



National Institute of  
Neurological Disorders  
and Stroke

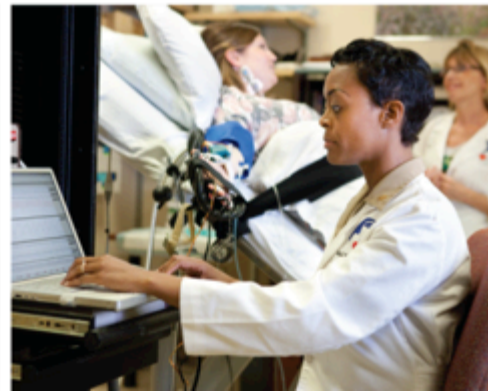
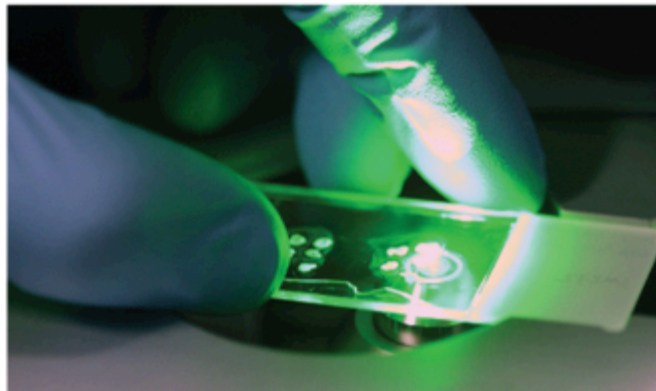
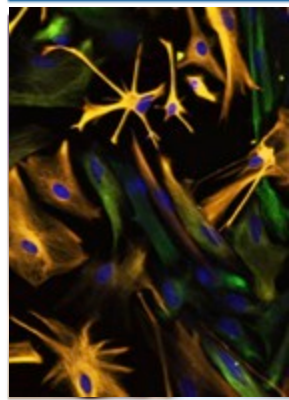
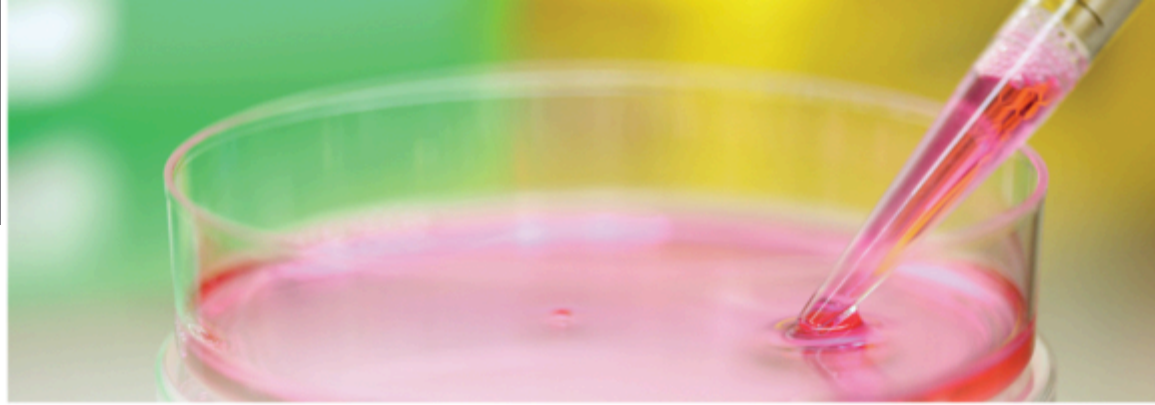
# NIH HEAL EPPIC-Net

*Early Phase Pain Investigation  
Clinical Network*

*Applicant Webinar  
August 23, 2019*



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



# EPPIC-Net Asset Applicant Webinar: Ground rules

- For clearest audio, please mute your microphone
- Please note that the webinar is public and is being recorded
- The webinar recording will be posted on NIH websites and will be available for later viewing
- Please save all questions for the end
  - You can e-mail questions to the speakers during the webinar or use Q&A panel or the "chat" feature on Webex
- The purpose of the webinar is to provide information on the asset application submission and review process.
- Please do not ask about specific assets or applicants during the webinar. Questions about specific assets or studies can be emailed to EPPIC-Net staff.

# EPPIC-Net Asset Applicant Webinar: Agenda

- **Welcome and introductions- Barbara I. Karp, MD, EPPIC-Net Program Director**
- **Welcome and HEAL Initiative introduction- Rebecca Baker, PhD, Director, NIH HEAL Initiative**
- **EPPIC-Net Overview, purpose**
- **Infrastructure**
- **Asset solicitation**
- **Application overview**
- **Funding information**
- **Preliminary application guide**
- **Review process – Marilyn Moore-Hoon, PhD; SRO NINDS**
- **eRA Commons – Laurie Roman, PhD, MBA; NIH/OD/OER/ORIS/eRA**
- **Q and A – all presenters**

# NIH HEAL (Helping to End Addiction Long-term) Initiative

Rebecca G. Baker, Ph.D.  
Director, HEAL Initiative, Office of the Director,  
National Institutes of Health





# Long

- Trans-NIH research initiative to:
  - Improve prevention and treatment strategies for opioid misuse and addiction
  - Enhance pain management
- Goals are scientific solutions to the opioid crisis
- Coordinating with the HHS Secretary, Surgeon General, federal partners, local government officials and communities

