# NCATS NEW PROJECTS WITH HUMAN SUBJECTS RESEARCH

# ADDENDUM

## **SECTION I**

Read each section and complete according to the instructions provided.

|  |  |
| --- | --- |
| **Name of UL1 Pilot Study Principal Investigator (PI) or KL2 Scholar** *(Designated Study PI)* | Click here to enter text. |
| **Title\* of Proposed Research Protocol***\*This must match the title on the IRB-Approval documentation* | Click here to enter text. |
| **Type of Proposed Research** | [ ]  **UL1 Pilot Project** [ ]  **KL2 Scholar Project** |
| **UL1 PILOTS and KL2 PROJECTS** |
| **Category 1 Research**Requires entry & document upload into HSS and official NCATS approval by GMS before human subjects research begins. | [ ]  **Greater Than Minimal Risk** *(as designated by institution and/or IRB)*[ ]  [**Clinical Trial**](https://grants.nih.gov/policy/clinical-trials/definition.htm) **(NIH-defined)** *(regardless of the risk level, based on NIH definition)* |
| **Category 2 Research**Requires entry & document upload into HSS and notification of NCATS before human subjects research begins. | [ ]  [**Exempt**](https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML) **Exemption #** [ ] **1** [ ] **2** [ ] **3** [ ] **4** [ ] **5** [ ] **6** [ ] **7** [ ] **8** **Existing data with identifiers** [ ]  Yes [ ]  No [ ]  [**Minimal Risk**](https://www.hhs.gov/ohrp/sites/default/files/revised-common-rule-reg-text-unofficial-2018-requirements.pdf) **\****All NIH-defined clinical trials are considered Category 1 research even if proposed research might otherwise be considered Minimal Risk.* |
| **Does the study include a** [**foreign component**](https://ncats.nih.gov/funding/grantees/approval#foreign-components)**?** | [ ]  Yes\* [ ]  No *\*Official NCATS Prior Approval notice must be received from GMS prior to study start. This is the same NCATS review requirement as Category 1 submissions.* |
| **Title and PI of Parent Study** (if proposed research is ancillary to another study) | Click here to enter text. |
| **Is this study collecting genomic data?** **See:** [**NIH Genomic Data Sharing**](https://osp.od.nih.gov/scientific-sharing/genomic-data-sharing/)  | [ ]  Yes [ ]  No |
| **Translational Stage(s) of Research****(**[**definitions**](https://ncats.nih.gov/translation/spectrum)**)** | [ ]  Preclinical [ ]  Clinical [ ]  Clinical Implementation [ ]  Public Health  |
| **NCATS Program Director/Program Officer (PO)** | Click here to enter text. |
| **NCATS Grants Management Specialist (GMS)** | Click here to enter text. |
| **Institutional Signing Official (SO)** | Click here to enter text. |
| **Institutional QA/QC Key Personnel**  | Click here to enter text. |

## **ADDENDUM**

## **SECTION II**

**Complete #1, #2, & #3 for all UL1 Pilot Project and KL2 Scholar Project requests in line with Instructions Section III below. Complete #4 for Category 1 UL1 Pilot Projects and Category 1 KL2 Scholar Project Prior Approval requests and/or any study containing a foreign component. *Reminder:*** *All Category 1 and/or studies with a foreign component must wait for official NCATS prior approval notice from GMS before human subjects research activities may begin.*

1. Provide a brief (< 500 words) summary of the specific aspects of the proposed study that will be supported by NCATS funds.

Click here to enter text.

1. List a line-item budget for each specific aspect to be supported with NCATS funds (list supplies, services, and personnel costs). Please note: KL2 Scholar salaries should not be included in the budget.

Click here to enter text.

1. 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.

Click here to enter text.

1. **List names of Key Personnel involved in the proposed Category 1 UL1 Pilot Project or KL2 Scholar Project and/or any study containing a foreign component.**

