SINGLE IRB &
the EXCEPTIONS REQUEST PROCESS
for
THE RESEARCH COMMUNITY
OCTOBER 18, 2017

National Institutes of Health

Office of Extramural Programs

LEARNING OBJECTIVES

- Recognize the key aspects of the NIH sIRB Policy
- Understand the requirements for compliance with NIH sIRB Policy
- Understand the process for requesting exceptions
- Know where to find information and resources

PRESENTATION OUTLINE

- Overview of the NIH sIRB Policy
- Implementation Guidance for Grants and R&D Contracts
- sIRB Exceptions Process for Grants and R&D Contracts
- Grant Application Budgets
- sIRB Under R&D Contracts
- Resources

OVERVIEW OF THE NIH SINGLE IRB POLICY

Speaker:
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GOALS of the SINGLE IRB POLICY

- Enhance and streamline IRB review for multi-site research
- Maintain high standards for human subjects protections
- Allow research to proceed effectively and expeditiously
- Eliminate unnecessary duplicative IRB review
- Reduce administrative burden
- Prevent systemic inefficiencies
- Compatible with final revised Common Rule requirement to use single IRBs for multi-site studies

NIH SINGLE IRB POLICY

- NIH-funded multi-site domestic studies involving non-exempt human subjects research are expected to use a single IRB
  - Conducting the same protocol
  - All Human Subjects; not just Clinical Trials
  - All new and re-competing applications/proposals
  - Grants and R&D Contracts

- Policy does not apply to:
  - Foreign sites
  - Career development (K), institutional training (T), and fellowship awards (F)
  - Current awards

NIH SINGLE IRB POLICY EXCEPTIONS

- **Policy-based Exceptions:**
  - When Federal, State, Tribal, local laws/regulations/policies require local review
    - Tribal regulations/policies given specific consideration in order to ensure that the importance of their role is recognized
    - Does not require NIH Exceptions Review Committee approval

- **Time Limited Exceptions:**
  - When ancillary studies are part of ongoing studies or parent studies
    - Do not require sIRB until the parent study is expected to comply with the sIRB policy

NIH SINGLE IRB POLICY EXCEPTIONS (CONT'D)

- **Compelling Justification or Other Exceptions:**
  - When there is a compelling justification for local IRB review
    - Requires NIH Exceptions Review Committee approval

NIH SINGLE IRB POLICY

Published in NIH Guide and Federal Register: June 21, 2016

- Full Policy: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html
- Notice of Extension: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-076.html
- Cost Scenarios: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-109.html
- Implementation: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-004.html
- Exceptions: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-003.html

Effective Dates (Extended)

- All competing grant applications (new, renewal, revision or resubmission)

  Application due dates on/after **January 25, 2018**

- Contract proposals

  Solicitations issued on/after **January 25, 2018**

POLICY IMPLEMENTATION FOR GRANTS and R&D CONTRACTS

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SINGLE vs CENTRAL IRB

A Single IRB is selected on a study-by-study basis; usually is an existing IRB that agrees to serve as the IRB of record for a particular study.

A Central IRB reviews for all sites participating in a program that usually includes more than one multi-site study. Often is established specifically for this purpose (e.g., NCI Central IRB).

Unless required by the FOA or contract solicitation you do not have to create a Central IRB. For many studies your institution's IRB can serve as the single IRB of record.

POSSIBLE IRB MODELS

IRB models that would meet the policy:

1. Existing IRB can agree to serve as sIRB
   - Awardee or participating site
2. Independent/Unaffiliated IRB
3. Central IRB organized to review specific projects

Single IRB of record does not have to be the IRB of the parent award.

It is the best IRB for the study.

NOTE: sIRB must be registered with OHRP and must have membership to adequately review the proposed study

CHOOSING the SINGLE IRB

- **FOA or solicitation** may **describe any specific requirements** to meet policy (such as intent to set up a Central IRB for project)

1. **All sites known** at time of application/proposal
   - A. Single award with sub-award sites
   - B. Linked Awards w/ same protocol (each site has award)

