Welcome to the
Pre-Application Webinar for RFA-NS-19-022:

Biological Measures for Prognosing and Monitoring of Persistent Concussive Symptoms in Early and Middle Adolescents: Center Without Walls (PCS-EMA CWOW) (U54 Clinical Trial Not Allowed)

National Institute of Neurological Disorders and Stroke

Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institutes of Health

Turning Discovery Into Health

***RFA-NS-19-022*: Biological Measures for Prognosing and Monitoring of Persistent Concussive Symptoms in Early and Middle Adolescents: Center Without Walls (PCS-EMA CWOW) (U54 Clinical Trial Not Allowed)**

Participating Institutes: NINDS & NICHD

This FOA solicits multicenter applications from multidisciplinary groups to:

1) **discover** and **validate** a set of ***objective* biological measures** that underlie post-injury disability and will improve accuracy for prognosis and monitoring of persistent concussive symptoms that result from concussion and/or repetitive head impacts,

2) **develop a clinically useful risk stratification algorithm** that incorporates these biological measures with current clinical and self-report measures,

3) **provide** the broader scientific community with a **data resource** related to pediatric concussion using data sharing through the Federal Interagency TBI Research (FITBIR) database and the NINDS biomarker repository, BioSEND.

Mechanism, Budget and Key Dates

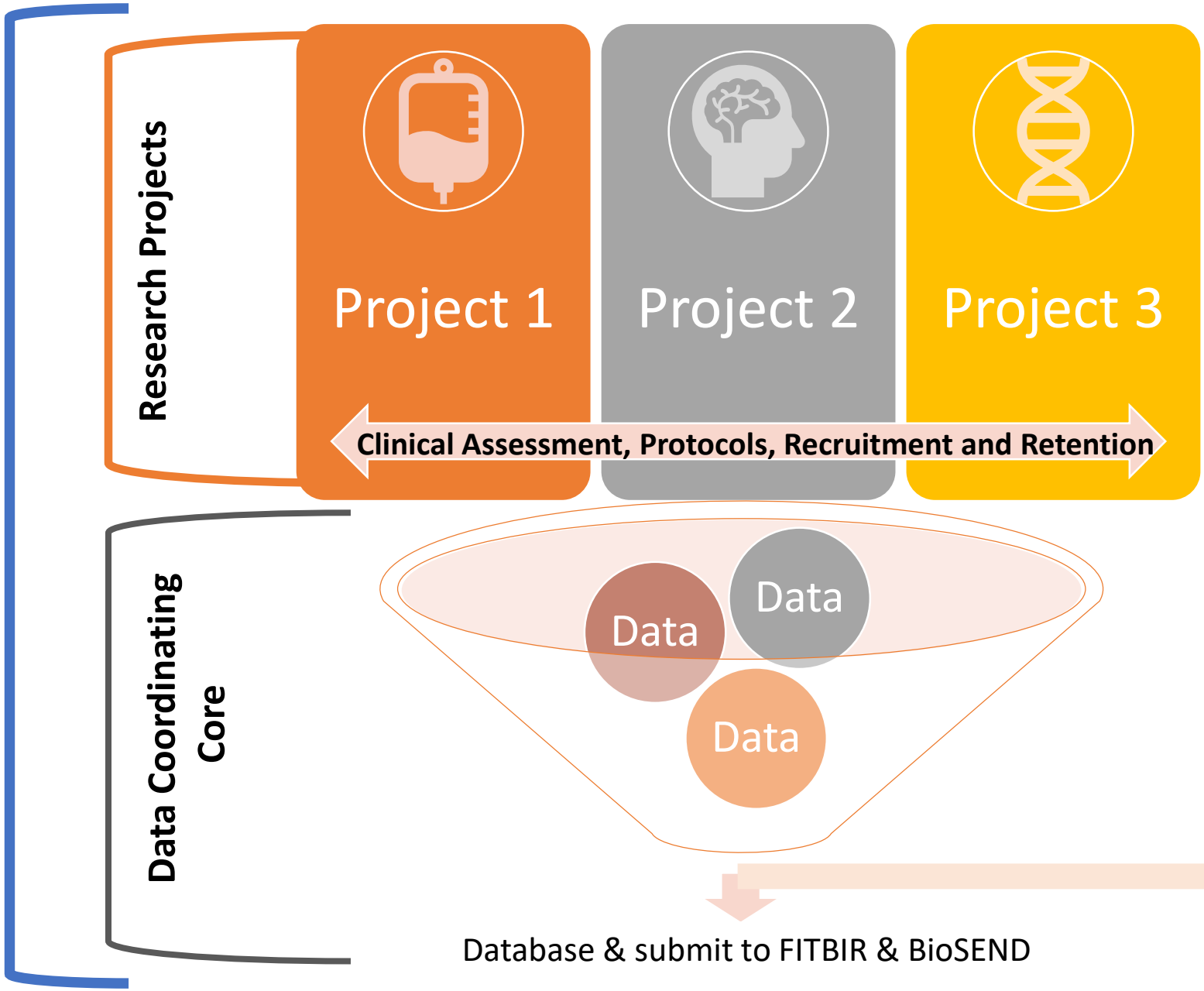
Mechanism: U54 CWOW grant mechanism – Cooperative agreement

