HEAL Programs for Pain

Discovery
- Acute to Chronic Pain Signatures
- Discover and Validate Novel Targets

Preclinical Development
- Preclinical Screening Platform
- Small Molecules and Biologics Development
- Device Development

Clinical Trials
- Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints
- Data & Asset Sharing Partnership
- Early Phase Pain Investigation Clinical Network

Implementation/Dissemination
- Back Pain Research Consortium
- Hemodialysis Pain Effectiveness Research Network
- Pragmatic and Implementation Studies for the Management of Pain
NINDS Networks
Organizational and Funding Structure

- Increased trial quality
- Balanced portfolio
  - Allows logical ordering of incoming trials
  - Creates a pipeline for future trials
- Stable infrastructure and research capacity
  - Improved subspecialty input via working groups
  - Stable funding for research and training
- Improved data sharing
  - Single data center with uniform governance
  - Fosters the use of CDEs
- Manages trials competing for similar patients
  - Commitment to consider **ALL** eligible patients
- Coordinates with non-profits, industry, and international partners
- Trains the next generation of clinical trialists
EPPIC-NET Set-up Status

Infrastructure

Select CCC, DCC, Hubs

RFAs 19-NS-023, 024,025: Feb 2019

Hub re-issue
RFA 19-NS-036: July 2019

Application Templates and Processes

Preliminary Asset Template

Review #1

Dossier Template

Review #2

Protocol Template

Review #3

IMPLEMENTATION
August 1-8
- CCC/DCC/1st hub Awards
- Finalize submission & review processes
- Launch preliminary application

August 9-17
- CCC, DCC: Joint meetings together and with 1st hubs
- Eppic-Net leadership committees set up and meet
- Website set up by DCC

August 17-24
- Publicity implementation
- Webinar for potential applicants
- Trial run of submission process

August 25-September 1
- Refine submission process based on trial run
- Continue CCC/DCC/Hub & Spoke set up

September 3
OPEN FOR ASSET APPLICATIONS
September 2019
- Preliminary application submission and review

October 2019
- Dossier preparation, submission and review

November 2019
- Protocol preparation, submission and review

December 2019

2020
- February
  - FUNDING AND IMPLEMENTATION OF FIRST TRIALS
- January
EPPIC-NET Set-up Status

Infrastructure

Select CCC, DCC, Hubs
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Application Templates and Processes

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Protocol Template

IMPLEMENTATION

Review #1
Review #2
Review #3
EPPIC NET - Building a Clinical Network

Clinical Coordinating Center (CCC)
- Use a centralized IRB and Master Trial Agreements
- Match Hubs/Spokes to the protocol/asset
- Identify and train site investigators/staff
- Standardize CRFs and methodologies
- Work with DCC; develop SOPs and quality controls
- Distribute funds with NINDS oversight

Clinical Hubs & Spokes
- Identify individual investigators
- Conduct trials
- Collect and report data to DCC and CCC

Data Coordinating Center (DCC)
- Receive and centralize data
- Provide statistical/analysis reports
- Harmonize data, including that from BacPac, and for transfer to central repository when available
- Monitor safety/ provide reports to DSMB and other monitors
- Create and manage biorepository for samples throughout HEAL

NIH
- Interact with all EPPIC-Net components
- Provide oversight of budget and milestones

Funding for infra-structure components are U24 Cooperative Agreements
EPPIC-NET Set-up Status

Infrastructure

Select CCC, DCC, Hubs
RFAs 19-NS-023, 024,025: Feb 2019
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Application Templates and Processes

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Protocol Template

IMPLEMENTATION

Review #1
Review #2
Review #3
1. **Manage diversity** - Assets (small molecules, biologics, and devices) proposed by academia and industry

2. **Pursue rigor** - A non-grant/contract process to rigorously review all applications at multiple steps

3. **Level the playing field** - NIH provides free resources to assist applicants through the process

4. **Accelerate time** - Clinical trials are commenced within short time of initial proposal (6-8 months)
Early Phase Pain Investigation Clinical Network + Data and Asset Sharing

**Improve quality, consistency, efficiency of early phase pain clinical trials**

- EPPIC-net will test compounds and devices judged highly meritorious in peer review that come from industry and academia
- Clinical Coordination Center, Data Coordination Center, 11 specialized clinical sites (hub and spoke design)
- Incentivize, accelerate Phase II trials
- Focus on well-defined pain conditions with high-unmet need
- Reduce the time to start, enroll, run, and complete trials
- Incorporate biomarker studies
- Accommodate platform trial designs

**Data and Asset Sharing Partnership**

- EPPIC-net Data Coordination Center will host data from EPPIC-Net and BacPac for later transfer to HEAL central repository
- EPPIC-Net DCC will serve as the biosample repository for all HEAL programs
- FNIH and the HEAL Partnership Committee will encourage submission of assets for EPPIC-Net clinical trials
Clinical studies may come to the network from several sources:

(1) Clinical trials to test the efficacy of therapeutic candidates (“assets”) such as *small molecules, biologics, and medical devices* as contributed by academic or industry partners. **NOT-NS-19-043**

(2) Clinical research studies aimed at understanding the biological basis of different pain states or *validation of biomarkers* for their utility in phase 2 studies → from other NIH FOAs.