   } Site IRB or Independent IRB to serve as sIRB; Identify in application

2. Sites not **known until after review**
   - A. Multiple site awards plus an award for central coordinating entity

   → Central entity can serve or responsible for sIRB

   - B. Multiple site awards without a central coordinating entity

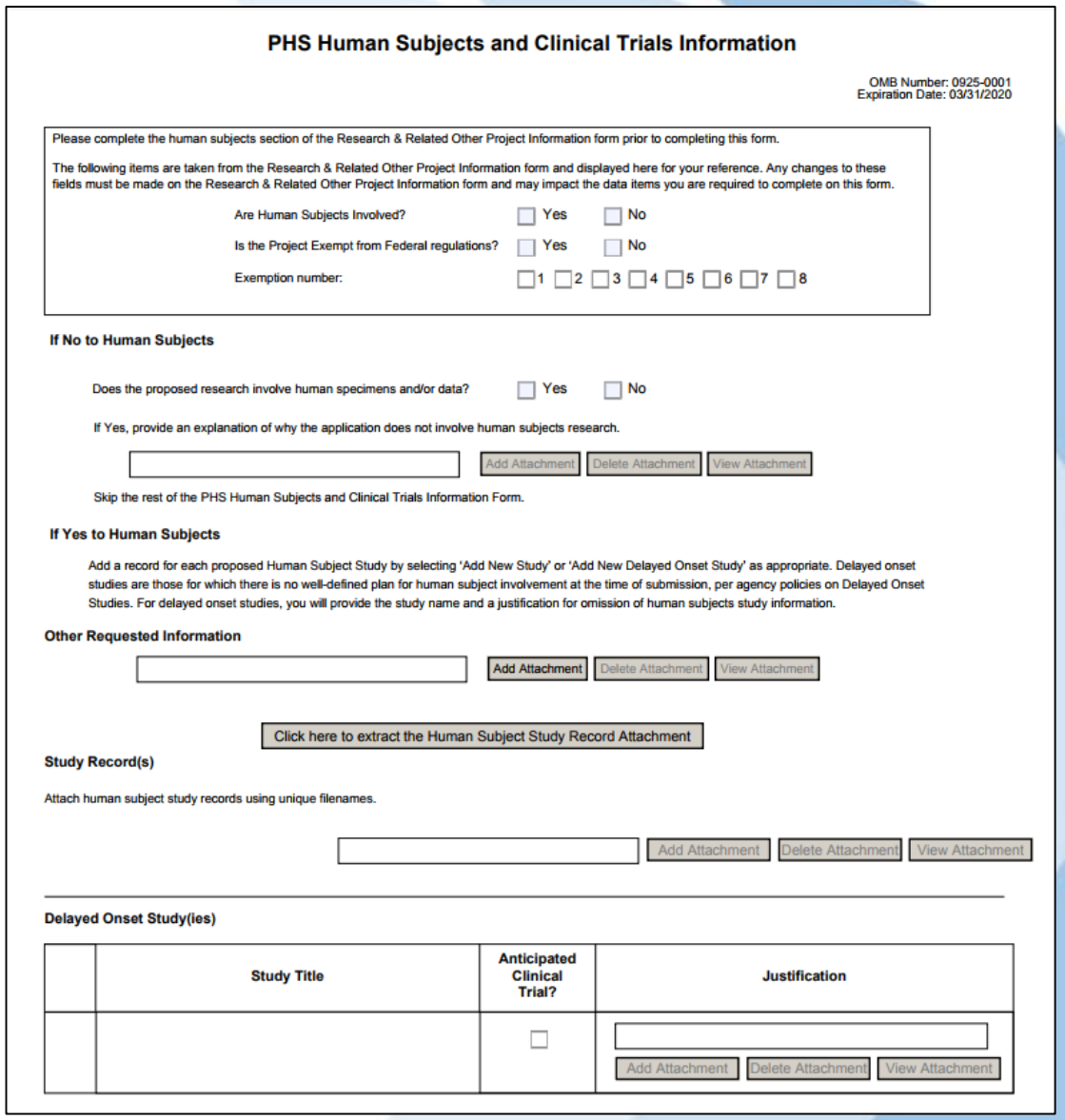
   → For Cooperative agreements – IC work with awardee sites to select the sIRB
   or
   Require sites use a Central IRB

CHOOSING the BEST IRB

- Participating sites should work together ahead of time to determine the best IRB for the study
- Make sure that reliance agreements are in place and up to date
- May include working with local IRBs to determine the best IRB, gather relevant local context and policies

INTRO TO FORMS-E

- NOT-OD-17-062
- Due dates on/after January 25, 2018
- 5 sections
- All human subjects research
  - Some Clinical Trials specific
- Individual study records; one/protocol
- Structured data
  - Some information shuffled a bit
- Aligns with ClinicalTrials.gov information
- Section 3.2 – Single IRB Plan



PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Please complete the human subjects section of the Research & Related Other Project Information form prior to completing this form.

