GENERAL GUIDELINES FOR COMPLETING THE PRELMINARY APPLICATION

- Applicants are strongly encouraged to talk to EPPIC-Net staff before submitting a preliminary application.
- EPPIC-Net will not consider assets without preliminary data in humans
- Please read the objective review criteria for ROA OTA-21-005 that can be found on the EPPIC-Net website. Complete the application with information that best addresses the review criteria (https://www.ninds.nih.gov/sites/default/files/roapreliminaryapplication_rerelease_508c.pdf)
- Please be reminded assets remain the property of the asset owner
- All information provided in the application is kept confidential.
- Required documents for the preliminary application include:
  - The preliminary application
  - Cover letter for NIH review only
  - Freedom-to-operate letter
  - Pdf files of cited references
- Do not submit documents or attachments in addition to or other than those listed above.
- All documents must be submitted in .pdf format
- APPLICATIONS MISSING REQUIRED DOCUMENTS OR WITH ADDITIONAL DOCUMENTS OR ATTACHMENTS WILL BE ADMINISTRATIVELY WITHDRAWN WITHOUT REVIEW

LINE-BY-LINE INSTRUCTIONS FOR COMPLETING THE EPPIC-NET PRELIMINARY APPLICATION

Applicant information

1. Applicant information: Provide applicant name, title, and degree. Other applicant information will be entered directly into eRA Commons.
2. Key Research Personnel Information (optional): You may identify one other key personnel for the application.

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 for study. [200 character limit]
4. Brief description of project with rationale:

   Identify the asset, the target population, and the type of pain to be studied. Describe the way in which the asset and proposed study address an unmet need in pain therapeutics and the opioid

crisis. Identify how the outcome of the proposed phase 2 clinical trial, if successful, would inform decisions regarding future research on the asset. Provide information on whether and how your asset offers an advantage over similar therapeutics. [500 word limit]

Asset information

5. Asset name
6. Asset status: identify if the asset is proprietary, marketed (commercially available), or other. If other, specify status.
7. Asset ownership: Identify the asset owner. If the applicant is the owner, select "self" and identify if the applicant is the originator or a licensee. If someone else is the owner, enter the name of the owner. If there is more than one owner, identify all owners in the supporting statement (see #8, below).
8. Authorization of asset availability and use: Whether the applicant is the owner or not, provide a statement of support from the applicant or asset owner confirming that the applicant has authorization to access and use the asset in the proposed study (freedom-to-operate) or that the asset is out-of-patent and not licensed and so is available for use in the study. The statement must be submitted as a .pdf document with the application in eRA Commons. *Applications that do not include a freedom-to-operate letter will be returned without review as nonresponsive.*
9. Asset type: if more than one asset type (e.g. a drug and a biomarker) is proposed for study, complete each applicable section
10. Drug: if the proposed asset is a drug, provide the following information
    a. Drug type: Select drug type. If "other," identify.
    b. Pharmacological class: Select class. If "other," identify.
    c. Mechanism of action: identify mechanism of action. If unknown, enter "Unknown".
    d. Target: identify the drug target
11. Device: if the proposed asset is a device, provide the following information
    a. Device contact with body: identify if the device is implanted, placed on the body surface, or true external (no body contact)
    b. Device interaction with the body: Identify if the device interacts with or modulates the body in any way or if it is solely recording or monitoring.
    c. Device target: identify the body organ or region the device is targeting.
    d. If the target is the brain, identify the target brain region or function. If there is no target brain region, write "not applicable".
12. Biomarker: if the proposed asset is a biomarker, provide the following information
    a. Purpose of biomarker: identify what the biomarker is a surrogate for.
    b. Sample needed: Choose the type of sample needed to assess the proposed biomarker
        i. If a body fluid is needed, select the type of body fluid. If "Other" or " blood derivative", identify.
        ii. If a tissue sample or biopsy is needed, chose what tissue is needed. If "other," identify the type of tissue sample/biopsy needed.
        iii. If the biomarker is an imaging biomarker, select the type of imaging. If "other," identify.
        iv. If the biomarker is a physiological measurement, select the type of test needed. If "other," identify.
        v. If the biomarker uses behavioral or observational data, describe.

Investigational New Drug (IND) /Investigational Device Exemption (IDE) information

13. State if asset is FDA regulated. If IND/IDE exempt or FDA regulations do not apply, explain why and skip to Item #15

a. State if an IND/IDE has been assigned for the asset. If so, provide the IND/IDE number and state if the IND/IDE is active and in good standing.