Clinical studies may not be limited to these two sources, so EPPIC-Net must be flexible enough to incorporate studies from other sources as directed by the NIH.
### EPPIC NET – Clinical Trial Selection

<table>
<thead>
<tr>
<th>WHAT:</th>
<th>WHO:</th>
<th>AWARD:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preliminary Asset Application</strong></td>
<td>Brief Asset Data</td>
<td>Applicant</td>
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<tr>
<td><strong>In Depth Asset Review: Dossier</strong></td>
<td>Complete Asset Dossier</td>
<td>Applicant and NINDS Contractor</td>
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<tr>
<td><strong>Clinical Trial Protocol review</strong></td>
<td>Clinical Trial Protocol</td>
<td>EPPIC-Net CCC* (with DCC, Hub PIs and Applicant)</td>
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**Objective Review Panel**
Evaluate assets based on template, full dossiers, and clinical protocols

- MDWG
- NINDS Council
- NIH HEAL Executive Committee

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**Other Transaction Awards are used to fund EPPIC-Net Clinical Trials**

*OT award made to CCC for distribution to Hubs/spokes for trial conduct. Asset owner does not receive funds; does receive access to EPPIC-Net for asset clinical trial.*
• Applicant information
• Asset information
• Freedom to operate
• Biological rationale
• Relevant prior studies (preclinical and clinical)
• Proposed indication
• Proposed treatment regimen
• Proposed outcomes measures (efficacy, biomarkers, and safety)
• Competing products
• Feasibility/logistics concerns
• Relevant Literature Citations
• Scientific rationale
• Clinical unmet need
• Target product profile (TPP)
• Target-disease connection
• Competitive analysis
• Preclinical Data Package
• Chemistry and manufacture, device specifications
• Biology, pharmacology, and physiology
• Clinical data to support the proposed trial
• Clinical Considerations for HEAL Program
• Non-scientific considerations
EPPIC-NET Application Templates and Processes

Preliminary template
- Completed with HPC/MDWG input
- Packet with information sheet, application, and instructions ready

Dossier template
- Completed with HPC/MDWG input
- Contract in place to prepare dossiers

Protocol template
- Protocol written by CCC with input from all stake-holders
- Based on NIH/FDA Clinical Trial Protocol Template
EPPIC-NET Preliminary Application Packet

4 Elements in Preliminary Application Packet

1. Information sheet- provides overview of HEAL, EPPIC-Net and application process

2. Preliminary Application fillable pdf

3. Line-by-line instructions for fillable pdf

4. Instructions for eRA Commons and ASSIST
EPPIC-NET APPLICATION PACKET INFORMATION SHEET

This packet contains:
1. This information sheet
2. The EPPIC-Net preliminary application: a fillable pdf form
3. Line-by-line instructions for completing the preliminary application
4. Instructions for application submission via eRA Commons

INFORMATION FOR EPPIC-NET APPLICANTS

The NIH HEAL Initiative
In April 2018, NIH launched the HEAL (Helping to End Addiction Long-term) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. A major goal of the HEAL Initiative is to spur the development of effective, non-addictive treatments to reduce the burden of illness due to pain and to reduce risk of addiction. Over the past 2 years, NIH has gathered input from experts from the U.S. Food and Drug Administration (FDA), academia, and the private sector to identify key gaps and opportunities for the development of new treatments for pain. Through these consultations, NIH identified the need for a sophisticated clinical trial network to design and execute innovative early phase trials of promising non-addictive pain therapies in well-characterized patient cohorts.
# EPPIC-NET Preliminary Application

## 1. Applicant Information:

1a. Title: _____  First Name: __________________________  MI: ____  Last Name: __________________________  Suffix: __

1b. Degree: _______  If other, identify: _______  

1c. Email: __________________________  Phone number: __________________________

1d. Organization: __________________________________________  Position at Organization: __________________________________________

### Mailing Address:

1e. Street Address: __________________________  Apt./Suite/Room #: __________________________

1f. Street Address (continued): __________________________________________

1g. City: __________________________  U.S. State: __________  ZIP: __________________________

1h. Country: __________  Non-US state/division: __________________________

## 2. Key Research Personnel Information (optional):

2a. Title: _____  First Name: __________________________  MI: ____  Last Name: __________________________  Suffix: __

2b. Degree: _______  If other, identify: _______

2c. Email: __________________________  Phone number: __________________________
LINE-BY-LINE INSTRUCTIONS FOR COMPLETING THE EPPIC-NET PRELIMINARY APPLICATION

**Applicant information**
1. Applicant information: Provide applicant name, title, degree, organization, position at organization, mailing address, email address and phone number.
2. Key Research personnel: Optional: Provide key personnel name, title, degree, organization, position at organization, mailing address, email address and phone number.

**Project identification**
3. Title of project: Provide a title that is descriptive of the project, including identification of the asset (e.g. drug, device, biomarker) and target population/type of pain being proposed. [200 character limit]
4. Brief description of project and rationale: Briefly describe the project (including identification the asset, the target population/type of pain) and the supporting rationale. [300 word limit]

**Asset information**
5. Asset name
6. Asset status: identify if the asset is proprietary, marketed or other. If other, specify status.
7. Asset ownership: Identify the asset owner. If the applicant is the owner, select "self" and identify
ERA Instruction Guide for EPPIC-Net OTA Submission

Use these instructions, together with the forms and information found in the EPPIC-Net application packet to complete your application. The EPPIC-Net website and information packet include specific instructions, forms and the Research Opportunity Announcement (ROA) number (see the section labeled "How to apply to EPPIC-Net" on the EPPIC-Net Application Packet information sheet) needed for your application submission.

Prepare to Apply

NIH typically makes awards to organizations, not individuals. At the time of submission, the Program Director/Principal Investigator (PD/PI) and their organization must be registered at ERA Commons. In addition to the PD/PI, an individual with the role of Signing Official (SO) is needed. If an application is awarded, additional registrations (e.g. System Award Management) will be required.

At each stage, EPPIC-Net applications must be submitted using NIH's ASSIST web-based application submission system. Users can access ASSIST directly or through eRA Commons. To complete the application, users must have access to a browser, a pdf generator, and Adobe Reader software.