12:05 pm: Overview of the NIH HEAL Initiative - Linda Porter, NINDS

12:15 pm: HEAL Pain Management Effectiveness Research Network: Infrastructure and services – Jane Atkinson, NCATS

12:35 pm: HEAL Pain Management Effectiveness Clinical Trials: FOA - Linda Porter, NINDS

12:55 pm: Q&A session – All

2:00 pm adjourn – earlier if we run out of questions
### NIH HEAL Initiative: Research Priorities

#### Opioid Use Disorder
- Therapies for addiction & overdose
- Real-world implementation research to optimize interventions
- Evaluate treatments, consequences of Neonatal Opioid Withdrawal Syndrome

#### Pain Management
- Understand neurobiology of chronic pain
- Accelerate discovery & development of non-addictive treatments
- Establish best pain management strategies

Human-based screening platforms and animal model screening platforms to advance investigational drugs and devices for new targets

Biomarker Discovery, Validation, and Implementation

Enhance targeting and reduce invasiveness of therapeutic devices
NIH HEAL Initiative: Clinical Research

Early Phase Pain Investigation Clinical Network and Partnership
- incentivize, accelerate early safety/efficacy trials
- compounds and devices from industry and academia
- well-defined pain conditions with high-unmet need

Back Pack Pain Research Consortium
- Link abnormalities to patient-reported symptoms and function
- Technology for discovery, diagnostics, and treatment
- trials for drugs, devices, complementary approaches
- Patient-centered algorithms to predict optimal treatment

Pain Management Effectiveness Research Networks and Trials
- Details to follow

Pragmatic & Implementation Studies for Management of Pain to Reduce Opioid Prescribing
- large-scale pragmatic trial or implementation science studies
- Embedded into health care systems
- electronic records of the health care system
- Focus on non-pharmacological approaches

Integrated Approach to Pain and Opioid Use in Hemodialysis Patients
- Evaluate integrated care
- Assessment/treatment co-morbid conditions & risk factors with opioids
- Enhance electronic health records to capture data
Program Goals

to establish the comparative effectiveness of existing therapies or effectiveness of existing or novel approaches for prevention and management of pain while reducing risk of addiction

• strengthen and inform current guidelines for pharmacologic and non-pharmacologic treatments for numerous pain conditions

• manage acute and chronic pain in patients from diverse communities

• provide patients and practitioners with a suite of effective strategies to alleviate pain that will reduce reliance on opioids

• improve the quality of life for patients and their families
What is Effectiveness Research?

the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, treat and monitor pain conditions in “real world” settings.

What interventions are of interest to NIH?

medications, biologics procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, complementary approaches, rehabilitation strategies, integrated approaches, and delivery system strategies in well controlled trials.
RFA-NS-19-021 Trial Innovation Network (TIN) Resources

TIN will provide these resources to all awardees:

- Single IRB services for the trial;
- Assistance with execution of the Master Clinical Trial Agreements with clinical sites;
- Developing final study protocol with study team;
- Finalizing recruitment and retention plans with investigators before trial initiation;
- Providing support for study design, statistical analyses and interpretation of results for manuscripts and publications;
- Developing associated trial documents, e.g.,
  - Manual of Procedures
  - Standard Operating Procedures
  - Case report forms
  - Training materials for study personnel
- Training clinical site investigators and staff for individual trials.
  - Training areas include, but are not limited to, regulatory requirements, Good Clinical Practice (GCP), adverse event reporting, human subject protections, informed consent, and NIH policies and procedures;

No letters of support are needed for TIN resources.
Trial Innovation Network (TIN) Resources provided to awardees (con’t.)

• Developing/ maintaining data management system for data collection, storage and adverse event reporting;
• Providing randomization support;
• Providing support for clinical operations and monitoring, project management, trial implementation, from study start-up through additional site selection as needed, enrollment, site management, study monitoring and close out. This includes assistance finding additional CTSA Program hub sites if needed in the UG3 and UH3 phase to meet enrollment goals;
• Monitoring and assisting with enrollment and retention;
• Preparing reports for Data and Safety Monitoring Boards; and
• Providing logistics for face to face meetings.