The following items are taken from the Research & Related Other Project Information form and displayed here for your reference. Any changes to these fields must be made on the Research & Related Other Project Information form and may impact the data items you are required to complete on this form.

Are Human Subjects Involved? ☐ Yes ☐ No

Is the Project Exempt from Federal regulations? ☐ Yes ☐ No

Exemption number: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8

If No to Human Subjects

Does the proposed research involve human specimens and/or data? ☐ Yes ☐ No

If Yes, provide an explanation of why the application does not involve human subjects research.

Add Attachment | Delete Attachment | View Attachment

Skip the rest of the PHS Human Subjects and Clinical Trials Information Form.

If Yes to Human Subjects

Add a record for each proposed Human Subject Study by selecting 'Add New Study' or 'Add New Delayed Onset Study' as appropriate. Delayed onset studies are those for which there is no well-defined plan for human subject involvement at the time of submission, per agency policies on Delayed Onset Studies. For delayed onset studies, you will provide the study name and a justification for omission of human subjects study information.

Other Requested Information

Add Attachment | Delete Attachment | View Attachment

Click here to extract the Human Subject Study Record Attachment

Study Record(s)

Attach human subject study records using unique filenames.

Add Attachment | Delete Attachment | View Attachment

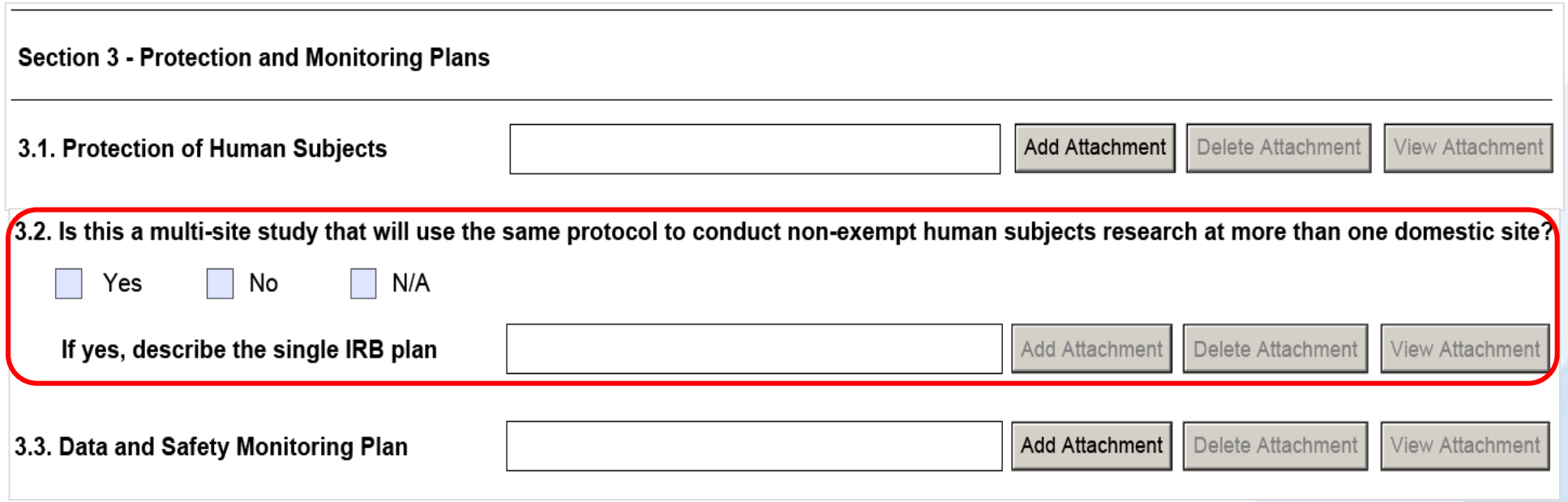
Delayed Onset Study(ies)

	Study Title	Anticipated Clinical Trial?	Justification
		☐	Add Attachment | Delete Attachment | View Attachment

Instructions available at: https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general-forms-e.pdf

IMPLEMENTATION

- sIRB should be identified by applicant/offeror in the sIRB plan
  - NOTE: New FORMS-E effective for due dates on/after January 25, 2018 (see NOT-OD-17-062).
- Application Guide Instructions https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm



If Yes, must add the Single IRB Plan as an attachment.

