



National Institute of  
Neurological Disorders  
and Stroke

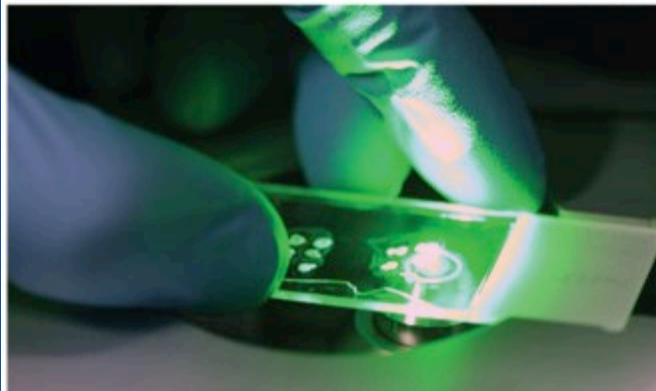
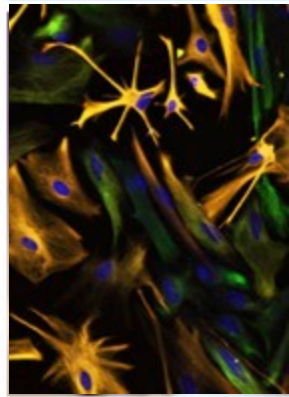
# NIH HEAL EPPIC-Net