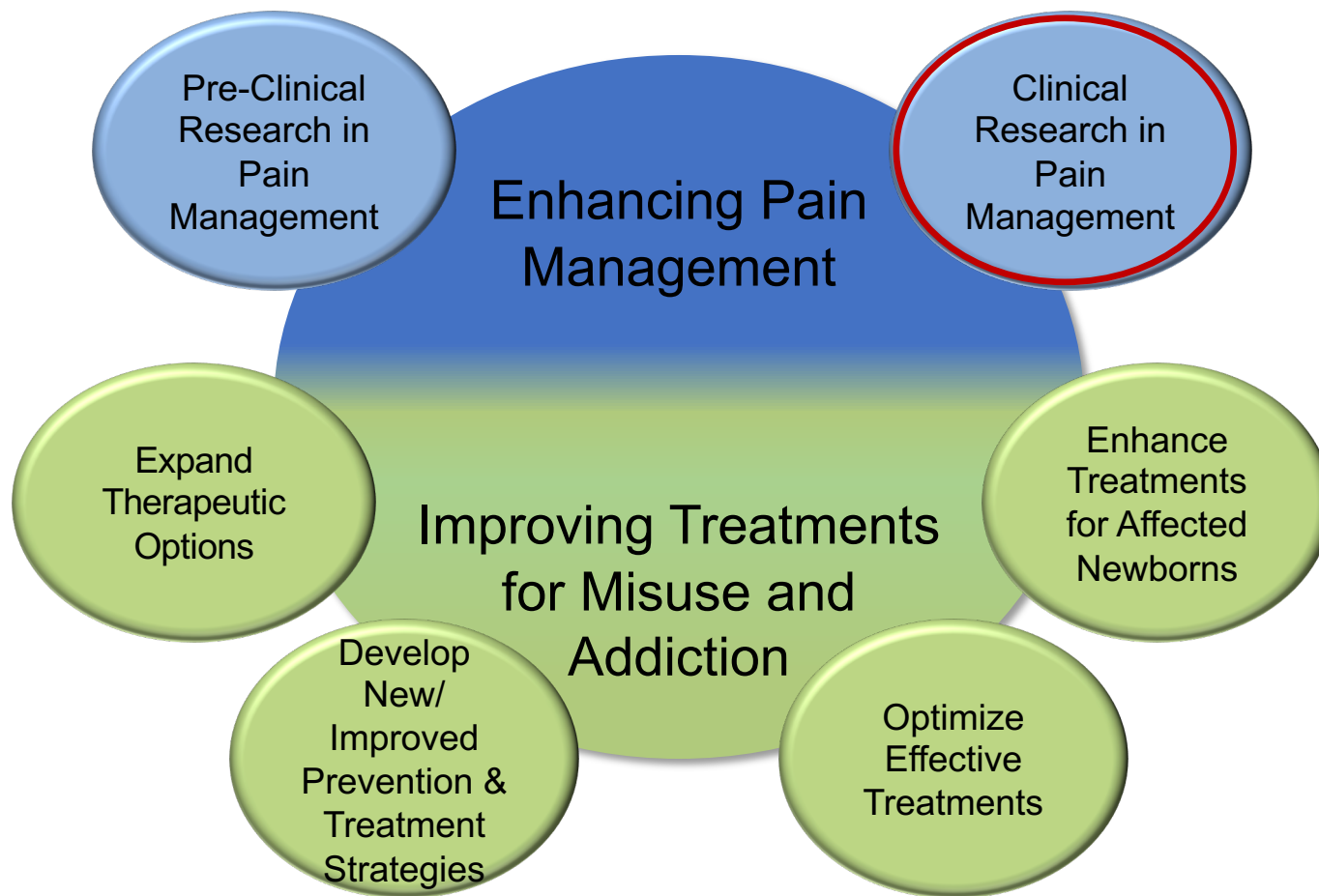


[www.nih.gov/heal-initiative](http://www.nih.gov/heal-initiative)

# Long

- \$500M/year Trans - NIH effort
  - Over \$850M to be obligated in FY2019
- 12 NIH Institute and Centers leading 26 HEAL research projects
  - Over 20 collaborating Institutes, Centers and Offices
  - From prevention research, basic and translational research, clinical trials, to implementation science
  - Multiple projects integrating research into new settings
- Released 40+ funding announcements for FY2019

# HEAL Initiative Research Overview



# Enhancing Pain Management

- Clinical Research in Pain Management
  - Characterize populations of patients with pain conditions
  - Test novel treatments in a new clinical trials network
    - Early Phase Pain Investigation Clinical Network (EPPIC Net)
    - Back Pain Research Consortium
  - Establish best strategies for management of acute and chronic pain
    - Pain Management Effectiveness Research Network
    - Integrated approach to pain and opioid use in hemodialysis patients
    - Pragmatic and Implementation Studies for the Management of Pain