Ks and Fs and exempt HS may check "N/A"

SINGLE IRB PLAN

- Name of the sIRB of record
- Indicate that:
  - All sites, including any added after award, agree to rely on sIRB
  - Sites will sign reliance agreement that will include a communication plan
  - Indicate who will maintain records of this agreement
- Exceptions
  - **Policy-based exceptions** - legal or regulatory: provide specific citation and indicate which sites are impacted
  - **Time-limited exceptions**, provide parent study information
  - **Compelling Justification exceptions,** identify sites and provide justification

Budget as if no *Compelling justification exception*

Several protocols may have one sIRB plan for all

You may either attach the same sIRB plan (with different file names) to different studies or attach a file that refers to the sIRB plan in another study within your application.

If delayed onset, in justification include statement that awardee will follow the policy and will provide sIRB info prior to start

Application Guide Instructions

SINGLE IRB PLAN ATTACHMENT

- Single IRB plan is an attachment
- No page limits
- sIRB should be identified by applicant/offeror in the sIRB plan within the application/proposal.
- Do not include the reliance agreement(s) or communication plans
- If study is delayed onset, include information regarding compliance with the NIH sIRB Policy in the delayed onset study justification; a complete sIRB plan must be provided to IC prior to initiating study

PEER REVIEW OF sIRB

- Information provided relating to sIRB **NOT** considered
  - in overall scoring

    OR
  - in overall rating of Protection of Human Subjects section

- Peer reviewers may note if policy appears to be applicable to the proposed research but application did not include a sIRB plan

- For grants, peer reviewers are encouraged to allow flexibility in budget requests while sIRB costing is still being assessed

REQUESTING A SINGLE IRB EXCEPTION FOR GRANTS AND R&D CONTRACTS

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NIH SINGLE IRB POLICY EXCEPTIONS

- **Policy-based Exceptions:**
  - **Do not require** NIH Exceptions Review Committee approval
- **Time-limited Exceptions:**
  - **Do not require** NIH Exceptions Review Committee approval
- **Compelling Justification Exceptions:**
  - **Requires** NIH Exceptions Review Committee approval

POLICY-BASED EXCEPTIONS

In the Single IRB Plan (separate PDF attachment):

- Identify the site(s) that are eligible for a policy-based exception
- Cite the law or policy that requires local IRB review

- Budget should be prepared as if policy-based exception site will use local IRB review, i.e. do not include policy-based exception sites in single IRB budget

- Prior notification is required for policy-based exceptions sites added after award

TIME LIMITED EXCEPTIONS

- **Ancillary Studies to Ongoing Research without a Single IRB:**
  - Not required to use a sIRB until the parent study is expected to comply with the sIRB policy.
  - Must be documented in the sIRB plan
    - Specify associated parent study
  - NOT-OD-18-003 provides guidance on exceptions to the NIH sIRB policy, including *time limited* exceptions

COMPELLING JUSTIFICATION EXCEPTIONS

In the Single IRB Plan (separate PDF attachment):

- Identify the site(s) for which an compelling justification is requested
- Provide compelling justification for local IRB review

- Budget should include costs associated with single IRB review only, i.e. prepare budget as if compelling justification exception **will NOT** be granted

- Prior approval is required for compelling justification exceptions sites added after award

COMPELLING JUSTIFICATION EXCEPTIONS (CONT'D)

- Will be evaluated by an internal NIH Exceptions Review Committee
- Program director will be point of contact for grant applicants
- CO will be point of contact for contract applicants
- sIRB exceptions are anticipated to be rare
- Case studies/FAQs will be developed to prevent repetitive requests

GRANT APPLICATION BUDGETS

Speaker:
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sIRB COSTS

- Policy allows, but does not require, sIRB costs to be direct charged.
- sIRB costs may be charged direct if:
  - Institution can differentiate the costs that are charged direct vs. indirect.
  - Cost incurred for the same purpose in like circumstances are treated consistently as either direct or indirect
- It is an institutional responsibility to determine if sIRB costs are appropriately classified as direct or indirect.
- Since cost principles remain unchanged, if using sIRB prior to the January 25, 2018 implementation date, applicants may choose to include sIRB costs in their direct cost budget.