*Early Phase Pain  
Investigation Clinical  
Network*

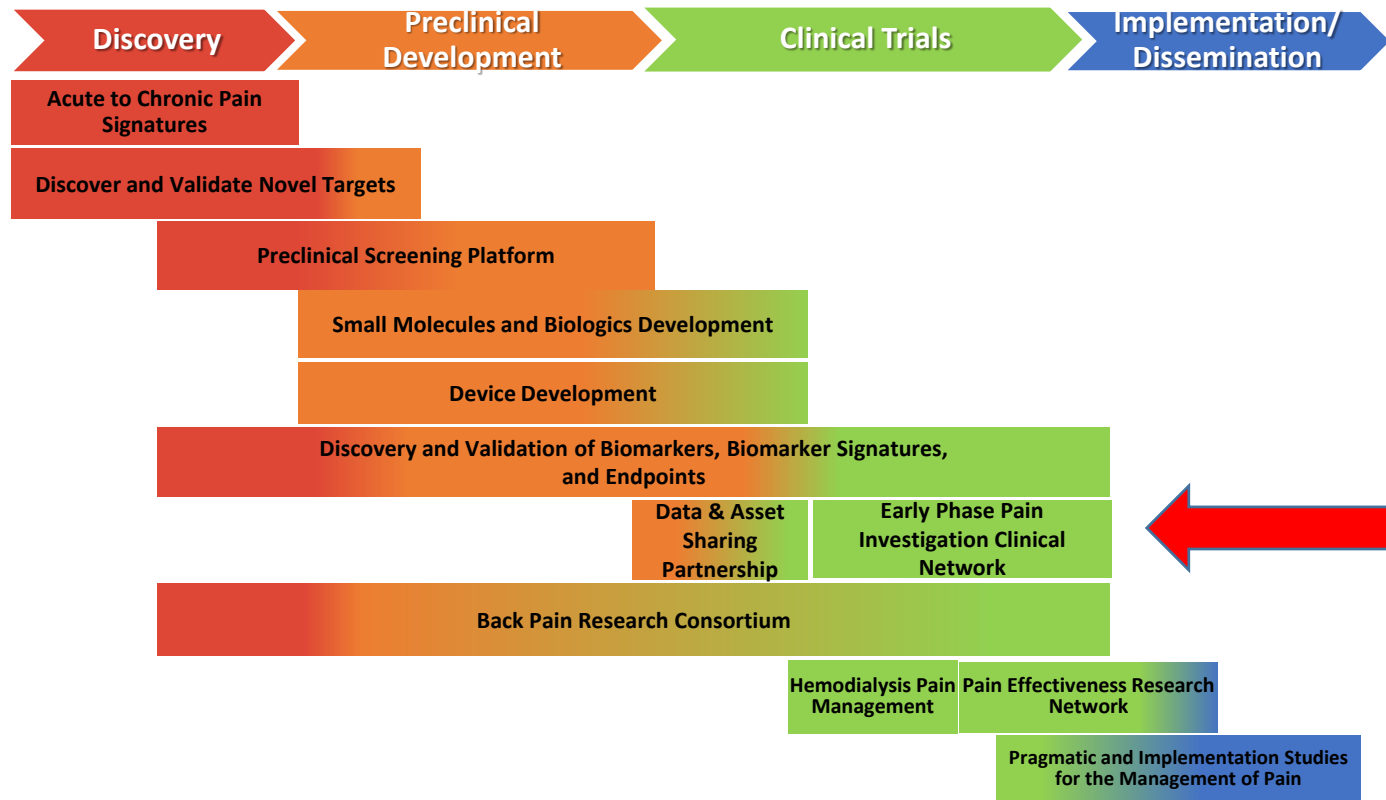


NIH • Helping to End Addiction Long-term

**Barbara Karp, MD**  
NIH/NINDS  
[barbara.karp@nih.gov](mailto:barbara.karp@nih.gov)



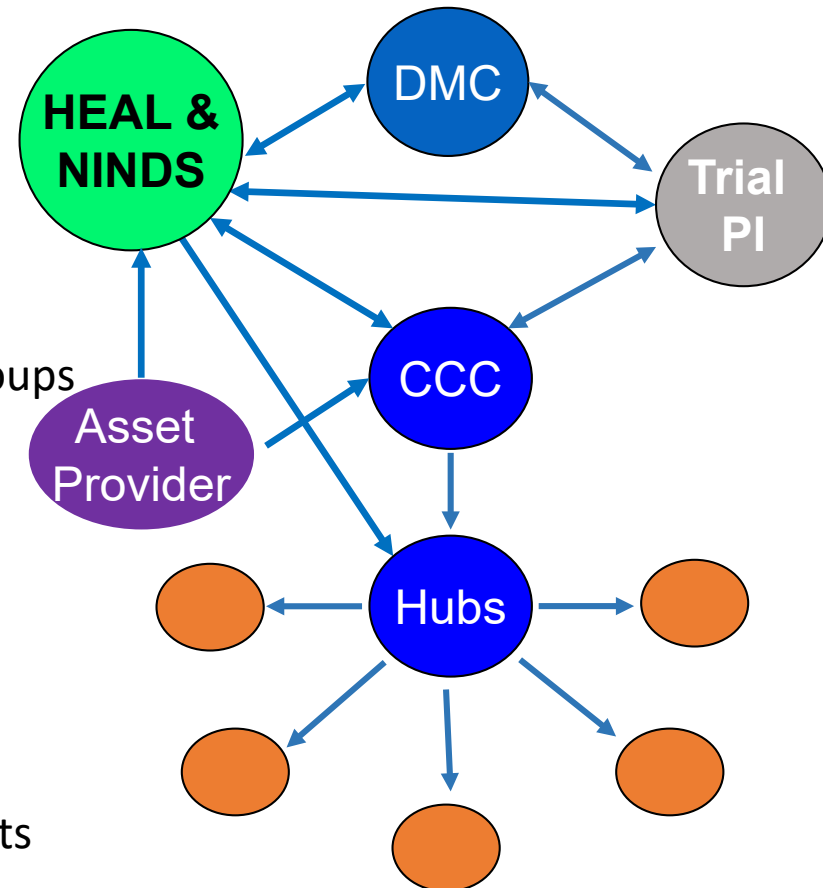
# HEAL Programs for Pain



# 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

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

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

## Application Templates and Processes

Preliminary Asset Template

Dossier Template

Protocol Template

Review #1

Review #2

Review #3

IMPLEMENTATION



- CCC/DCC/1<sup>st</sup> hub Awards
- Finalize submission & review processes
- Launch preliminary application

Aug 1-8



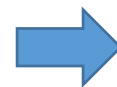
- CCC,DCC: Joint meetings together and with 1st hubs
- Eppic-Net leadership committees set up and meet
- Website set up by DCC