- Cooperative agreements have significant input from NIH program
  - (One Scientific & One Administrative Program Official)
- U54 Center Without Walls (CWOW) – **Multisite Center** grant
- Milestone Driven
- Research Projects – At least 3 hypothesis-driven research projects
- Center Cores – Administrative & Data Coordinating Core
- *Synergy*

Budget-
$2,250,000 per year in *Direct Costs* for a maximum of 5 years

Key Dates:
Letter of Intent: (non-binding) March 10th, 2019
Open Date: March 10th , 2019
Due Date: ***April 10th 2019*** (no late applications; continuous submission does NOT apply)
Start Date: Oct, 2019 (more likely Dec, 2019); goes to Oct NINDS Council

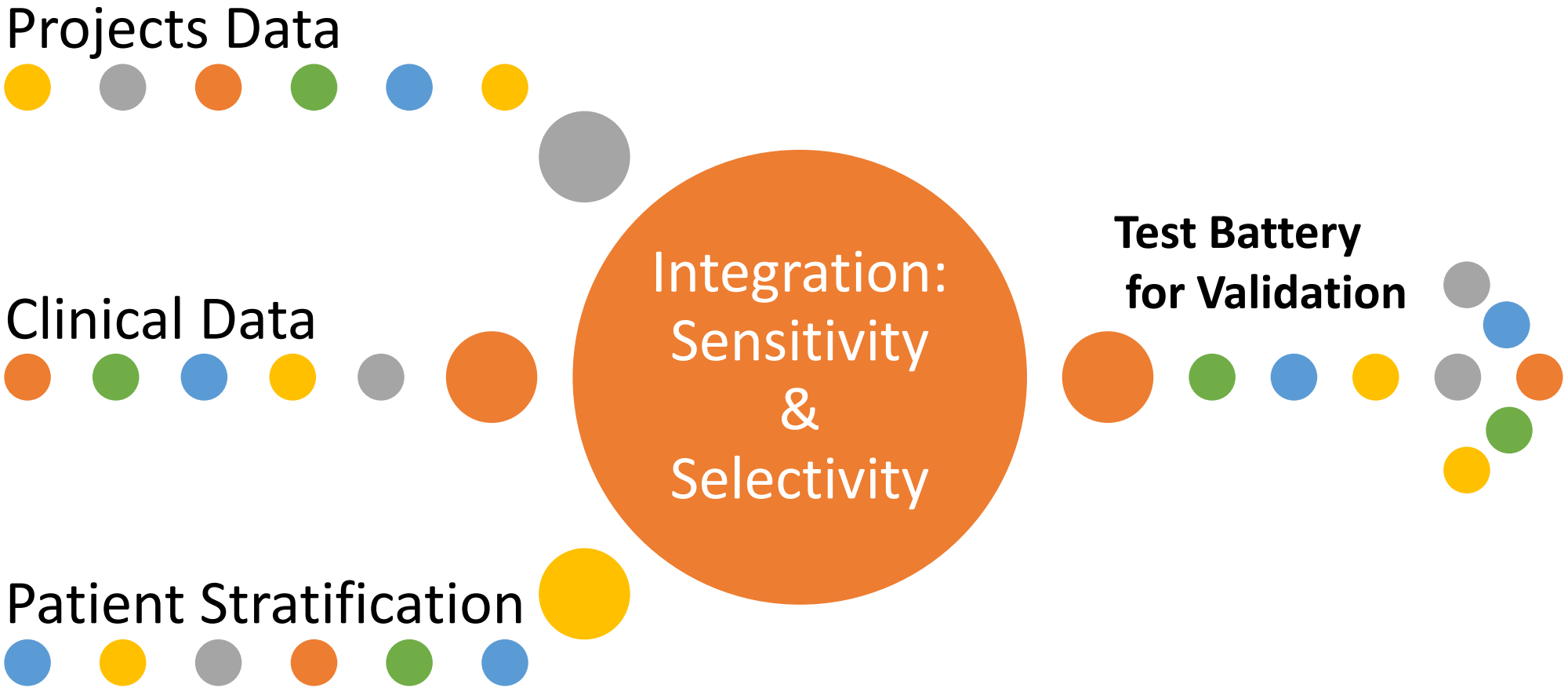
Discovery Phase



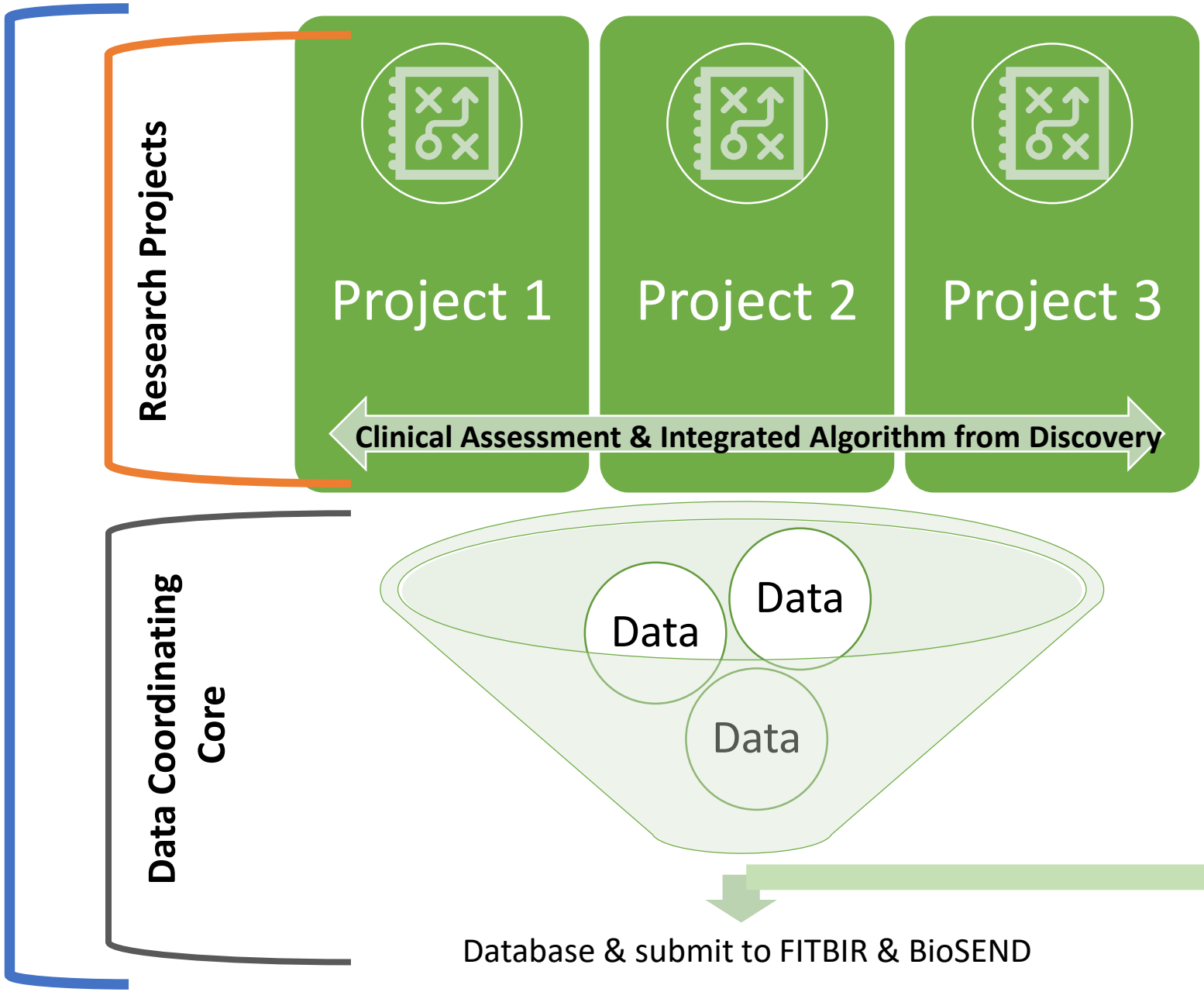
FITBIR
Federal Interagency Traumatic Brain Injury Research
INFORMATICS SYSTEM

Limited Dataset
(Rapid Data sharing in FITBIR)

Transition / Analytics Phase



Validation Phase – New Cohort



FITBIR
Federal Interagency Traumatic Brain Injury Research
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Limited Dataset
(Rapid Data sharing in FITBIR)

CWOW Details:

- Administrative Core:
  - The Administrative Core should coordinate the integration and management of activities within the Center.
  - Describe the Administrative Core personnel including scientific leadership, and administrative management and coordination of the proposed activities
  - Plan for holding regular meetings and facilitating communication between projects and cores (e.g., weekly teleconferences, an Annual Meeting, and site visits)
  - Plan to develop policies and procedures for providing access to data from both key investigators and collaborators
  - Provide clear diagnostic criteria that will be used in all Research Projects and operational definitions (e.g., persistent symptoms, concussion, etc…)
  - Provide training across research sites for clinical assessment batteries and biological sample collection
  - Clear and quantifiable milestones, including definition of a “limited dataset”