No letters of support are needed for TIN resources.
Budget guidance for all applications

• No costs should be included for the data coordination center, clinical coordination center or single IRB (if using the TIN single IRB). These resources will be provided by the TIN.

• Costs to clinical sites for enrollment and evaluation of participants or costs such as core laboratory costs, biospecimen shipping costs or costs for acquiring study agents should be included as study costs.

• Costs at the clinical sites must be budgeted on a per-subject or per-procedure basis. Applicants should provide a breakdown of the total per subject costs as part of the budget justification and should indicate how the cost for an item or procedure was determined.
Budget guidance for all applications (con’t)

• Costs for collection, analysis, storage, and shipping of biospecimens during the study duration should be included as a separate item.

• Specimens collected beyond those needed for the study or remaining at the close of study will be shipped and stored in the NIH HEAL common repository. Costs for shipping to the repository should be included in the budget. Costs for long-term storage in the HEAL repository will be covered through HEAL funds.

• Travel costs should include:
  • Costs for the investigator team to travel to a face to face kick-off meeting of the Program Steering Committee during the planning phase.
  • Costs for an annual one-day, in-person study investigator meeting for up to 6 persons from the investigator team.
## Summary Budget Guidance for Applicants

<table>
<thead>
<tr>
<th>Activity</th>
<th>Costs Included in applications</th>
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</thead>
<tbody>
<tr>
<td>Enrollment and evaluation of participants</td>
<td>Yes</td>
</tr>
<tr>
<td>Core Laboratory Costs</td>
<td>Yes</td>
</tr>
<tr>
<td>Shipping</td>
<td>Yes</td>
</tr>
<tr>
<td>Acquiring study agents</td>
<td>Yes</td>
</tr>
<tr>
<td>Costs for collection, analysis, storage of biospecimens during trial</td>
<td>Yes</td>
</tr>
<tr>
<td>Shipping to central HEAL repository during or at end of study</td>
<td>Yes</td>
</tr>
<tr>
<td>Costs for long-term storage of biospecimens in central HEAL repository</td>
<td>No</td>
</tr>
<tr>
<td>Data coordinating center</td>
<td>No</td>
</tr>
<tr>
<td>Clinical Coordinating Center</td>
<td>No</td>
</tr>
<tr>
<td>Single IRB costs if using TIN single IRBs</td>
<td>No</td>
</tr>
<tr>
<td>Travel costs</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Identifying CTSA clinical sites if needed

• Final date for grant submission: February 1, 2019, (see RFA-NS-19-021).

• Process for contacting individual CTSA sites
  • Determine number of participants to be enrolled.
  • Determine number of potential participants at applicant’s institution and institutions of any co-investigators.
  • Identify HEAL Point of Contacts (POC) at individual CTSA hubs to determine size of potential cohorts (see trialinnovationnetwork.org)
  • Determine whether CTSA hub wishes to participate in the trial (see next slide) and ask for a letter of intent for application.
HEAL Pain Management ERN CTSA site identification process

1. Trial PI goes to the [trialinnovation network.org](http://trialinnovation network.org) website.
2. Contacts HEAL POC at the individual CTSA hubs to find site PI and conduct a cohort assessment.
3. Individual CTSA provides cohort numbers and site PI name to trial PI.
4. Trial PI contacts site PI and asks for letter of intent to participate.
5. CTSA institution provides letter of intent to participate for grant application.
TRIAL INNOVATION NETWORK

NIH HEAL INITIATIVE SM
PAIN MANAGEMENT ERN & OTHER NIH HEAL FOAs

FUNDING

OPPORTUNITIES
FIND CTSA PROGRAM PARTNERS

EXPIRES ON
02/01/2019

LEARN MORE

INVESTIGATORS

submit your proposal

Hear from us within 5 business days.