 **Click here to enter text.**

# INSTRUCTIONS

## **SECTION I. NOTES**

* + [NIH policy,](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-179.html) requires that all Human Subjects Research (HSR) studies must be submitted via the [eRA Human Subjects System (HSS).](https://era.nih.gov/hss_overview.cfm)
		- HSS currently functions as a document repository, so e-mail should be used for communications between the submitter and NCATS Program and Grants Management staff.
		- The [HSS,](https://era.nih.gov/files/HSS_user_guide.pdf) [ASSIST,](https://era.nih.gov/files/assist_user_guide.pdf) and [Forms](https://grants.nih.gov/grants/how-to-apply-application-guide/forms-g/general/g.500-phs-human-subjects-and-clinical-trials-information.htm)-G User Guides are very useful.
		- NIH eRA HSS guidance received to date indicates that to enter a New Study, the UL1 or KL2 grant must indicate “yes” for human subjects research.
		- Inclusion enrollment monitoring is required for all human subjects research except KL2 scholar projects and HSR meeting the regulatory criteria for [Exemption 4](https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML#se45.1.46_1104). If you have questions about whether inclusion enrollment monitoring is required for your study, please contact your NCATS Program Officer.
			* NCATS compiles discrepancy reports for IER about every 2 months. These discrepancies are reported through the PO to the hub for corrections. Cumulative enrollment is expected to be monitored and updated regularly over the course of the study. IERs are required to be up-to-date prior to RPPR submission.
		- [Inclusion Across the Lifespan Policy](https://grants.nih.gov/policy/inclusion/lifespan.htm#:~:text=The%20purpose%20of%20the%20Inclusion%20Across%20the%20Lifespan,to%20all%20those%20affected%20by%20the%20researched%20diseases%2Fconditions.) requires providing age data for the enrolled participants.
	+ All new UL1 Pilot Projects and KL2 Scholar Projects with HSR must have IRB approval or institutional determination of exemption prior to submission and relevant documentation must be provided.