COSTS ASSOCIATED WITH sIRB REVIEW

- NOT-OD-16-109 provides sIRB costing guidance

- Primary activities:
  - Activities associated with conducting the ethical review of the proposed research protocol and the review of the template informed consent document.
  - These routine activities are usually included in F&A rate
- Secondary activities:
  - Activities associated with the review of site specific considerations (unlike circumstances) for all of the participating sites.
  - Project-specific activities “above and beyond” IRB review of human subjects research

EXAMPLES OF COST MODELS

- Fee structure established by institution
- Recharge or service center (specialized service facility; see 45 CFR 75.468)
- Remove all IRB costs from F&A pool
- Independent/commercial IRB
- Other options determined by institution

APPLICATION BUDGET PAGES

If requesting direct costs:

- The institution that is incurring sIRB costs should include the sIRB costs on their budget page.
  - Other sites that are not serving as the sIRB should not have IRB costs included in their budgets.
  - See NOT-OD-16-109 for table of examples
- List costs under the appropriate detailed budget category – Other Direct Costs category, or other categories as appropriate.
- Provide support for costs in narrative budget justification.

GRANT BUDGETS & EXCEPTIONS

- Policy-Based Exceptions & Time-Limited Exceptions
  - Applicant should account for the exception in the application budget, since these are standing exceptions
  - Sites not using the single IRB should not generate sIRB costs

- Compelling Justification Exceptions
  - The proposed budget must reflect any necessary sIRB costs without an exception (i.e., applicants should not assume that an exception will be granted when considering what sIRB costs to include in the budget)
  - If exception is approved: budget will be adjusted prior to award, to remove any sIRB costs for the excepted site(s)

SINGLE IRBs UNDER R&D CONTRACTS

Speaker:
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CONTRACT IMPLEMENTATION

- Applies to all solicitations issued on/after January 25, 2018 for NIH-funded multi-site research involving non-exempt human subjects research
- sIRB will be a requirement of the contract
- Same policy-based and *time limited* exceptions are allowed and must be specified in the proposal
- Compelling justification exceptions expected to be rare/infrequent

POTENTIAL sIRB MODELS

- Single Contract Award with Multiple Sites
  - One Contractor with Multiple Subcontract Sites
- Multiple Contract Awards with a Contract Research Organization (CRO) or Coordinating Center Responsible for sIRB
- Multiple Contract Sites with Separate sIRB
  - Standing IRB under Contract (NCI CIRB)
  - Separate IRB award for only the IRB (Stand Alone Contract or Task Order)

SINGLE CONTRACT AWARD WITH MULTIPLE SITES

- Single Contractor with Subcontractors
- sIRB is Responsibility of the Contractor
- sIRB may be the Contractor or a Subcontractor

MULTIPLE CONTRACT AWARDS WITH A CRO OR COORDINATING CENTER

- CRO/Coordinating Center is Responsible for sIRB

- Contracts with Individual sites require sites to accept CRO/Coordinating Center as sIRB

MULTIPLE CONTRACTS WITH SEPARATE sIRB

- sIRB may be an Existing sIRB or a separate contract or task order

- Contracts with Individual sites require sites to accept Government Provided sIRB (Contract/Task Order)

SINGLE VERSUS MULTIPLE CONTRACTORS

- Single Contractor
  - Use HHSAR 352.270-4(a)
  - Proposal will need to address sIRB
    - sIRB must be registered with OHRP
    - sIRB Membership must be adequate for review of the study
  - Contracting Officer Representative (COR) and Contracting Officer (CO) will consider acceptability of sIRB plan

- Multiple Contractors
  - Contract can use the Alternate I language of HHSAR 352.270-4(a)
  - Proposal needs to state the Contractor agrees to the sIRB provisions

PROPOSED sIRB PLAN – SINGLE AWARD

- Name of the sIRB of record
- Document:
  - Agreement that all sites accept sIRB
  - Procedures for meeting sIRB Policy
    - sIRB Composition
    - Records Maintenance
    - Reliance Agreements
    - IRB Approvals, etc.
- Exceptions
  - Policy Based – Indicate affected site(s) and the law/regulation requiring local IRB
  - Time Limited – Indicate parent study
  - Compelling Justification– Provide rationale

sIRB COSTS

- sIRB Costs may be Direct or Indirect
- sIRB costs should be proposed and billed in accordance with
  - Offeror's Accounting System
  - Negotiated Indirect Cost Rate Agreement
- Offerors must comply with FAR Parts 30 and 31

