GENERAL GUIDELINES FOR COMPLETING THE PRELIMINARY APPLICATION

- **Applicants are strongly encouraged to talk to EPPIC-Net staff before submitting a Preliminary Application**
- All information provided in the application is kept confidential
- EPPIC-Net will not consider assets without preliminary data in humans
- The preliminary application form and all other documents must be submitted as PDF documents (maximum allowed is 35MB; 25MB or less preferred)
- Please be sure to check the EPPIC-Net website immediately prior to submission to assure that the application is submitted under the current and correct ROA number
- Please read the objective review criteria in the ROA document and on the EPPIC-Net website. Provide information in the application that best addresses the review criteria

- **Do NOT submit documents or attachments in addition to or other than those listed above**
- **Do NOT submit documents or attachments longer than specified page limits**
- **Do NOT include hyperlinks**

APPLICATIONS THAT ARE MISSING REQUIRED DOCUMENTS, CONTAIN ADDITIONAL DOCUMENTS OR ATTACHMENTS, OR INCLUDE DOCUMENTS LONGER THAN SPECIFIED LIMITS, MAY BE ADMINISTRATIVELY WITHDRAWN WITHOUT REVIEW

Line-by-line Instructions for Completing the EPPIC-Net Preliminary Application

1. Applicant/PI Information

Provide applicant name, title, degree, and contact information. 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.

3. Project Identification

3a. Title of Project: Provide a title that is descriptive of the project, including identification of the asset, asset type (e.g., drug, device, biomarker), and target population/type of pain the asset is being proposed for. (**Limit 200 characters**)

3b. If this application is a re-submission for an asset previously reviewed, check the box and additionally identify what new information has been provided since the prior review to aid reconsideration. (**Limit 250 words**)

3c. Provide a 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. (**Limit 750 words**)

4. Asset Information

4a. Provide asset name.

4b. Select asset status: Identify if the asset is proprietary, marketed (commercially available), or other. If other, specify status.

4c. Asset ownership: Identify the asset owner(s). If the applicant is the owner, enter "Self"; if someone else is the owner, enter the name of the owner(s). If there is more than one owner, all owners must be listed in the supporting statement (see **#4e**, below).

4d. If the applicant is the owner, identify if the applicant is the originator or a licensee.

4e. Provide asset authorization: Whether the applicant is the owner or not, provide a statement of support from the applicant or asset owner(s) 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 administratively withdrawn as nonresponsive, and not reviewed.**

4f. Select asset type: If more than one asset type (e.g., a drug and biomarker) is proposed for study, complete each applicable section (4g-4i).

4g. Drug: If the proposed asset is a drug, provide the following information:

i. Drug Type: Select drug type. If "Other", identify.
ii. Pharmacological Class: Select class. If "Other", identify.
iii. Mechanism of Action: Identify mechanism of action. If unknown, enter "Unknown".
iv. Target: Select drug target. If "Other", identify.

4h. Device: If the proposed asset is a device, provide the following information:

i. Device contact with body: Identify if the device is implanted, placed on the body surface, or true external (no body contact).
ii. Device interaction with participant: Identify if the device interacts with or modulates the body in any way or if it is solely recording or monitoring.
iii. Device target tissue/organ: Identify the body organ or region the device is targeting.
iv. If brain, identify target brain region or function. If there is no target brain region, enter "not applicable".

4i. Biomarker: If the proposed asset is a biomarker, provide the following information:

i. Purpose of biomarker: Identify what the biomarker is a surrogate for.
ii. Sample type needed: Choose the type of sample needed to assess the proposed biomarker.
    a. If a body fluid is needed, select the type of body fluid. If "Blood derivative", identify.
    b. If a tissue sample or biopsy is needed, chose what tissue is needed. If "Other", identify the type of tissue sample/biopsy needed.
    c. If the biomarker is an imaging biomarker, select the type of imaging. If "Other", identify.

d. If the biomarker is a physiological measurement, select the type of test needed. If "Other", identify.
e. If the biomarker uses behavioral or observational data, describe.