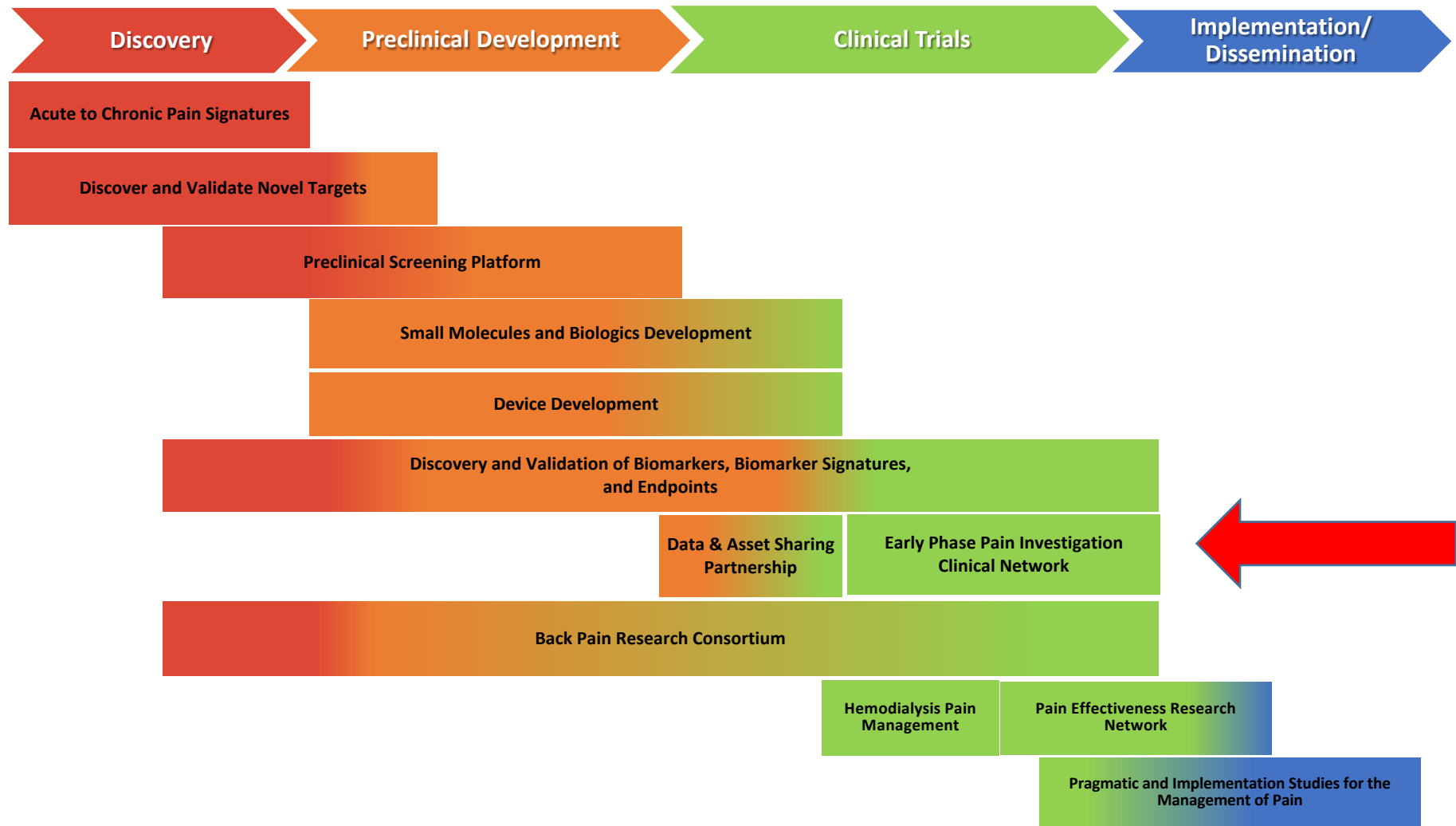


# NIH HEAL EPPIC-NET

Barbara Illowsky Karp, M.D.  
Program Director: EPPIC-Net  
National Institutes of Neurological Disorders and Stroke  
National Institutes of Health



# HEAL Programs for Pain



# EPPIC-Net Purpose

The goals of EPPIC-Net are to provide academic and industry investigators with expert infrastructure and support for early-phase clinical testing of pain therapeutics across populations and the lifespan AND to reduce reliance on opioids by accelerating early-phase clinical trials of non-addictive pain therapeutics, including drugs and devices.

# EPPIC-Net Overview

## EPPIC-Net will:

- **Test new pain treatments (compounds and devices judged highly meritorious in peer review that come from industry and academia) in early-stage trials**
- **Incentivize, accelerate Phase II trials; Reduce the time to start, enroll, run, and complete trials**
- **Focus on well-defined pain conditions with high-unmet need; provide well-characterized pain patient cohorts for EPPIC-Net clinical trials, incorporating deep phenotyping**
- **Provide proof-of-concept testing of potential biomarkers and new non-addictive treatments**
- **Validate biomarkers for utility in assessing target engagement or pain outcomes**
- **Develop and test innovative clinical trial paradigms to engineer adaptive, ever-improving early-phase testing of new pain therapies**

# EPPIC-Net & NIAMS BACPAC

**EPPIC-Net is collaborating with the NIAMS Back Pain Consortium (BACPAC) Research program. BACPAC is focused on chronic low back pain research using novel, inter- and multidisciplinary integrated approaches and novel analytics for discovery of disease mechanisms and features for deep patient phenotyping and identification of new targets for intervention.**

**More information can be found in the following notices:**

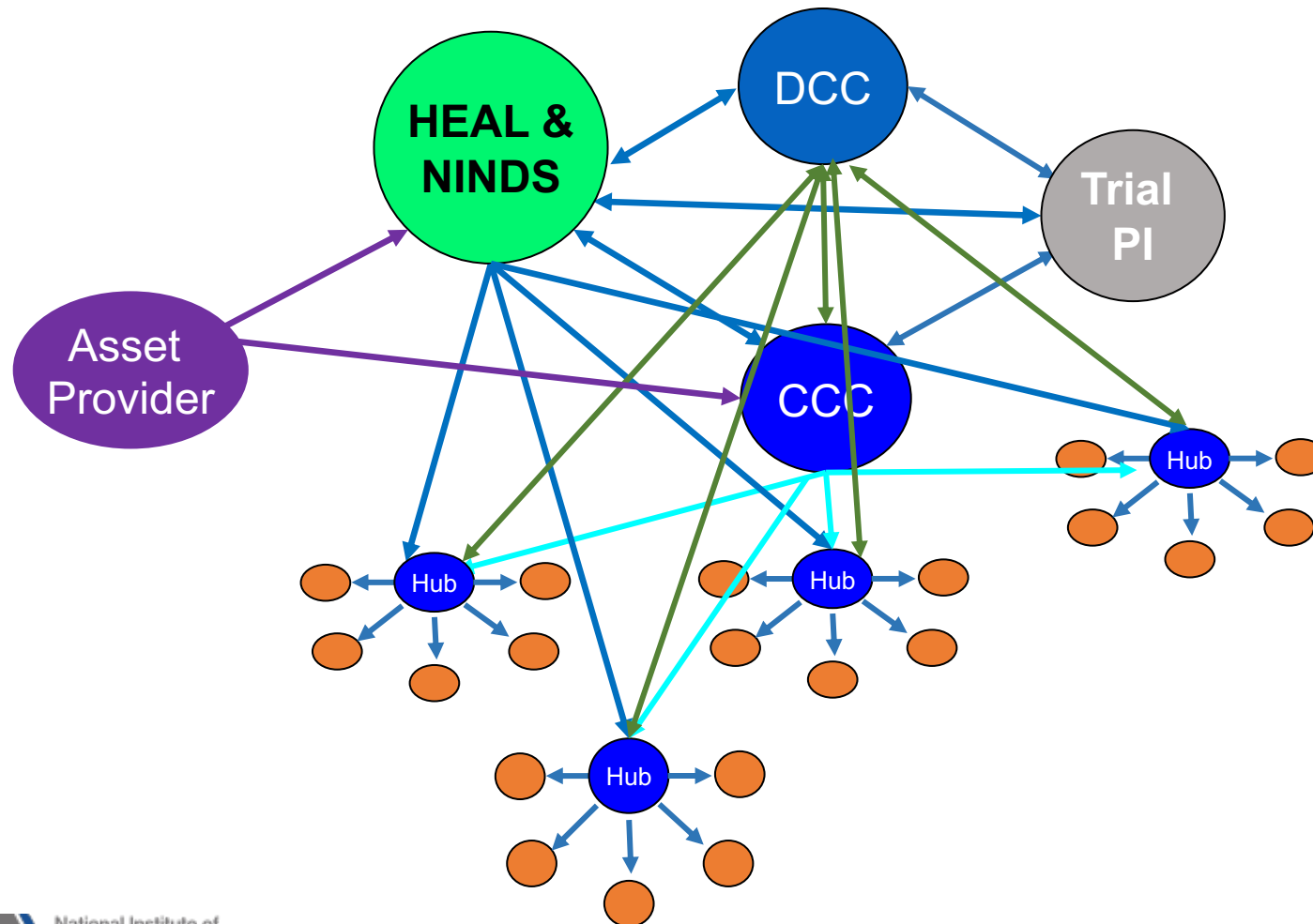
- NOT-AR-19-022 (<https://grants.nih.gov/grants/guide/notice-files/NOT-AR-19-022.html>)
- NOT-AR-19-023 (<https://grants.nih.gov/grants/guide/notice-files/NOT-AR-19-023.html>)
- NOT- AR-19-024 (<https://grants.nih.gov/grants/guide/notice-files/NOT-AR-19-024.html>)
- NOT-AR-19-025 (<https://grants.nih.gov/grants/guide/notice-files/NOT-AR-19-025.html>)