CWOW Details:

- Overall:
  - Describe the PCS-EMA CWOW's goals and objectives, background information, scientific premise, and the overall importance of including biological measures into the prognosis and monitoring of concussive symptoms in a pediatric population
  - Provide a strategy for achieving the goals defined for the overall Center
  - Describe how each research project and core relates to that strategy, and a transition plan for moving from discovery and external validation of the biological measures to a risk stratification algorithm
  - Describe study leadership and management
  - Determine the “limited dataset” that will be made available for sharing on a rolling basis no more than 1-year after being collected (see the NIH ABCD data sharing plan as an example)

CWOW Details:

- Research Projects:
  - Use standardized outcome and non-outcome measures and instruments (e.g., NINDS Common Data Elements (CDEs)) when possible.
  - Test Hypothesis-driven Objective Markers in coordination with clinical research measures.
  - Projects should focus on recruitment of EMA (11-17 years old) participants and must provide strong justification for inclusion of ages outside this range.
  - Enroll from multiple points of care (e.g., Emergency Departments, urgent care clinics, primary care, concussion/sports medicine clinics, or other specialty clinics) and include participants with a variety of injury mechanisms (e.g., falls, sports, abusive head trauma, automobile accidents).
  - Data from each Research Project should be collected at as many sites as possible in the discovery phase.
  - Description must include analytic plans for determining the sensitivity and selectivity of each measure and any combination of measures.

CWOW Details:

- Data Coordinating Core:
  - The Data Coordinating Core (DCC) must provide a data management plan capable of coordinating and curating data collected across all PCS-EMA CWOW research projects.
  - Provide a thorough list of all CDEs and Unique Data Elements (UDEs) that will be collected in all projects.
  - Submit to the FITBIR informatics platform and be able to coordinate with the NINDS biomarker repository, BioSEND in compliance with the NOT-NS-17-029.

CWOW Details:

- Milestones:
  - Applicants should propose annual milestones that provide clear go/no-go decision points for evaluating a project's continued success or emergent difficulties and will be used to evaluate the application not only in peer review but also in consideration of the awarded project for funding of non-competing award years.
  - Achievement of milestones will be evaluated by NINDS Program staff, and funding of non-competing award years will depend on milestone accomplishments.
  - Milestones should also include clear quantitative thresholds for determining whether specific or a combination of biological measures will move on from the discovery to the validation stage.
  - Data Submission to FITBIR will also be included as a Milestone.

CWOW Details:

- Review:
  - Applications will be reviewed by the NINDS Scientific Review Group.
  - Prior to review all applications will be screened by NINDS Program staff for responsiveness to the FOA.
  - Applicants should carefully read the Review Criteria listed in the FOA as those will instruct Reviewers for scoring.

FAQs:

Q1) Do we have to use the definition of “persistent symptoms” as written in Section 1 of the FOA that describes responsive designs?

Answer: NO, the times selected (3 days and 30 days) were only meant to be examples. Each application should operationally define persistent symptom and include justification of their choice.

Q2) Do each of the Research Projects need to be based in separate sites?

Answer: NO. Though this FOA requires the CWOW (by definition) to be multisite, there are a variety of ways to incorporate 3 research projects. The research projects are based on specific hypotheses, not by sites.

FAQs:

Q3) Can we enrich our sample in the discovery phase by only recruiting participants with a specific injury mechanism (e.g., sports concussion)?

Answer: NO. Both phases should include recruitment of multiple injury mechanisms and from multiple Points of Contact (emergency rooms, primary care offices, concussion clinics, sports medicine clinics, etc…).

Q4) Should we include the cost of the BioSEND repository in our budget?

Answer: YES. The NINDS contract with BioSEND does NOT support the full costs of biospecimen processing and storage. The estimate obtained from BioSEND should be included in your budget.

FAQs:

Q5) Is the $2,250,000 budget for each year?

Answer: YES, NINDS and NICHD contributions account for $2.25M in DIRECT costs per year for each year up to 5 years.

Q6) Does a separate budget need to be created for the NINDS and NICHD funds?

Answer: NO. NINDS will distribute the funds each year and the two institutes will use internal processes to transfer the NICHD funds to NINDS for distribution.

Q7) Do we have to use the Neuroimaging protocols from the projects listed in the FOA?

Answer: NO. However, it is recommended that, when possible, alignment with other large natural history studies of TBI or children is included.

Questions??

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Thank you to:

Diana Cummings, Ph.D.