For all asset types, complete items 4j-4p.
Note: Copies of the FDA filing, Investigator Brochure, etc. are not required and should not be included in the submission.

***Investigational New Drug (IND)/Investigational Device Exemption (IDE) Information**

4j. State (yes/no) if asset is FDA-regulated or whether it's IND/IDE exempt.

If asset is not FDA-regulated, skip to item #5a, otherwise complete 4k.

4k. State (yes/no) if an IND/IDE has been assigned for the asset. If yes, provide the IND/IDE number and state if the IND/IDE is active and in good standing.

If IND is granted and in good standing, skip to Item 4p, if not, complete 4l-o.

4l. State (yes/no) 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.
4m. State (yes/no) if adequate data is available to support an IND/IDE filing at the time of application to EPPIC-Net.
4n. State (yes/no) if an IND/IDE application has already been filed with the FDA.
4o. State expected time to receive an IND/IDE.
4p. Investigator Brochure (IB): State (yes/no) 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. (**Do NOT** submit the IB, or proprietary data with the preliminary application.)

For items 5-6, provide citations for selected published research articles and reports that demonstrate the asset's suitability and readiness for a Phase 2 clinical trial. You may also reference unpublished data. Unpublished data should be provided in summary form, with summaries limited to 5 pages per citation. In addition, upload each cited article or summary of unpublished data as a PDF document attachment to the application. Attachments are limited to no more than 18 articles/summaries, total (i.e., 3 documents per question, for questions 5a, 5b, 5c, 6a, 6b, & 6c). Applications with attachments beyond these limits will be withdrawn administratively without review.

5. Relevant prior data on asset:

5a. 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 documents with the application, in accordance with instructions provided above.
5b. Preclinical efficacy studies to support completion: 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 documents with the application, in accordance with instructions provided above.

5c. 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 documents with the application, in accordance with instructions provided above.

6. Clinical Studies Citations

6a-6c. Phase 1, 2, 3 studies completed: If Phase 1, 2, or 3 clinical studies have been completed, provide citations for up to 3 references, reports, or publications for each phase and include ClincalTrials.gov Identifier/NCT number. Submit copies of the cited references as PDF documents with the application, in accordance with instructions provided above.

If Phase 1, 2, and/or 3 clinical studies have been completed, provide information for #7a-g.

7. Cumulative Information from Prior Studies:

7a. Cumulative number of human subjects studied: Provide cumulative number of individuals studied across all human studies to date.
7b. 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.
7c. 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.
7d. Site(s) of prior studies: Identify where prior studies were conducted. If outside the USA or EU, identify.
7e. 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.
7f. Addiction Potential: Indicate if the asset has been tested for addiction potential.

- If tested, state (yes/no) if asset is known to have addiction potential or not.
- If "no" addiction potential is indicated, provide information on how addiction potential was assessed.

7g. 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.

8. Proposed Study Information:

8a. Pain Acuity: Identify if the proposed study is targeting acute pain, chronic pain, or the transition from acute to chronic pain.
8b. Pain Type: Choose the type of pain proposed to be studied. If "Other", identify.

Population:
8c. Disease/Condition to be studied: Identify the pain disease or condition proposed for the study.
8d. Population to be studied: Identify whether the proposed study includes patients,

healthy/unaffected subjects or both.
8e. Special populations: Identify whether the proposed study includes children, cognitively impaired adults or other vulnerable groups. If other or multiple vulnerable populations, identify.

Proposed Treatment Regimen (For Drugs and Devices):
8f. 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, enter "N/A".

9. Outcomes:

9a. Primary outcome measure for efficacy: Describe the proposed primary study outcome measure for efficacy.
9b. Primary outcome measure for safety: Describe the proposed primary study outcome measure for safety.

10. Additional Information:

10a. 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. **(Limit 200 words)**
10b. Feasibility/Logistics Concerns: State (yes/no) 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. **(Limit 100 words)**
10c. 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. **(Limit 50 words)**
10d. 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. **(Limit 50 words)**