## **SECTION II. DOCUMENT PREPARATION, SUBMISSION, & INSTRUCTIONS**

* **Confirm** that all sections of HSS and the Addendum are completed accurately and that all required documents are included prior to submission and NCATS notification.
* **Formatting**
1. Include footers on individual PDF documents to identify (IRB-approval, biosketches, etc.) prior to combining into a single PDF document.
2. HSS only accepts PDFs and only one **combined** PDF per study uploaded to Section 2.7 or 5.1 (see below). Convert each required document into a PDF and then combine into a single PDF file in the order specified under each category, below, when applicable.
3. Do not scan to convert to PDF, as the quality will degrade.
* **Category 1:** Greater Than Minimal Risk studies and [NIH-defined Clinical Trials](https://grants.nih.gov/policy/clinical-trials/definition.htm)
	+ See Section III for a summary of NCATS required documents and eRA HSS sections to be completed.
	+ Collect specified documents as PDFs, add footers to each PDF, combine into a single PDF file in the following order, and name the combined PDF file *HSRPA1 \_CTSA Institution\_ Study PI Last Name\_Date*
		1. Addendum Sections I and II (the first 2 pages of this document)
		2. Certification of IRB-Approval
		3. Biosketches for the PI and key personnel
		4. Institutional letter attesting to completion of Human Subjects Training for PI and key personnel
		5. IRB-Approved Protocol
		6. IRB-Approved informed consent, verbal consent transcript, assent and parental permission documents, or documentation of IRB waiver (as applicable)
		7. Study Timeline
			- Greater than Minimal Risk - add the Study Timeline to the combined PDF
			- NIH-Defined CTs – upload Study Timeline to Section 2.7 as single PDF
	+ Enter new study into eRA [HSS](https://era.nih.gov/help-tutorials/hss?q=hss_overview.cfm) and upload the combined PDF to HSS Section:
		- 5.1 for NIH-Defined Clinical Trials
		- 2.7 for Greater than Minimal Risk studies
	+ SO submits the new study and required documents via eRA [HSS](https://era.nih.gov/hss_overview.cfm)
	+ SO notifies NCATS via email to assigned PO, GMS and mailbox NCATSPriorApprovalRequest@mail.nih.gov with the suggested SUBJECT line: NCATS CTSA Pilot/KL2 project HS Study XXX *{insert HSS study number}* Notification. HSR study/trial may not begin until approval is received from the Grants Management Specialist (GMS).
* **Category 2:** Minimal Risk and Exempt Studies
	+ See Section III for a summary of NCATS required documents and eRA HSS sections to be completed.
	+ Collect specified documents as PDFs, add footers to each PDF, combine into a single PDF file in the following order, and name the combined PDF file *HSRPA2\_CTSA Institution\_ Study PI Last Name\_Date*
1. Addendum Sections I and II (the first 2 pages of this document)
2. Certification of IRB-Approval
3. Study Timeline
	* Enter new study into eRA [HSS](https://era.nih.gov/hss_overview.cfm)
		+ Upload the combined PDF file to HSS Section 2.7
	* SO submits the new study and required documents via eRA [HSS](https://era.nih.gov/hss_overview.cfm)
	* SO notifies NCATS via email to assigned PO, GMS, and mailbox NCATSPriorApprovalRequest@mail.nih.gov with the suggested SUBJECT line: NCATS CTSA Pilot/ KL2 project HS Study XXX *{insert HSS study number}* Notification. Submission by the SO serves as institutional verification of the Minimal Risk or Exempt determination and completion of Human Subjects Training for PI and key personnel.
	* Failure to submit the required documentation prior to project start may result in non-compliance enforcement actions.
* **Foreign Component:** Category 1 and Category 2
	+ Any prior approval submission containing a foreign component must submit the prior approval according to the Category 1 or Category 2 instructions outlined above.
	+ No project should be authorized to move forward until official NCATS prior approvals are received via a revised Notice of Award or formal approval documentation provided by the assigned GMS. Engaging in foreign component activity prior to receiving NCATS prior approval will result in non-compliance enforcement action.
	+ The prior approval process will involve a primary review by NCATS and, unless rejected by NCATS, a secondary review through the NIH Fogarty International Center and/or U.S. Department of State. Due to the requirements for a multi-step review and oversight, the prior approval review process can take no less than 30 days, possibly significantly longer. Furthermore, NCATS reserves the right to reject any project that it deems ineligible, unallowable, and/or inappropriate given its scope of work.
	+ Information Required for FACTS Clearance:
		- Collaborator information (Name, Country, Institution/Site, Address, Phone, Email)
		- Whether the project involves HSR
		- Whether the Federal Wide Assurance (FWA) is established
		- Whether the project involves VAS (What is the animal assurance #)
		- Description of the research (preferably in plain language)
		- Amount of funding proposed to be sent to the site
	+ Compile all the required documentation into one PDF file. Submission components include:
		- Description of the planned activity to be conducted in a foreign country, with assistance of a collaborator employed by a foreign entity or a non-United States vendor, and/or with financial support or resources from a foreign entity.
		- Identification of countries with which international cooperative activities are planned.
		- Description of special resources or characteristics of the research project (e.g., human subjects, animals, disease, equipment, and techniques), including the reasons the facilities or other aspects of the proposed project are more appropriate than a domestic setting.
		- Description of how the scientific environment in which the research will be done contributes to the probability of success (e.g., institutional support, physical resources and intellectual rapport).
		- Discussion of ways the proposed studies will benefit from unique features of the scientific environment or from unique subject populations, or how studies will employ useful collaborative arrangements.
		- Specific explanation of why this activity cannot be completed in the United States.
		- For training requests: the name of the scholar/trainee and a detailed justification for the foreign training, including the reasons the facilities, the mentor, the timeline and/or other aspects of the proposed experience are more appropriate in a foreign setting.
		- If human/animal research, select agents and/or highly pathogenic agents are involved: a description of the plans for ensuring appropriate research protocol review and approval.
		- If multiple performance sites are involved: a description of the resources available at each site.
		- If any funds will be provided, detailed budget.
		- Timeline of planned activities.
	+ All requests must be submitted by the AOR from the grantee institution via email to NCATSPriorApprovalRequest@mail.nih.gov with a copy to the PO and GMS assigned to the grant.

## **SECTION III.** **SUMMARY OF NCATS REQUIRED DOCUMENTS & ERA HSS SECTIONS TO BE COMPLETED**

|  |  |  |
| --- | --- | --- |
| **NCATS REQUIRED DOCUMENTS** | **Category 11** | **Category 22** |
| **STUDY CATEGORY** | **Clinical Trial** | **Greater Than Minimal Risk Study** | **Minimal Risk3, Exempt 1-3; 5-8 Study6** | **Exemption 4** |
| **COMPLETE HSS SECTIONS5** | **1-6** | **1, 2, 3.1 & 3.2** | **1, 2, 3.1 & 3.2** | **1, 3.1 & 3.2** |
| **Addendum** | **√** | **√** | **√** | **√** |
| **Certification of IRB-Approval** | **√** | **√** | **√ or****√** |  |
| **Institutional Exemption Determination** |  |  | **√** |
| **Biosketches for PIs and key personnel** | **√** | **√** |  |  |
| **Institutional letter attesting to completion of Human Subjects Training for PI and key personnel4** | **√** | **√** |  |  |
| **IRB-Approved Protocol** | **√** | **√** |  |  |
| **IRB-Approved informed consent, verbal consent transcript, assent and parental permission documents, or documentation of IRB waiver (as applicable)** | **√** | **√** |  |  |
| ***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.)*** |

**1****Category 1 Human Subjects Research** that meets the [NIH definition of a clinical trial](https://grants.nih.gov/policy/clinical-trials/definition.htm). *Answered “Yes” to all the questions in HSS* *Section 1.4* - *Clinical Trial Questionnaire.* OR Human Subjects Research study deemed Greater than Minimal Risk by IRB.