# EPPIC Network Advantages

- Increased trial quality
- Balanced portfolio
  - Allows logical ordering of incoming trials
  - Creates a pipeline for future trials
- Stable infrastructure and research capacity
  - Stable funding for research and training
- Required data sharing
  - Single data center with uniform governance and quality assurance
  - Use of CDEs within EPPIC-Net and within HEAL
  - Data will be submitted to central HEAL data repository for broad use/sharing
- Biosample repository and sharing
- Manages trials competing for similar patients
- Coordinates with non-profits, industry, and international partners
- Trains the next generation of clinical trialists



# EPPIC Net Infrastructure



# EPPIC NET – Infrastructure Defined

## Clinical Coordinating Center (CCC)

- Manages centralized IRB arrangements and Master Trial Agreements
- Match Hubs/Spokes to the protocol/asset
- Identify and train site investigators/staff
- Standardize CRFs, CDE's and methodologies
- Work with DCC; develop SOPs and quality controls
- Distribute funds with NINDS oversight

## Data Coordinating Center (DCC)

- Receives, processes and centralizes data
- Provide statistical/analysis reports
- Harmonizes with data from other HEAL studies
- Monitors safety/provides reports to DSMB and other monitors
- Creates data repository; Manages EPPIC-Net data
- Biorepository for EPPIC-Net and other HEAL projects

## Clinical Hubs & Spokes

- Identifies individual investigators
- Conducts trials
- Collects and reports data to DCC and CCC

## NIH

- Selects Assets for study
- Interacts with all EPPIC-Net components
- Provides oversight of studies
- Oversees budget and milestones

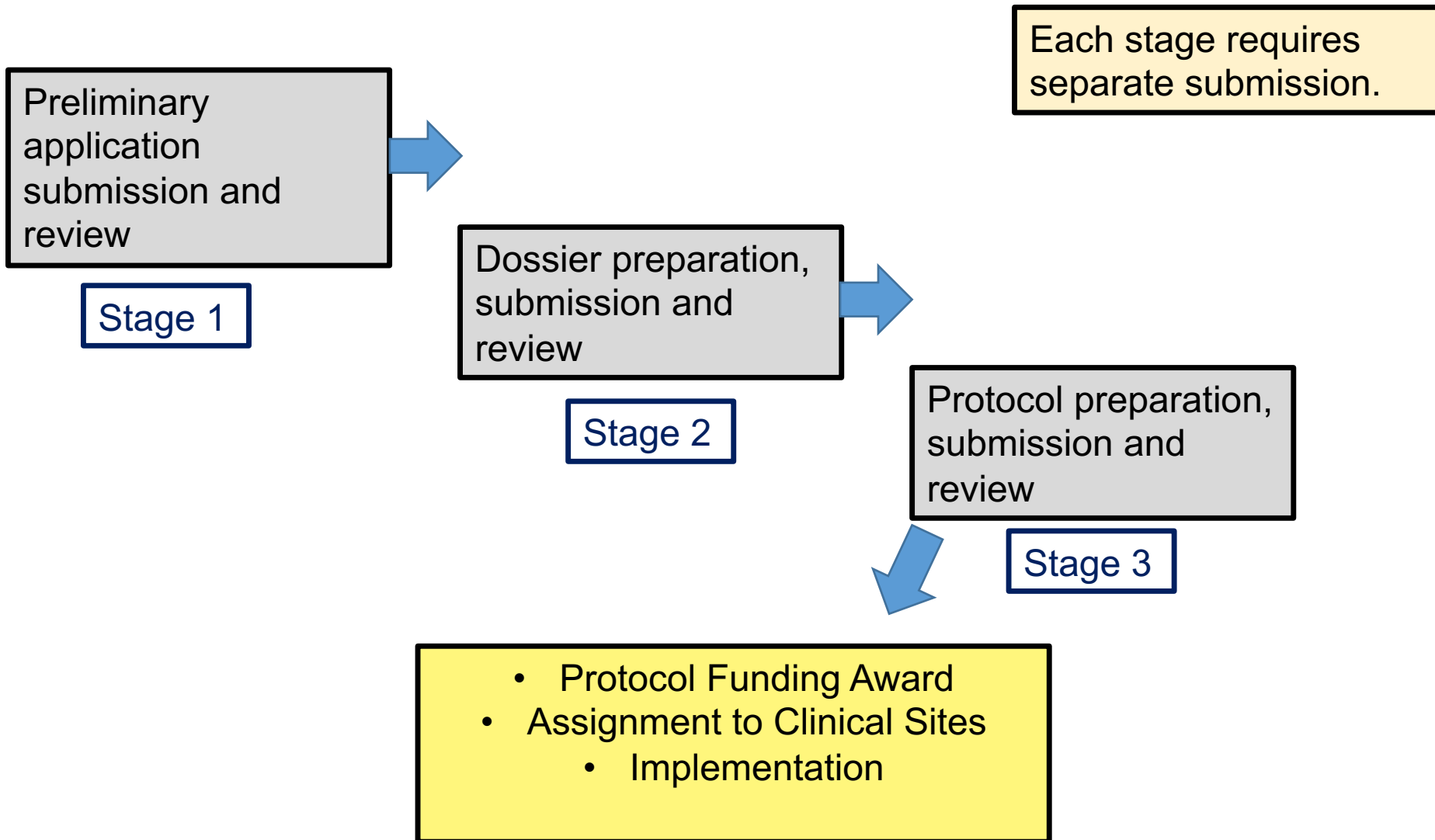
**Funding for infra-structure components are U24 Cooperative Agreements.**

