ Actual
6.5. Reporting of results in ClinicalTrials.gov	○ Anticipated ○ Actual
6.6. Is this an applicable clinical trial under FDAAA?	○ Yes ○ No

4. CTSI-CN NCATS Support Team

Contacts:

GW Finance: Budget and NCATS prior approval requirements
Lydia Prentiss, Sponsored Projects Administrator, lydiaprentiss@gwu.edu

CNH Finance: Budget questions
Valery Yankov, Finance Program Lead, vyankov@childrensnational.org

CNH: NCATS prior approval requirements
Rachel Pentlarge, Senior Grants and Contracts Specialist, rspentlar1@childrensnational.org

CTSI-CN Regulatory Team for consultations and specific questions related to NCATS prior approval process

Dylan Marashi, dmarashi@childrensnational.org
Debra Paxton, dapaxton@gwu.edu

4. Relevant Websites

Links:

NCATS delayed onset page: https://ncats.nih.gov/ctsa/funding/prior-approval-paga

NIH human subjects tools and links: https://grants.nih.gov/policy/humansubjects/research.htm

NIH application instructions (choose section G.500 for human subjects page): https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/general-forms-f.pdf

5. Questions and Answers