**2****Category 2 Human Subjects Research** study deemed Minimal Risk by the IRB or study has been determined by the institution to meet the criteria for Exemptions 1-8 under [45CFR46](https://www.ecfr.gov/cgi-bin/text-idx?SID=c55504b292fe7481954eb30808ae2336&mc=true&node=pt45.1.46&rgn=div5).

**3All NIH-defined clinical trials are considered Category 1** research even if proposed research might otherwise be considered Minimal Risk.

**4Institutional letter attesting to completion of Human Subjects Training for PI and key personnel**:NIH policy ([NOT-OD-00-039](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html) & [NOT-OD-01-061](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html)) requires education on the protection of human research participants for PI and all key personnel; insert signed letter.

**5Utilize** [**G.500 – PHS Human Subjects and Clinical Trials Information**](https://grants.nih.gov/grants/how-to-apply-application-guide/forms-g/general/g.500-phs-human-subjects-and-clinical-trials-information.htm)as a guide during the preparation of any HSS Section required for Category 1 or Category 2 Prior Approval submissions.

**6**Existing data with identifiers is included in this category**.**

|  |  |  |
| --- | --- | --- |
| **eRA HSS SECTIONS to be COMPLETED6** | **Category 11** | **Category 22** |
| **STUDY CATEGORY** | **Clinical Trial** | **Greater Than Minimal Risk Study** | **Minimal Risk3, Exempt 1-3; 5-8 Study9** | **Exemption 4** |
| **HSS Section 1 – Basic Information** |
| **1.1** | Study Title | **√** | **√** | **√** | **√** |
| **1.2** | Is this Study Exempt from Federal Regulations? | **√** | **√** | **√** | **√** |
| **1.3** | Exemption Number | **√** | **√** | **√** | **√** |
| **1.4** | Clinical Trial Questionnaire | **√** | **√** | **√** | **√** |
| **1.5** | Provide the ClinicalTrials.gov Identifier | **√** |   |   |  |
| **HSS Section 2 – Study Population Characteristics** |
| **2.1** | Conditions or Focus of Study | **√** | **√** | **√** |  |
| **2.2** | Eligibility Criteria | **√** | **√** | **√** |  |
| **2.3** | Age Limits | **√** | **√** | **√** |  |
| **2.3.a** | Inclusion of Individuals Across the Lifespan | **√** | **√** | **√** |  |
| **2.4** | Inclusion of Women & Minorities | **√** | **√** | **√** |  |
| **2.5** | Recruitment and Retention Plan | **√** | **√** | **√** |  |
| **2.6** | Recruitment Status | **√** | **√** | **√** |  |
| **2.7** | Study Timeline | **√** | **√** | **√** |  |
| **2.8** | Enrollment of First Participant (Section 6.3) | **√4** | **√4** | **√4** |  |
| **2.9** | Inclusion Enrollment Report(s) | **√7** | **√7** | **√7** |  |
| **HSS Section 3 – Protection and Monitoring Plans** |
| **3.1** | Protection of Human Subjects | **√** | **√** | **√** | **√** |
| **3.2** | Is this a multi-site study? | **√5** | **√5** | **√5** | **√5** |
| **3.3** | Data and Safety Monitoring Plan | **√** | **Optional** | **Optional** | **Optional** |
| **3.4** | Data and Safety Monitoring Board | **√** | **Optional** | **Optional** | **Optional** |
| **3.5** | Overall Structure of the Study Team | **√** | **Optional** | **Optional** | **Optional** |
| **HSS Section 4 – Protocol Synopsis** |
| **4.1** | Study Design | **√** |   |   |  |
| **4.1.a** | Detailed Description | **√** |   |   |  |
| **4.1.b** | Primary Purpose | **√** |   |   |  |
| **4.1.c** | Interventions | **√** |   |   |  |
| **4.1.d** | Study Phase | **√** |   |   |  |
| **4.1.e** | Intervention Model | **√** |   |   |  |
| **4.1.f** | Masking | **√** |   |   |  |
| **4.1.g** | Allocation | **√** |   |   |  |
| **4.2** | Outcome Measures | **√** |   |   |  |
| **4.3** | Statistical Design and Power | **√** |   |   |  |
| **4.4** | Subject Participation Duration | **√** |   |   |  |
| **4.5** | FDA-Regulated Intervention? (IND/IDE) | **√** |   |   |  |
| **4.7** | Dissemination Plan | **√** |   |   |  |
| **HSS Section 5 – Other Clinical Trial Attachments** |
| **5.1** | Other Clinical Trial Attachments | **√** |   |   |  |
| **HSS Section 6 – Clinical Trial Milestone Plan8** |
| **6.1** | Study Primary Completion Date | **√8** |  |  |  |
| **6.2** | Study Final Completion Date | **√8** |  |  |  |
| **6.3** | Enrollment and Randomization | **√8** | **√8** | **√8** |  |
| **6.4** | Completion of primary endpoint data analyses | **√8** |  |  |  |
| **6.5** | Reporting of results in ClinicalTrials.gov | **√8** |  |  |  |
| **6.6** | Is this an applicable clinical trial under FDAAA? | **√8** |  |  |  |