# EPPIC-Net Asset Solicitation

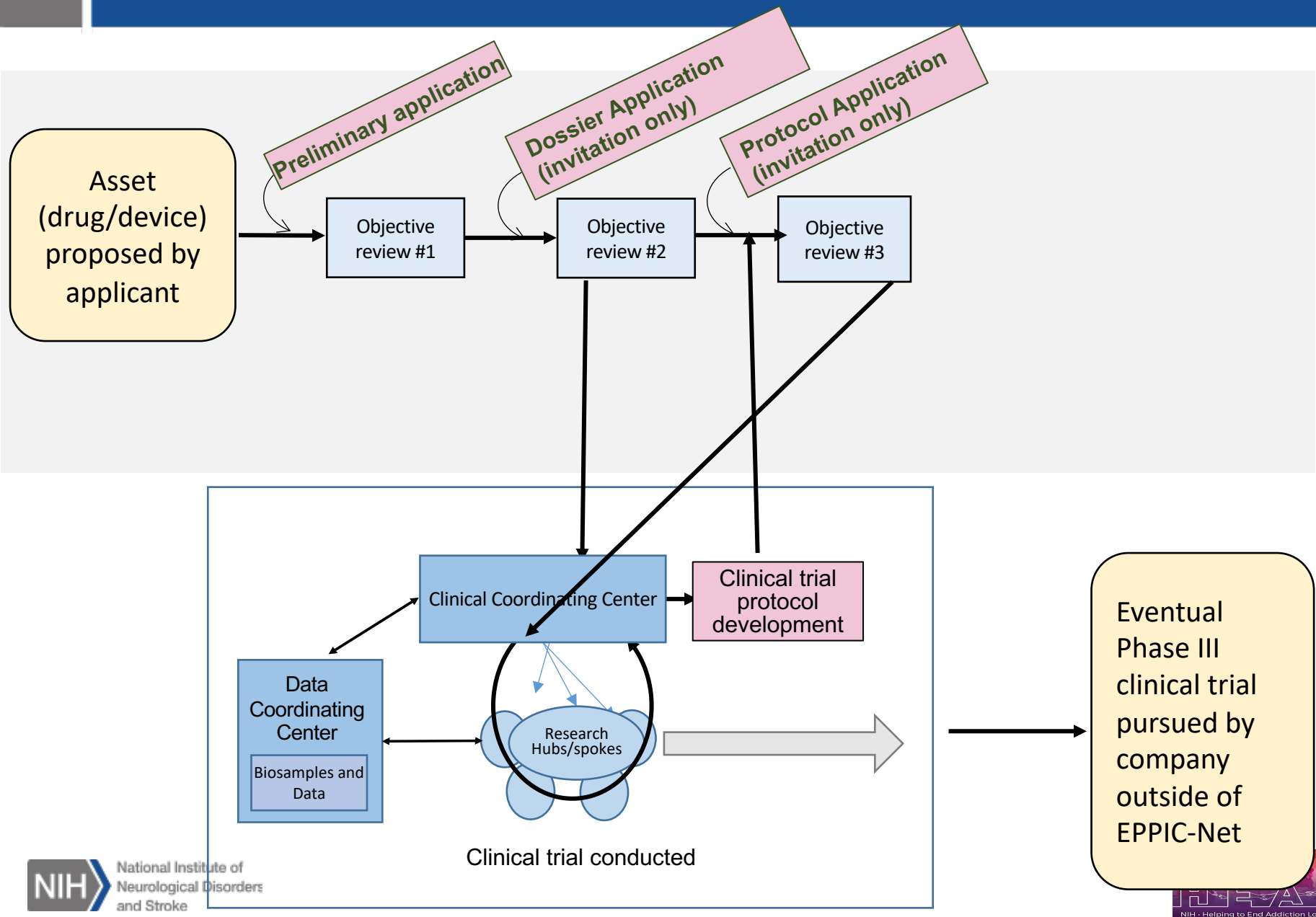
Those from Industry, Academia (and Elsewhere) are invited to submit applications for assets to be studied within EPPIC-Net

- EPPIC-Net is seeking non-addictive therapeutics for targeted pain conditions that currently lack adequate treatment
- Drug, biologics, and device assets considered
- All pain conditions considered
- Studies addressing pain across the age spectrum encouraged
- Assets that serve for proof-of-concept testing considered
- Re-purposed drugs considered
- Phase 2 ready with existing IND/IDE desirable
- The asset and IP remain the property of the asset owner; Confidentiality agreements implemented as needed. Technology transfer agreement (CRADA or other) defines relationship between EPPIC-Net and asset owner.

# EPPIC NET – 3 stage application process

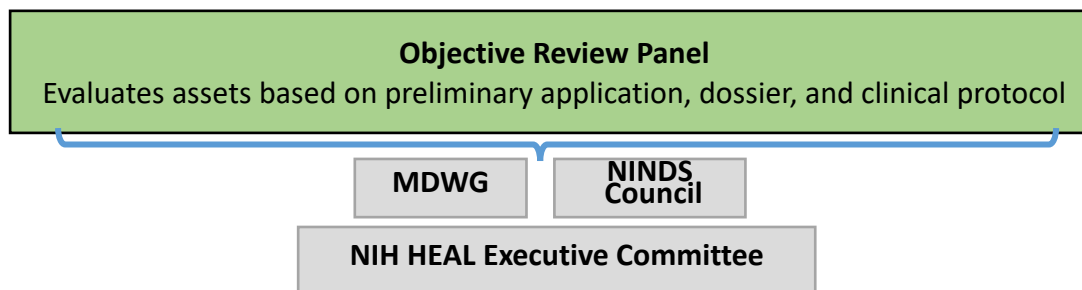


# EPPIC-Net Application Overview



# EPPIC NET – Funding information

	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” (OT) 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; Asset holder gains access to EPPIC-Net for asset clinical trial.**