Aug 9-17



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

Aug17-24



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

Aug 25-Sept 1



**OPEN FOR ASSET APPLICATIONS**

Sept 3



2019

Preliminary  
application  
submission and  
review

Dossier preparation,  
submission and  
review

Protocol preparation,  
submission and  
review

September



October



November



December

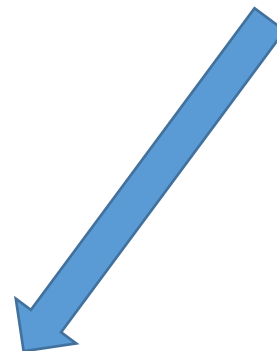
2020

**FUNDING AND  
IMPLEMENTATION OF  
FIRST TRIALS**

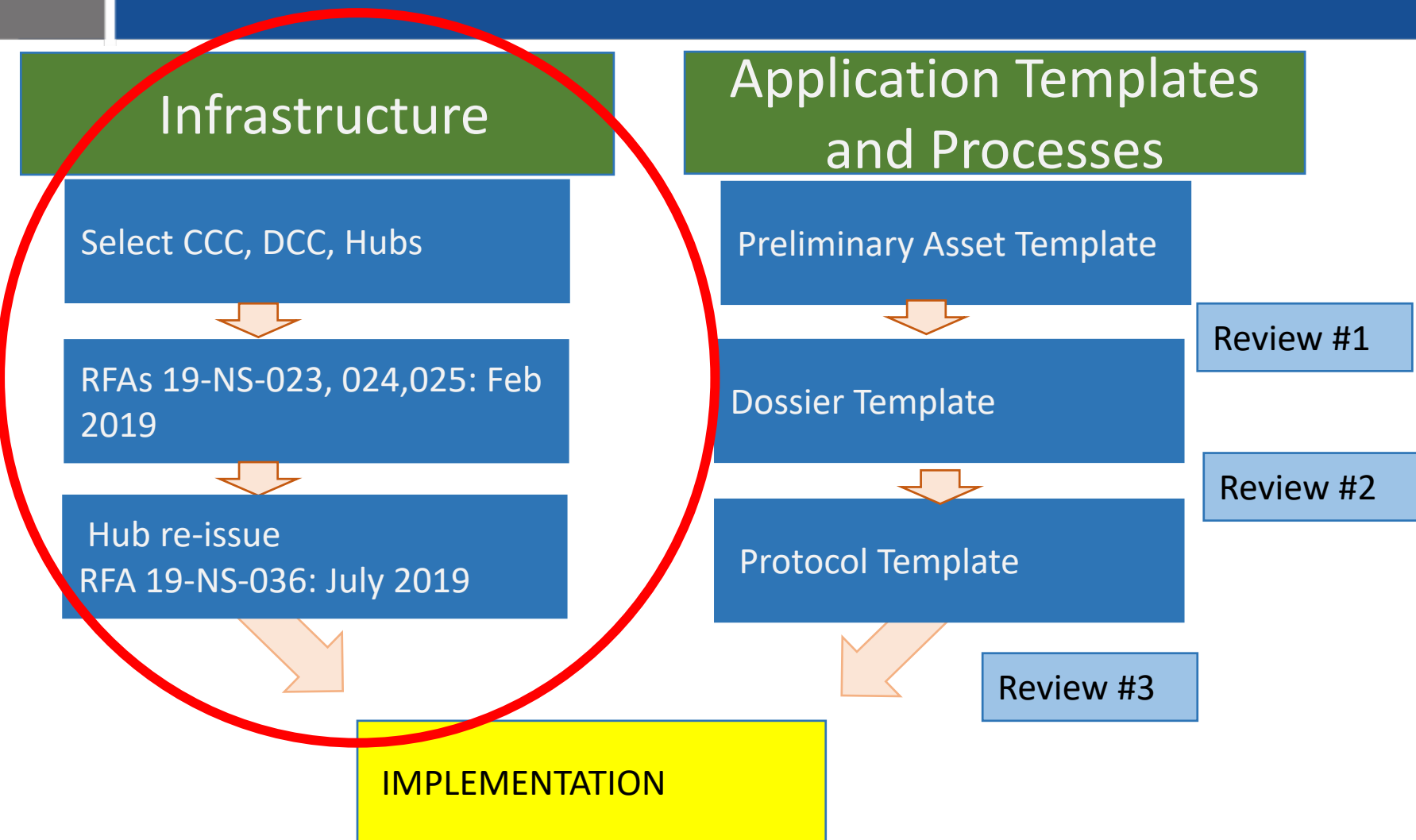
February



January



# EPPIC-NET Set-up Status



# 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

## 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

## Clinical Hubs & Spokes

- Identify individual investigators
- Conduct trials
- Collect and report data to DCC and CCC