For FDA-regulated assets without a current active IND/IDE, indicate

b. If there has been a pre-IND/IDE meeting with the FDA regarding a clinical trial with the asset. If so provide the meeting date.
c. If adequate data is available to support an IND/IDE filing at the time of application to EPPIC-Net.
d. If an IND/IDE application has already been filed with the FDA.
e. Expected time to receive an IND/IDE

14. Investigator brochure: State if there is an IB for the proposed asset and if the asset owner is willing to share the IB or proprietary data with HEAL/EPPIC-Net. [Note: assets submitted to EPPIC-Net remain the property of the asset owner. Confidentiality of submitted materials will be protected.]

Relevant prior research on asset

For questions 15-18, provide citations for selected research publications and reports that demonstrate the asset's suitability and readiness for a phase 2 clinical trial. You may reference unpublished data. In addition, upload each cited article or a summary of unpublished data as a PDF document attachment. The attachments are limited to no more than 18 articles/reports (3 per each question 17, 18, 19, 20a, b, c).

15. Background key literature citations. Provide citations for 3 key references specific to the proposed asset that provide background and context for the proposed clinical trial. Submit copies of the cited references as pdf files with the application.
16. Preclinical efficacy studies to support indication completed. If preclinical efficacy studies have been done, provide citations for up to 3 references, reports or publications. Submit copies of the cited references as pdf files with the application.
17. IND/IDE enabling studies completed to support IND/IDE. If IND/IDE enabling studies were done, provide citations to 3 key references, reports or publications supporting asset profile and readiness for clinical trial. Submit copies of the cited references as pdf files with the application.
18. Phase I, II, III studies completed. If phase I, II, or III clinical studies have been completed, provide citations for up to 3 references, reports or publications for each phase and include ClinicalTrials.gov Identifier/NCT number. Submit copies of the cited references as pdf files with the application.
19. If Phase I, II, and/or III clinical studies have been completed, provide the following information:
    a. Cumulative number of human subjects studies: provide cumulative number of individuals studied across all human studies to date
    b. Dose range studied in humans: provide the dose range studied for the proposed asset (drug or device, as applicable) across all human studies to date. Dosing information should include the dose, concentration, and frequency of drug administration, device settings and exposure information, or any other relevant information about human administration.
    c. Number of doses/duration of exposure/route in humans. Provide information regarding the maximum number of doses, exposure duration, and type/route of exposure for the proposed asset, whether drug or device, in all human studies to date.
20. Site(s) of prior studies. Identify where prior studies were conducted. If outside the USA or EU, identify site(s)
21. Known frequent and/or serious adverse effects (animal and/humans). Identify and summarize

frequent and/or serious adverse events from preclinical and clinical studies to date

22. Addiction potential: Indicate if the asset has been tested for addiction potential, and, if tested, if it is known to have addiction potential or not. If “no” addiction potential is indicated, provide information how addiction potential was assessed.
23. Evidence of efficacy for intended indication. State if there is evidence of asset efficacy for the proposed indication in prior preclinical or clinical studies. If so, state if efficacy was demonstrated or if there was only a trend towards significance.

Proposed study information

24. Pain Acuity: Identify if the proposed study is targeting acute, chronic pain, or the transition from acute to chronic pain.
25. Pain Type: Choose the type of pain proposed to be study. If other, identify.

Population

26. Disease/condition to be studied: Identify the pain disease or condition proposed for the study
27. Population to be studied: Identify whether the proposed study includes patients, unaffected subjects or both
28. Special populations: Identify whether the proposed study includes children, cognitively-impaired adults or other vulnerable groups. If other or multiple vulnerable populations, identify.
29. Proposed treatment regimen: provide the dose, route of administration, frequency of administration, and duration of exposure for the asset drug or device proposed for use in the EPPIC-Net study. If a particular category is not applicable, write in "n/a"

Outcomes

30. Primary outcome measure for efficacy: describe the proposed primary study outcome measure for efficacy.
31. Primary outcome measure for safety: describe the proposed primary study outcome measure for safety.

Additional information

32. Summarize currently available treatments for the proposed condition: state what treatments are currently available and how the proposed asset may differ and offer an advantage. For biomarkers, describe currently available biomarkers for the proposed biomarker target and what advantage the proposed biomarker offers.
33. Feasibility/logistics concerns: Check "yes" if there are any feasibility/logistical barriers and identify the concern(s): e.g., whether it would be difficult/not feasible to recruit an adequate number of subjects within a reasonable period of time; whether the drug or device may be too costly for use in the study, whether the asset is scalable to the necessary level (whether an adequate pharmaceutical grade drug could be produced, distributed and stored in numbers great enough to support study, or whether an adequate number of devices would be available for all study sites). Explain any concerns identified.
34. Availability of asset: Identify when the asset could be ready in adequate supply to support the study Explain any barrier to availability within 90 days of receipt of funding.
35. Readiness to start clinical trial: Once approved for funding, identify how long it would take to start the trial. Explain any barriers to starting within 90 days of receipt of funding.