# EPPIC NET Preliminary Application

**EPPIC-Net Preliminary application packet is available at**

<https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative/early-phase-pain-investigation-clinical-network-eppic-net>

<https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/NINDS-Role-HEAL-Initiative/NINDS-Role-HEAL-Initiative-EPPIC>

**Preliminary application packet includes**

- 1. Information sheet with contact addresses**
- 2. Preliminary application (fillable .pdf)**
- 3. Line-by-line application instructions**
- 4. eRA Commons submission instructions**

# EPPIC-NET Preliminary Application

- Applicant information
- Asset information
- Freedom to operate
- Biological rationale
- Relevant prior studies (preclinical and clinical) with relevant literature citations
- Proposed indication
- Proposed treatment regimen
- Proposed outcome measures (efficacy, biomarkers, and safety)
- FDA/regulatory status
- Feasibility/logistics concerns



## EPPIC-Net Preliminary Asset Application

### Applicant Information:

1a. Title:  First Name:  MI:  Last Name:  Suffix:   
1b. Degree:  If other, identify:

### Project Identification:

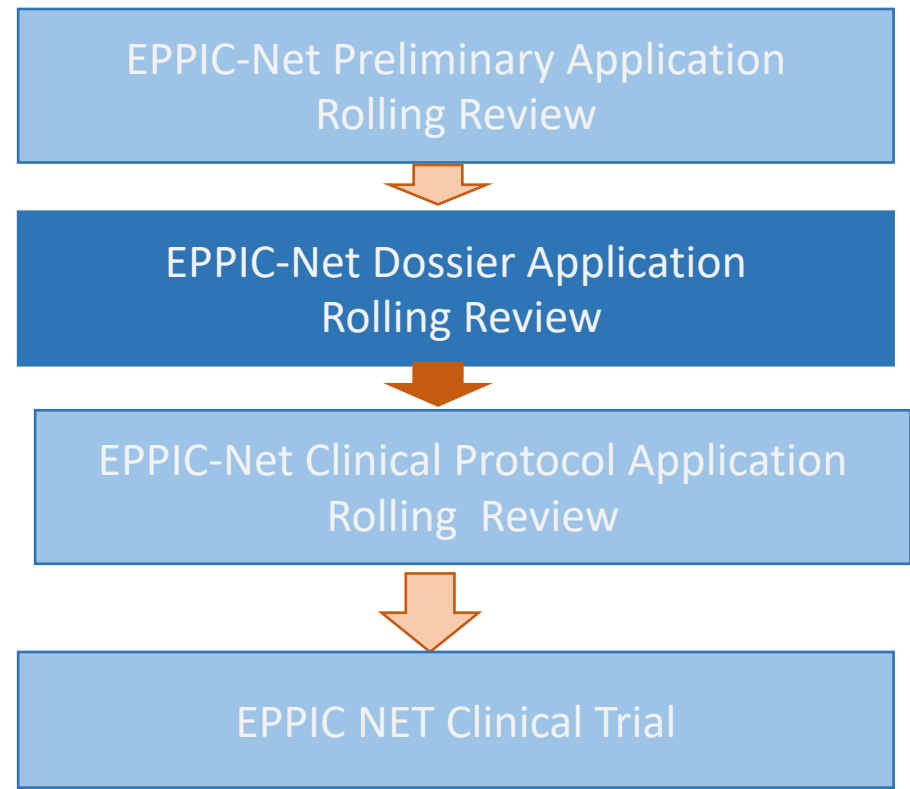
2. Title of Project (limit 200 characters):

3. Brief description of project with rationale (limit 300 words):

# EPPIC-NET Dossier Application

Applications selected through rigorous review process will work with an NIH contractor to prepare the Stage 2/Dossier application

- Scientific rationale
- Clinical unmet need
- Target product profile (TPP)
- Target-disease connection
- Preclinical Data Package
- Chemistry/manufacture, device specifications
- Biology, pharmacology, physiology
- Clinical data to support proposed trial
- Clinical considerations for HEAL Program
- Non-scientific considerations



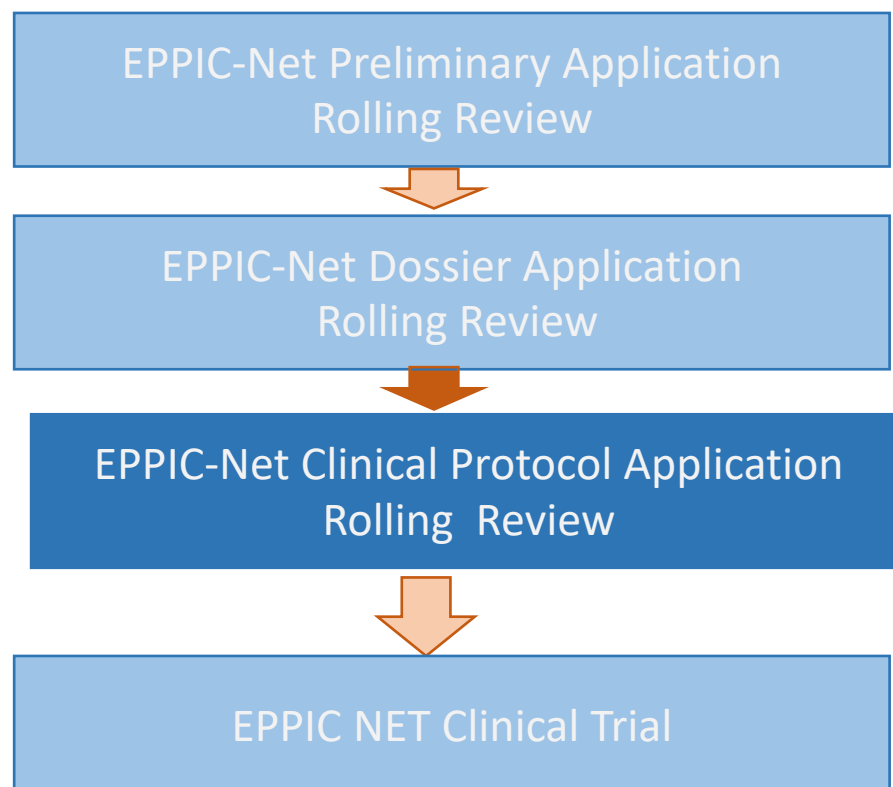
# EPPIC-NET Protocol Application

Dossier applications selected through rigorous review process will work with EPPIC-Net infrastructure (led by CCC) to prepare the Stage 3/Protocol application