TRIAL INNOVATION NETWORK
Operational innovation, excellence, and collaboration.

The Trial Innovation Network continues to accept new proposals!
Click the button below to get started.

Get Started now!

158 total proposals submitted

WELCOME!
The Trial Innovation Network is a collaborative national network that focuses on operational innovation, excellence and collaboration and will leverage the expertise and resources of the CTSA Program.

NETWORK LOGIN
NIH HEAL INITIATIVE℠ PAIN MANAGEMENT ERN & OTHER NIH HEAL FOAs

The NIH launched the HEAL (Helping to End Addiction Long-term) Initiative℠ to speed scientific solutions to stem the national opioid public health crisis. The NIH HEAL Initiative will bolster research across NIH to improve treatments for opioid misuse and addiction and enhance pain management. The HEAL Pain Management Effectiveness Research Network (ERN) will address pain management by supporting clinical trials that compare the effectiveness of existing therapies, including combinations or novel approaches using existing therapies, to prevent or manage pain in ways that reduce the risk of addiction. Clinical trials will be conducted within the existing NCATS CTSA Program - Trial Innovation Network.

Things you need to know:
- Due to the timing of the HEAL Pain Management ERN FOA and to avoid any conflicts of interest, the Trial Innovation Network (TIN) will not accept proposals requesting initial consultations for RFA-NS-19-021.
- The Trial Innovation Network (TIN) will provide data coordination services, clinical coordination services, single IRB functions, biostatistical support, and recruitment and retention support for awarded studies. Those submitting applications in response to

https://trialinnovationnetwork.org/heal-pain-ern-other-heal-foas/
Other factors to note

• This FOA may NOT be used for applications that propose testing interventions to establish initial efficacy of drugs, devices or biologics for approval by the Food and Drug Administration (FDA).

• Applicants **must** include a milestone plan as a separate attachment.
  • Separate milestones must be included for the UG3 planning phase and the UH3 trial implementation phase.

• Applicants **must** include a schedule of events as a separate attachment.
Other factors to note (con’t)

• Trial implementation phase can be up to four years.
• It is expected that each trial will be overseen by a Data and Safety Monitoring Board.
• Read the RFA carefully, including the review criteria.
• Note the governance structure outlined in the Terms and Conditions.
What if my proposal is not a fit?

**EPPIC**
early phase efficacy and safety trials

**PRISM**
pragmatic trials in health care settings

**SIREN**
trials in emergency room settings

non-HEAL solicitations
## Anticipated RFA NS -19-021 Timeline

<table>
<thead>
<tr>
<th>Event</th>
<th>Date/Details</th>
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<tbody>
<tr>
<td>Receipt date</td>
<td>February 1, 2019</td>
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<tr>
<td>Review Date</td>
<td>TBD</td>
</tr>
<tr>
<td>Award date</td>
<td>September, 2019</td>
</tr>
<tr>
<td>Begin planning year</td>
<td>October, 2019*</td>
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<tr>
<td>Kick off Meeting</td>
<td>November, 2019*</td>
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</tbody>
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*approximate dates – check the webpage*
Trans-NIH-HEAL Pain Research Networks

- Kick off meeting
- PRO data base
- Common data elements
- Central Data Repository
- Biospecimens
Overview of Cooperative Agreements

- Used when substantial programmatic involvement is anticipated between the federal agency and the recipient
- Supports the recipients' activities through a partnership role
- The primary role and responsibilities reside with the awardees
- The Cooperative Agreement Terms and Conditions of Award in the FOA outlines the roles and expectations of the PD/PI and NIH Program Staff
Resources

NIH Pain Consortium Webpage
Information for applicants RFA NS -19-021
https://painconsortium.nih.gov/Funding_Research/
NIH-HEAL-Effectiveness-Research-Program-Pain
Questions on the FOA
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Questions?

Please submit using the Webex Q&A box