**1Category 1 Human Subjects Research** that meets the [NIH definition of a clinical trial](https://grants.nih.gov/policy/clinical-trials/definition.htm) (*Answered “Yes” to all the questions in HSS* *Section 1.4* - *Clinical Trial Questionnaire)* OR Human Subjects Research study deemed Greater than Minimal Risk by IRB.

**2Category 2 Human Subjects Research** study deemed Minimal Risk by the IRB or study has been determined by the institution to meet the criteria for Exemptions 1-8 under [45 CFR 46](https://www.ecfr.gov/cgi-bin/retrieveECFR?gp&amp;SID=83cd09e1c0f5c6937cd9d7513160fc3f&amp;pitd=20180719&amp;n=pt45.1.46&amp;r=PART&amp;ty=HTML)

**3All NIH-defined clinical trials are considered Category 1** research even if proposed research might otherwise be considered Minimal Risk.

**4Section 2.8 Enrollment of First Participant:** This field is now Section 6.3 in HSS.Do not complete this field if you answered “YES” to the question “Using an Existing Data Set or Resources?” in the Inclusion Enrollment Report.

**5Section 3.2 Multi-site Studies**: Answer "Yes/No;" or select N/A only if: a. You answered “Yes” to “Question 1.2 Is this Study Exempt from Federal Regulations?” or b. You are a training grant applicant; or c. You are a fellowship applicant (sIRB policy does not apply to situations b, and c.). If you answer "YES" - Multi-site studies using the same protocol: Attach Plan describing how you will comply with the NIH policy on the use of single-IRB for multi-site research. N/A should be checked for K scholars.

**6Utilize** [**G.500 – PHS Human Subjects and Clinical Trials Information**](https://grants.nih.gov/grants/how-to-apply-application-guide/forms-g/general/g.500-phs-human-subjects-and-clinical-trials-information.htm)as a guide during the preparation of any HSS Section required for Category 1 or Category 2 Prior Approval submissions.

**7Section 2.9 Inclusion Enrollment Report(s)** is not required forKL2 Scholar projects and Category 4 Exempt HSR.

**8Section 6.3 Anticipated Enrollment of 1st participant** is required for all prior approval submissions except Exempt Category 4. *Even though Section 6 was initially created for clinical trials, the enrollment start/end dates must be included and updated for ALL HSR projects before submitting the RPPR.*

For clinical trials, the other fields in Section 6 will populate when the NCT number is entered in Section 1.5 and the ‘populate’ button is pushed. However, this is not required for prior approval submission but must be populated within 21 days of enrollment of the first participant. *The information from clinicaltrials.gov will populate the HSS fields so ensure the clinicaltrials.gov entry is current upon HSS completion.*