- Protocol will be based on NIH/FDA template

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

- Full trial information and plan
- Human subjects protections addressed
- Stage 3 application includes proposed budget and study timeline
- Stage 3 applicant is CCC in coordination with asset owner



# EPPIC-Net Review process and criteria

**Marilyn Moore-Hoon, PhD**  
**Scientific Review Officer**  
**NINDS**



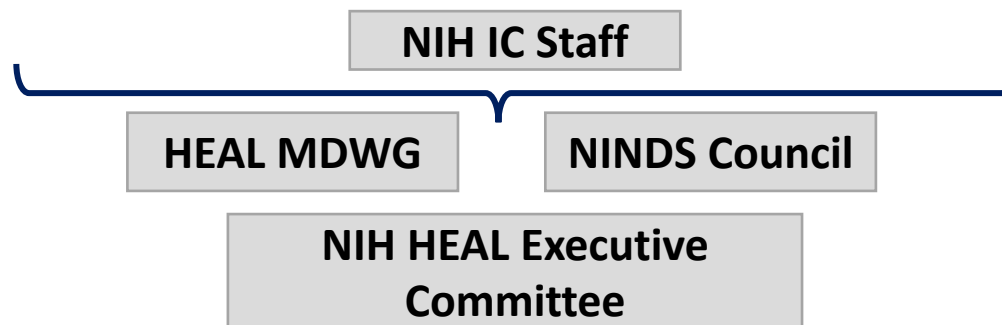
Objective Reviews are  
**NOT**  
using the standard  
NIH Peer Review process!!!



# EPPIC NET – Review process and criteria

	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

**Objective Review Panel**  
Evaluates assets based on template, full dossier, and clinical protocol



## Goals of Objective Review

- To get expert input for NINDS/HEAL consideration of EPPIC-Net awards
- To have a fast, streamlined review process
- To get reviewers' individual opinions on each proposed therapeutic.
  - Consensus is *not* the goal. Scores will *not* be stated out loud at the meeting or averaged after the meeting – each reviewer's score stands alone.
- Conflicts of Interest (COI) will be managed using standard review COI policy as a guide.

## Objective Review Panel Composition

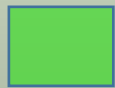
- 25-30 Core panel members. Same panel for all stages of review (different members may be present)
- Expert ad hoc reviewers as needed to cover science, rigor, and methodology
- As a therapeutic moves through the application stages – stage appropriate expertise will be included.

## Review Timeline

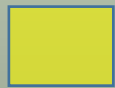
- Review of applications for all stages should be completed within 2 months of receipt.
- Applications are submitted on a rolling basis: meeting cut-off dates will be posted on the EPPIC-Net webpage:
  - e.g. “All applications received by Oct 1 will go to review at the end of Oct meeting.”
- Applicants will be notified of the outcome, but **NO** Summary Statements provided
  - Feedback will focus on therapeutics of interest

## Application Review

Pre-meeting individual reviewer assessment will identify 3-4 key strengths and weaknesses and an initial recommendation for a color “Bin”:



**GREEN** – Meritorious – will be discussed



**YELLOW** – Meritorious, but concerns noted – may be discussed



**RED** – Not deemed meritorious – will not be discussed.

## Stage 1 Review Criteria

- Significance
- Approach
- Viability/Feasibility



## Significance

- Do the asset and approach appropriately target a specific type of pain with high unmet therapeutic need?
- Do the asset and approach represent a marked improvement over existing pain therapies?
- Will the asset and proposed study notably advance the field of pain therapy?

## Approach

- Is the strategy for testing this asset in a Phase 2 Clinical Trial realistic?
- Will the asset be scalable?
  - Are there plans to have enough asset available for a Phase 2 Clinical Trial?
  - Will the asset be scalable for eventual clinical use?
- Is there a reasonably rapid timeline for bringing this asset to a clinical trial?
- Are novel methods, assays, or approaches proposed?
- Are safety and biohazard considerations for use of the asset in humans clearly addressed

## Viability/Feasibility

- Is the asset appropriate for the proposed indication?
- Does the study information provided, support a Phase 2 Clinical Trial?
- Is there a path forward for eventual clinical adoption?
- Are there barriers to use of the asset in the proposed study or eventually in the clinic?
- Have safety and regulatory IND/IDE studies been completed, indicating readiness for a Phase 2 Clinical Trial?

## Stage 2 and 3: Objective Review

- Same Objective Review panel with additional ad hocs for proper science and stage evaluation.
- Different criteria matched to stage of review
- Stage 3 will be similar to an NIH standard review to ensure consideration of required policies such as *The Protection of Human Subjects* and *Inclusion Across the Lifespan*.

# EPPIC-Net eRA Commons

Laura M. Roman, MBA, PhD  
eRA/OER



# EPPIC-Net: Preparation, Submission & Tracking


## eRA Commons

### Registrations

- Submitting organization must be registered at eRA Common
- Organization must have individual with role of Signing Official
- Streamlined Commons registration process: no DUNS required for submission
- PD/PI must have Commons ID and be affiliated with submitting organization

# EPPIC-Net: Preparation, Submission & Tracking

## Application Preparation & Submission in ASSIST

- NIH's System to System solution
- Application preparation, submission & tracking in a single system
- Streamlined submission- single form + attachments
- Use opportunity provided in EPPIC-Net (OTA-XX-XXX) 
- if PI completes profile in eRA Commons, can use Commons ID to prepopulate select fields

# EPPIC-Net: Preparation, Submission & Tracking

Application Submission System & Interface for Submission Tracking (ASSIST)  
Sponsored by the National Institutes of Health

Welcome

Welcome to the Application Submission System & Interface

INITIATE APPLICATION  
Funding Opportunity Announcement #  
(Example: PA-XX-XXX or LITC-ABCD-XX-000)

The National Institutes of Health posts Funding Opportunity Announcements (FOAs) in the [NIH Guide for Grants & Contracts](#) and in [Grants.gov's Search Grants](#). Each resource has robust search functionality to identify opportunities of interest. ASSIST can only be used to prepare and submit applications when explicitly stated in the FOA.