EXCEPTIONS UNDER CONTRACTS

Budget as if no compelling justification exception

- **Policy Based Exceptions**
  - Identify Site(s) Affected
  - Cite Law or Policy that requires local IRB
- **Time Limited Exceptions**
  - Identify parent study
- **Compelling Justification Exceptions**
  - Identify Site(s) Affected
  - Provide Compelling Justification
  - Exceptions are only considered for proposals in the competitive range
  - Must be reviewed and approved by NIH Exceptions Review Committee

BUDGET PROPOSALS

- Proposal should **NOT** budget for compelling justification exceptions
  - Budget may be adjusted if exception is granted
- Compelling justification exceptions *in competitive range* must be submitted to NIH Exceptions Review Committee by Contracting Officer.
- If a request for compelling justification exceptions is granted, costs may be revised during negotiations.

PEER REVIEW OF sIRB –

- Information provided relating to sIRB **NOT** considered
  - in overall scoring

    OR
  - in overall rating of Protection of Human Subjects section
- Peer reviewers may note if policy appears to be applicable to the proposed research but the proposal did not include a sIRB plan

SUMMARY: COMPELLING JUSTIFICATION EXCEPTIONS

- Exception site(s) should be identified in sIRB plan in the proposal
- Offeror must provide compelling justification for exception(s)
- Reminder: Budget as if no compelling justification exception granted
- Compelling justification exception requests will only be considered for offerors in the competitive range

CONTRACT EXCEPTIONS PROCESS

- Contracting Officer submits compelling justification exception requests to the NIH Exceptions Review Committee
- NIH Exceptions Review Committee will make a decision based upon the justification and supporting documentation
- Request may be denied based on the NIH Exceptions Review Committee's past precedent
- Contracting Officer will communicate NIH Exceptions Review Committee's decision to Offeror during Negotiations
- Budget negotiations may be impacted by the NIH Exceptions Review Committee's decision

SINGLE IRB CHALLENGES & RESOURCES

Speaker:
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CHALLENGES

- **Infrastructure/Technologies**
  - Capacity to facilitate tracking and sharing of sIRB related documents across multiple sites
- **Negotiation of Reliance/Authorization Agreements**
  - Willingness to use a Master Agreement
  - Ability to clearly define roles and responsibilities of sIRB and local IRBs
- **Budget Development Challenges**
  - Cost considerations vary across studies

NCATS SMART IRB RELIANCE PLATFORM

- **Single IRB Authorization Agreement**
  Eliminates time and effort required to negotiate agreements for each new study.
- **Supports National Collaboration**
  All CTSA Institutions signed
  >240 additional institutions signed
- **Guidance & Resources**
  SOPs, educational materials, tools, and checklists help clarify roles, responsibilities
- **Expertise across the Nation**
  Ambassadors and IRB experts available to help with adoption and implementation
- **Flexible and inclusive**
  SMART IRB is open all FWA holding institutions.
  It supports all kinds of research – biomedical, social/behavioral and observational, regardless of funding
- **Online Sharing**
  Centralized systems support sign-on and reliance arrangements (in pilot)
  SMARTIRB.org
- **Trial Innovation Network Central IRBs**
  Will operationalize SMART IRB Agreement and SOPs
  TrialInnovationNetwork.org