**9**Existing data with identifiers is included in this category**.**

## **SECTION IV. HSS SUBMISSION PROCESS**

* + All new HSR UL1 Pilot Projects and KL2 Scholar Projects require entry of a new study into the HSS.
	+ You can find HSS video tutorials [here](https://era.nih.gov/help-tutorials/era-training-hss.htm)
	+ Once in the HSS module, the PI/SO/QA/QC Personnel clicks the “Add New Study” button and enters all required study-related information. Complete HSS fields and attach HSS and NCATS specified documents. You can find screenshots and instructions for HSS completion starting on page 123 of the [ASSIST User Guide](https://era.nih.gov/files/assist_user_guide.pdf).
* Once the study is saved, it will be added to the *Study Record* table.
* Please ensure that these steps have been taken when entering a New Study:
	+ Save & Keep Lock/Save & Release Lock: PI, SO, or QA/QC Personnel
	+ Ready for Submission: PI, SO, or QA/QC Personnel
	+ Submit: SO only
	+ After submission of a study by the SO, the study status must be changed manually to “Work In Progress.” This will allow another New Study to be added.
* SO notification to NCATS of submission of a new HSR study to HSS: see Section III above for instructions.

## **SECTION V. HSS BACKGROUND INFORMATION**

* eRA Human Subjects System

NIH developed the Human Subjects System (HSS), which consolidates human subjects and clinical trial information in one place, as part of its larger effort to comply with 21st Century Cures requirements to enhance accountability and transparency in NIH clinical research. HSS is a shared system, used both by principal investigators and signing officials on one hand and by NIH staff on the other. The system was launched in June 2018 and replaced the Inclusion Management System (IMS) used for reporting participant sex/gender, race, and ethnicity information. HSS is accessed via the Human Subjects link in eRA Commons (via the Status tab or the RPPR tab). The Human Subjects link will only be visible if the application/grant is marked “yes” for human subjects research.

* CTSA Award Recipient Features in HSS
	+ Pre-award (post review) for just-in-time information or correction of human subjects data
	+ Post-award to add/update human subjects study information; create new inclusion enrollment reports; or view/edit/update existing enrollment data when submitting a Research Performance Progress Report (RPPR)
		- Complete study start and end date in section 6.3 (Note: start and end date for clinical research and clinical trials can be updated in this section).
	+ Off-cycle updates as required in the Funding Opportunity Announcement or terms and conditions of award, e.g., to add a New Study for Prior Approval
	+ Provide interim data as requested by NIH staff
	+ Inform NIH of ClinicalTrials.gov registration

Important Note: The Human Subjects and Clinical Trials Information form appears for all recipients with human subjects studies. However, those who submitted competing applications prior to January 25, 2018 only need to update inclusion data via the Human Subjects link in the RPPR. The remaining fields (e.g., milestones) are not required to be filled out.

Those who submitted applications on or after January 25, 2018, may need to fill out more fields than the inclusion data for their RPPR.

## **SECTION VI. NCATS REVIEW PROCESS & RESPONDING TO REQUESTS FOR CLARIFICATION OR ADDITIONAL INFORMATION**

*Reminder: Award funds may be spent on non-human subjects research activities before NCATS Prior Approval as long as other NCATS prior approval requirements do not apply (e.g., for research involving live vertebrate animals and/or foreign component).*

* + Category 1
		- NCATS will conduct a review, primarily of the safety aspects of the described study/trial, and an administrative review of required documents. NCATS will initiate review of the request and notify (via email) the PI/SO of the outcome within 30 calendar days. NCATS may request clarification or revisions via email to the SO. SOs should:

 a. Submit any clarifications/revisions into the eRA HSS module, and

 b. Send an email response to NCATS that includes a description of the changes to the documents.

* + - Please note that if a request is returned for any reason, the 30-day turnaround time resets. HSR study/trial may not begin until approval is received from the GMS.
	+ Category 2
		- NCATS will conduct a timely, high-level review to confirm that the described study appears to meet Category 2 criteria and will conduct an administrative review of required documents. NCATS may submit questions to the institution and require the site to stop HSR activities if the submitted documentation does not support Category 2 criteria.
	+ Foreign Components
1. The AOR submits an official request to add a foreign study site to the award to GMS and PO.
	1. The PO reviews the request and upon internal NCATS approval submits through the Foreign Award and Component Tracking System (FACTS) for additional review.
2. For most countries, the request is approved and sent back to NCATS.
3. NCATS/GMS sends official approval to the AOR. Human subjects activity may not begin until this official approval is received by the institution. This process may take 30 calendar days or more and if any clarification or revisions are requested the turnaround time resets.
4. The foreign component and Category 1 or 2 prior approvals may be submitted concurrently. However, the foreign component will need to be approved before the Category 1 or 2 prior approval is formally issued.