[Home](#) > [Search for Applications](#) > [Initiate Application](#)

SEARCH FOR

Initiate Application for ROA #: OTA-18-005

ROA INFORMATION:

ROA Number: OTA-18-005

Opportunity Title: OT Research Opportunity Test June

Offering Agency: National Institutes of Health

Opportunity Open Date:

Opportunity Close Date:

Agency Contact: NIH Contact

Application Identifier:

Application Project Title \*  
(describe title in 200 characters)

Lead Applicant Organization: \*  
---- Choose Organization ----

Lead Applicant Organization Address:

Contact Project Director/Principal Investigator

Enter PD/PI Information below or

First Name:

Middle Name:

Last Name:

Enter opportunity announcement # here\*

\*Research Opportunity Announcement (ROA) # will be posted on EPPIC-Net website on Sept 3

Enter title for application





# EPPIC-Net: Preparation, Submission & Tracking

Actions ?

RETURN TO APPLICATION

MANAGE ACCESS

PREVIEW CURRENT FORM

VALIDATE APPLICATION

VIEW STATUS HISTORY

UPDATE SUBMISSION STATUS

COPY APPLICATION

DELETE APPLICATION

Home > Search for Applications > Application Search Results > Application Information

Hide Navigation

Application Information ?

Summary

OTA Core

NIH Other Transaction Application Form  
OTA Core v1.0 ?

Edit

Submission Type

Application Information

Application Identifier: 21115

Application Project Title: Clinical Center for All of Us NIH Program

PD/PI Name: AARONS, GREGORY

Organization:

Project Period:

Status: Ready for Submission

Status Date: 2018-05-16 10:50:09.000 PM EDT

Submit Application

Submit Application

# EPPIC-Net: Preparation, Submission & Tracking

Summary

OTA Core

OTA Core > Contact PD/PI Record

OTA Core - Contact PD/PI Record

OTA Core v1.0 ?

Edit

☒ Expand

Credential, e.g., agency login

Populate fields from Credential

Prefix

--- Select Prefix --- ▾

\* First Name

Middle Name

\* Last Name

Suffix

--- Select Suffix --- ▾

Position/Title

Department

\* Organization Name

Division

\* Street 1

Street 2

\* City

County/Parish

State

CA: California

Province

\* Country

USA: UNITED STATES

Zip/Postal Code

Phone Number

Fax Number

\* Email

9. Attachments

Attachments

Add Attachment

Attachment

Equipment.pdf

Save and Keep Lock

Save and Release Lock

Cancel and Release Lock



# EPPIC-Net: Preparation, Submission & Tracking

Actions ?

RETURN TO APPLICATION

MANAGE ACCESS

PREVIEW CURRENT FORM

VALIDATE APPLICATION

VIEW STATUS HISTORY

UPDATE SUBMISSION STATUS

CONFIRM APPLICATION

DELETE APPLICATION

Home > Search for Applications > Application Search Results > Application Information

Hide Navigation

Application Information ?

SummaryOTA Core

NIH Other Transaction Application Form  
OTA Core v1.0 ?

Edit

Submission Type

Application Information

Application Identifier:21115

Application Project Title:Clinical Center for All of Us NIH Program

PD/PI Name:AARONS, GREGORY

Organization:

Project Period:

Status:Ready for SubmissionSubmit Application

Status Date:2018-05-16 10:50:09.000 PM EDTSubmit Application

# EPPIC-Net: Preparation, Submission & Tracking

## ASSIST

Submission Date:	2019-04-01 10:28:06 AM
Submitting AOR:	ROMANL_SO
ASSIST Submission Status:	Submitted
Submission Status Date:	2019-04-01 10:28:06 AM

## Agency

[View Agency Submission Errors and Warnings](#)

Agency Tracking #:	<a href="#">4271519</a> (To View Commons Status and Application Details) <a href="#">To View Commons Post Submission Actions</a>
Agency Status:	PROCESSED
Agency Status Date:	2019-04-01 10:28:11 AM

Close

© 2019 NIH. All Rights Reserved.

Screen Rendered: 04/01/2019 11:00:21 AM | Screen Id: ASSIST0095@1047

# EPPIC-NET TIME-LINE

2019

Preliminary  
application  
submission and  
review

Dossier preparation,  
submission and  
review

Protocol preparation,  
submission and  
review

September



October



November



December

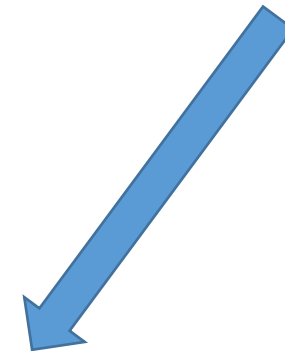
2020

**FUNDING AND  
IMPLEMENTATION OF  
FIRST TRIALS**

February



January



# EPPIC-NET Final comments

EPPIC-Net opens for applications on **Sept 3, 2019**. Please check the website for updates, the ROA # needed to complete the application, and to join the EPPIC-Net list-serv



## EPPIC-Net Contacts:

### EPPIC-Net Program Director:

Barbara Illowsky Karp, M.D.

[barbara.karp@nih.gov](mailto:barbara.karp@nih.gov)

(o) 301-496-0150

### EPPIC-Net Program Manager

Rebecca Hommer, M.D.

[rebecca.hommer@nih.gov](mailto:rebecca.hommer@nih.gov)

### EPPIC-Net Program Assistant

Nancy Bowen, Dr.PH, MPH

[nancy.bowen@nih.gov](mailto:nancy.bowen@nih.gov)

(301) 827-6865

## HEAL Contacts:

<https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative>

## eRA Commons Contacts:

Service desk:

<https://grants.nih.gov/support/index.html>

Laura M. Roman, PhD, MBA

301 451-5966

301 642-4207 (mobile)

[Laura.roman@nih.gov](mailto:Laura.roman@nih.gov)

**THANK YOU FOR YOUR INTEREST IN  
NIH HEAL AND EPPIC-NET**



National Institute of  
Neurological Disorders  
and Stroke