## 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

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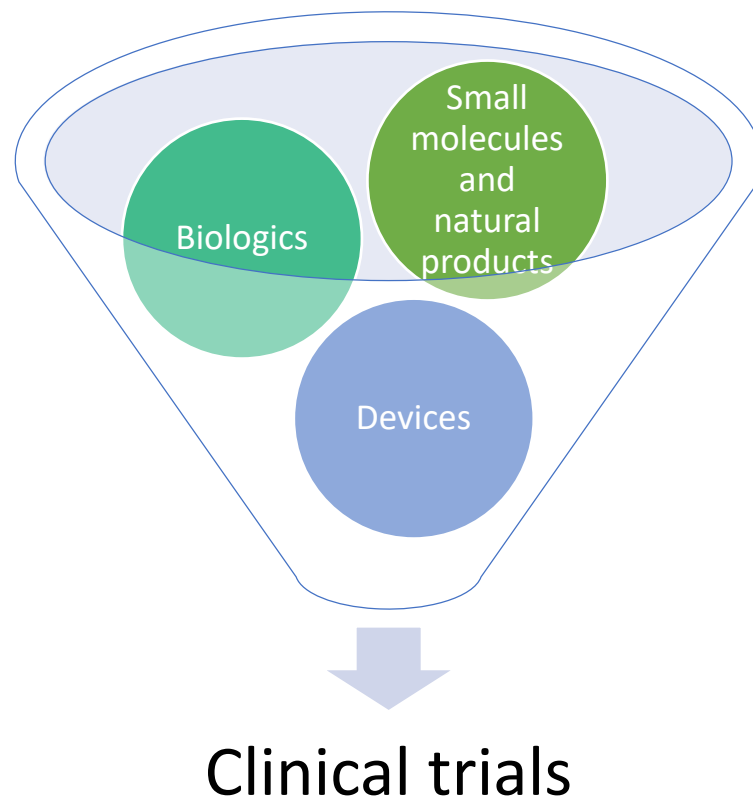
Review #2

Review #3

IMPLEMENTATION

# EPPIC NET Asset Entry and Review Process

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



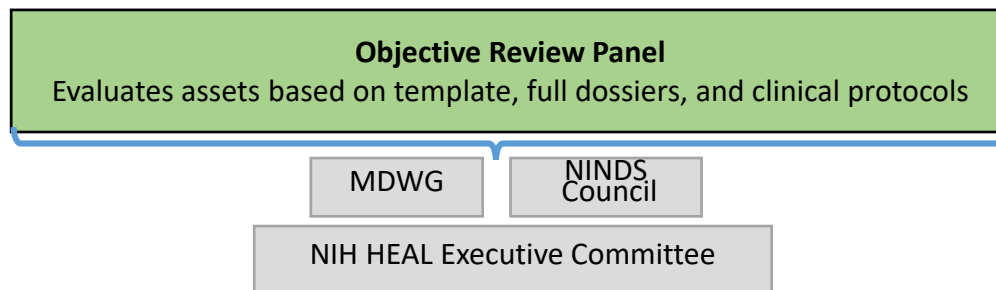
## Clinical studies may come to the network from several sources:

- (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

	WHAT:	WHO:	AWARD:
<b>Preliminary Asset Application</b>	Brief Asset Data	Applicant	NO
<b>In Depth Asset Review: Dossier</b>	Complete Asset Dossier	Applicant and NINDS Contractor	NO
<b>Clinical Trial Protocol review</b>	Clinical Trial Protocol	EPPIC-Net CCC* (with DCC, Hub PIs and Applicant)	YES



## 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.

# EPPIC NET Preliminary Application

- 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

EPPIC-Net Preliminary Application  
Rolling Review



EPPIC-Net Dossier Application  
Rolling Review



EPPIC-Net Clinical Protocol Application  
Rolling Review



EPPIC NET Clinical Trial

# EPPIC NET Dossier Application

- 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 Preliminary Application  
Rolling Review



EPPIC-Net Dossier Application  
Rolling Review



EPPIC-Net Clinical Protocol Application  
Rolling Review



EPPIC NET Clinical Trial



# 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
- <https://grants.nih.gov/policy/clinical-trials/protocol-template.htm>





# 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 Preliminary Application Information Sheet



## 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: \_\_\_\_\_

# EPPIC-NET Preliminary Application Instructions



## 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

# EPPIC-NET Submission Instructions (eRA Commons)



## 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.



THANK YOU!