**Process Overview**

# APPENDIX

## **SECTION I. DEFINITIONS**

* NIH Definition of [Clinical Research](https://grants.nih.gov/grants/glossary.htm#ClinicalResearch): Research with human subjects that is: 1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. It includes: (a) mechanisms of human disease, (b), therapeutic interventions, (c) clinical trials, or (d) development of new technologies. 2) Epidemiological and behavioral studies. 3) Outcomes research and health services research.
* NIH Definition of [Clinical Trial](https://grants.nih.gov/policy/clinical-trials/definition.htm): A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.
* HHS Definition of [Human Subjects Research](https://grants.nih.gov/policy/humansubjects/research.htm): According to 45 CFR 46 Link to Non-U.S. Government Site - Click for Disclaimer, a human subject is "a living individual about whom an investigator (whether professional or student) conducting research:
* Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
* Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.”
	+ New Study means that a study was not included in the grant application; studies are identified and added after award. You include none of the required supporting material with the application. A new human subjects project must be entered into the HSS as a NEW STUDY and may require Prior Approval from your NCATS Program Director and Grants Management Official. *Reminder: NCATS requires that IRB approval or institutional determination of exemption be obtained prior to entry into the HSS.*

## SECTION II. PAY PARTICULAR ATTENTION TO THE FOLLOWING

* **Most Common Issues with Prior Approval Requests**
	1. Inaccurate/incomplete HSS fields
	2. Incomplete submissions (missing, inaccurate, or inconsistent documents; inadequate information)
	3. Overall quality of the materials
	4. Adherence to NIH and NCATS policies
* **NCATS Phase III Clinical Trial Policy (NIH Guide Notice** [**NOT-TR-18-025**](https://grants.nih.gov/grants/guide/notice-files/NOT-TR-18-025.html)**)**
	+ NCATS is prohibited from direct funding of NIH-defined Phase III CT unless the target is a [rare disease or condition](https://www.govinfo.gov/content/pkg/USCODE-2015-title21/html/USCODE-2015-title21-chap9-subchapV-partB-sec360bb.htm), and follows specific steps prior to funding (public notice for ≥120 days )
	+ Please refer to NIH-approved definitions of clinical trials [here](https://grants.nih.gov/policy/clinical-trials/glossary-ct.htm)
* **Accurate completion of the Human Subjects System “PHS Human Subjects and Clinical Trials Information” Section, including accurate identification of clinical trials**
	+ Pilot Project study investigator/KL2 Scholar should review the available resources to clarify definitions (i.e., case studies, FAQs and decision tree) at <https://grants.nih.gov/policy/clinical-trials/definition.htm> and consult with a clinical trial specialist at the CTSA hub or a designated [point of contact for quality assurance/quality control](https://grants.nih.gov/grants/guide/notice-files/NOT-TR-20-014.html) (QA/QC) before submitting information to include in the study record to the institutional POC.
	+ If a pilot/project is extended (without need for a [prior approval request](https://ncats.nih.gov/ctsa/funding/prior-approval-paga) for carryover of the budget) due to unforeseen circumstances but the science, scope, and risk level remains the same as the originally submitted and approved pilot, the extended project can proceed without an additional prior approval if all prior documentation covers the extended period.
	+ If a study meets the criteria for an NIH-defined clinical trial, the UL1/TL1 Pilot Project study investigator/KL2 Scholar must comply with the registration and reporting requirements for Applicable Clinical Trials (<https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf>) and/or the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information.
* **Inclusion Enrollment Information:**
	+ The Planned Enrollment Table in the Inclusion and Enrollment Report (IER) ASSIST 2.9 must be accurate (number of participants, racial categories, and ethnic categories) and must match the described project and all supporting documentation. Note: The Actual (Cumulative) Enrollment Table must be updated in the IER (ASSIST 2.9) at the time of submission of the annual RPPR including and [age at enrollment](https://grants.nih.gov/policy/inclusion/lifespan.htm#:~:text=The%20purpose%20of%20the%20Inclusion%20Across%20the%20Lifespan,to%20all%20those%20affected%)
	+ <https://era.nih.gov/erahelp/assist/Content/ASSIST_Help_Topics/3_Form_Screens/PHS_HS_CT/Incl_Enroll_Rprt.htm>
	+ Inclusion policies: <https://grants.nih.gov/policy/inclusion.htm>
* **Research Involving Prisoners**
	+ In addition to Subpart C of the Common Rule (45 CFR 46), an institution that intends to conduct HHS-supported research involving prisoners as subjects must certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a), including the finding that the proposed research represents one of the permissible categories of research under 45 CFR 46.306(a)(2).
	+ In general, research involving prisoners cannot be designated as exempt from regulatory requirements. However, the revised Common Rule exempts (46.104(b)(2) research “aimed at involving a broader subject population that only incidentally includes prisoners”.
	+ More detailed information about Biomedical and Behavioral Research Involving Prisoners as Subjects:
		- Subpart C—Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects: <https://www.ecfr.gov/cgi-bin/text-idx?SID=c55504b292fe7481954eb30808ae2336&mc=true&node=pt45.1.46&rgn=div5>
		- Guidance on Approving Research Involving Prisoners: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/prisoner-research-certification/index.html>
		- Prisoner Research Certification: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/prisoner-research-certification/index.html>
		- Prisoner Research FAQs: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/prisoner-research/index.html>
* **Foreign Components**
	+ Adding a foreign component under a grant to a domestic or foreign award requires NCATS prior approval. This includes the addition of a performance site or research project in a country other than that specified in the competing application and/or a change in the performance site within a foreign country. The transfer of work by a domestic award recipient to a foreign entity also requires NCATS prior approval. For more information on the submission of a prior approval request to add or change a foreign component, please refer to the NCATS website ([here](https://ncats.nih.gov/funding/grantees/approval#foreign-components)).
* **Human Fetal Tissue Policy**
	+ CTSA Hubs must contact the assigned Program Officer and Grants Specialist of any potential use of human fetal tissue prior to submitting the research project in to the HSS system. Any proposed use of human fetal tissue research supported via direct funding and/or voluntary committed cost share requires NCATS prior approval before the study may begin. Please refer to recent guidance issued by NIH on the proposed use of human fetal tissue. [https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-111.html](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-111.html%20)