Sign up for the newsletter

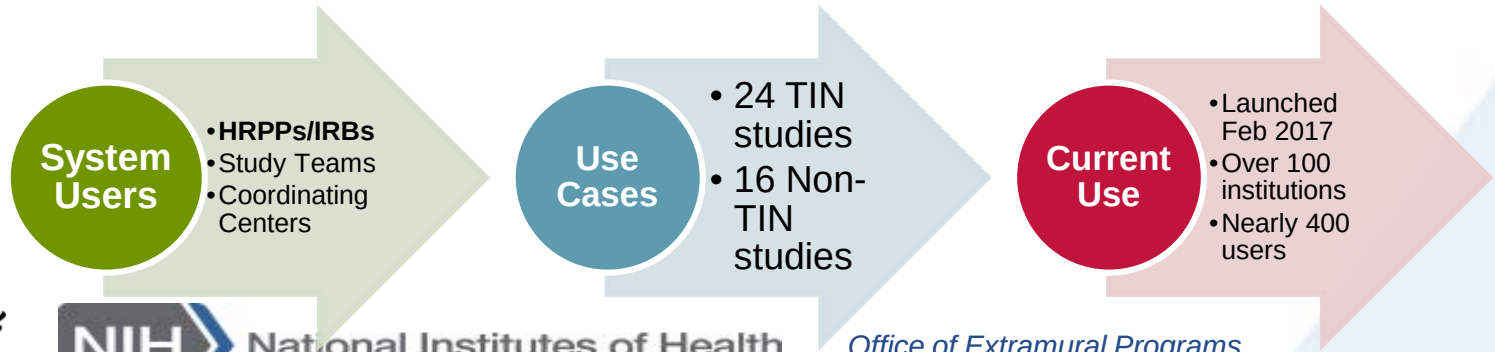
SMART.IRB.Model@ncats.nih.gov or help@smartirb.org

SMART IRB EXCHANGE

"The Exchange" is a web-based platform developed to support the IMPLEMENTATION of sIRB review from study start up to study close.

- A tool for **IRBs** to document and track IRB reliance relationships
- A tool for **IRBs** and **study teams** to manage documents for Participating Sites
- A tool for **IRBs** to streamline and automate study-related notifications to Participating Sites
- A tool for **coordinating centers** to monitor study start up and manage approvals
- ***Coming Soon:*** *A tool for* ***IRBs*** *and* ***study teams*** *to centralized the capture of local considerations*

- **Supported by the Duke-Vanderbilt Trial Innovation Center (TIC)**



Sign onto the SMART IRB Exchange Portal Access Form (IT agreement)

Learn More:

https://trialinnovationnetwork.org/smart-irb-exchange/

Contact Us:

admin@SMARTIRBExchange.org

KEY TAKE-AWAY MESSAGES

- Effective date: **January 25, 2018** for competing grant applications and R&D contract solicitation publications
- Applies to: Domestic sites conducting the same non-exempt human subjects research protocol
- Does not apply to:
  - Ks, Ts, and Fs
  - Foreign sites

KEY TAKE-AWAY MESSAGES: EXCEPTIONS

- Three types of exceptions
  - Policy-based – legal requirement for local IRB review
    - NIH should be informed
    - Cite law in Single IRB plan
  - Time limited exceptions
    - NIH should be informed
    - Site parent study
  - Compelling justification exceptions
    - Requires NIH approval
    - Must have compelling justification

KEY TAKE-AWAY MESSAGES : EXCEPTIONS PROCESS

- Applicant/offeror should identify exception requests in sIRB Plan
- Policy-based exceptions are automatic
- Time limited exceptions allowed for ancillary studies with ongoing parent studies
- Compelling justification exceptions must be approved by NIH Exceptions Review Committee
- Request may be denied based on the NIH Exceptions Review Committee's past precedent

KEY TAKE-AWAY MESSAGES: PEER REVIEW

- Single IRB plan does NOT factor into score or overall rating of HS section

- Reviewers and SROs will note if sIRB plans not addressed in application or proposal

sIRB IMPLEMENTATION RESOURCES

- Policy Web Page: https://grants.nih.gov/policy/clinical-trials/single-irb-policy-multi-site-research.htm
- Guide Notices: OD-16-094, OD-17-076, OD-16-109 (costs), OD-18-003, OD-18-004
- OSP Webpage: https://osp.od.nih.gov/clinical-research/irb-review/
  - Implementation FAQs: https://osp.od.nih.gov/clinical-research/implementation-of-the-sirb-policy/
  - Cost FAQs: https://osp.od.nih.gov/clinical-research/nih-policy-on-the-use-of-a-single-irb-for-multi-site-research-faqs-on-costs/
- OER Webinars: https://grants.nih.gov/news/virtual-learning/upcoming_webinars.htm
- Mailboxes
  - SingleIRBpolicy@mail.nih.gov
  - GrantsCompliance@nih.gov
- SMART IRB: https://smartirb.org/
- SMART IRB Exchange: https://trialinnovationnetwork.org/home-page/smart-irb-exchange/
- Clinical Trials Transformation Initiative (CTTI): https://www.ctti-clinicaltrials.org/projects/central-irb

THANK YOU