## **SECTION III. RESOURCES**

* + OER Inclusion inbox for HSS and inclusion policy-related questions: inclusion@od.nih.gov
	+ <https://humansubjects.nih.gov/>
	+ [45CFRPart46](https://www.ecfr.gov/cgi-bin/text-idx?SID=c55504b292fe7481954eb30808ae2336&mc=true&node=pt45.1.46&rgn=div5)
	+ https://era.nih.gov/hss\_training.htm
	+ <https://era.nih.gov/files/HSS_user_guide.pdf>
	+ https://era.nih.gov/files/assist\_user\_guide.pdf
	+ [https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/format-](https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/format-attachments.htm)  [attachments.htm](https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/format-attachments.htm) (required format of attachments)
	+ <https://ncats.nih.gov/ctsa/funding/prior-approval-faq>
	+ <https://grants.nih.gov/policy/clinical-trials/human-subjects-system.htm>
	+ [https://era.nih.gov/erahelp/assist/Content/ASSIST\_Help\_Topics/3\_Form\_Screens/PHS\_HS\_CT/PHS\_Summary.htmh](https://era.nih.gov/erahelp/assist/Content/ASSIST_Help_Topics/3_Form_Screens/PHS_HS_CT/PHS_Summary.htm)
	+ <https://ncats.nih.gov/ctsa/funding/prior-approval-faq#clarification>
	+ <https://grants.nih.gov/grants/funding/inclusion-basis-on-sex-gender-race-ethnicity-faq.htm#5510>
	+ <https://grants.nih.gov/grants/funding/women_min/inclusion_training.htm>
	+ <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-g/general-forms-g.pdf>
	+ <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-g/multi-project-forms-g.pdf>

Join the QA/QC Discussion Forum to connect with others who submit NCATS prior approval.

* The QA/QC Discussion Forum (DF) can be accessed from the CLIC website: <https://clic-ctsa.org/groups/discussion-forums>
* Scroll down to the ***NCATS CTSA Program Quality Assurance/Quality Control Group***
* For questions or other assistance with the DF, please contact support@ctsa.io.
* Contact the Discussion Forum: ctsa-qaqc-discuss@ctsa.io.

**For assistance with this Addendum or requested content, please contact** **NCATSDOPAinquiry@mail.nih.gov**

**For assistance with the eRA HSS, please contact the eRA Service Desk** <https://grants.nih.gov/support/index.html>

**Toll-free:** 1-866-504-9552 (Press 1 for eRA Commons or ASSIST)

**Phone:** 301-402-7469 (Press 1 for eRA Commons or ASSIST)

**Hours:** Mon-Fri, 7 a.m. to 8 p.m. ET (closed on federal holidays)