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.

Project identification

2. 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]
3. 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

4. Asset name
5. Asset status: identify if the asset is proprietary, marketed or other. If other, specify status.
6. 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).
7. 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. The statement must be submitted as a .pdf document with the application in eRA Commons.
8. Asset type: if more than one asset type (e.g. a drug and a biomarker) will be present in the proposed study, complete each applicable section
9. 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
10. 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".
e. Expected FDA classification. Select Class I, II, or III. For definitions, see https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device
f. Expected FDA device classification name. For definitions, see https://www.fda.gov/medical-devices/classify-your-medical-device/product-code-classification-database
g. Expected FDA Classification Product Code(s): For codes, see https://www.fda.gov/medical-devices/classify-your-medical-device/product-code-classification-database

11. 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 uses behavioral or observational data, describe.

<u>Investigational New Drug (IND) /Investigational Device Exemption (IDE) information</u>

12. IND/IDE: state if there is an active FDA IND or IDE for the proposed asset. If there is, provide the IND/IDE number and state if it is in good standing
13. Investigator brochure: State if there is an IB for the proposed asset
14. Willing to share data with HEAL/EPPIC-Net: State 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.]

<u>Relevant prior research on asset</u>

15. Background key literature citations. Provide citations for 3 key references that provide background and context for the proposed clinical trial
16. 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.
17. Preclinical efficacy studies to support indication completed. If preclinical efficacy studies have been done, provide citations for up to 3 references, reports or publications.
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 publication for each phase and include ClinicalTrials.gov Identifier/NCT number.
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 across all human studies identified to date

b. Dose range studied in humans: provide the dose range for the proposed asset (drug or device, as applicable) across all human studies identified to date
c. Number of doses/duration of exposure/route in humans. Provide the information for proposed asset (drug or device as applicable) across all human studies identified to date

20. 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
21. Site(s) of prior studies. Identify where prior studies were conducted. If outside the USA or EU, identify site(s)
22. Evidence of efficacy for intended indication. State if there was 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

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

Population

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

Outcomes

30. Primary outcome measure for efficacy: describe the primary study outcome measure for efficacy.
31. Primary outcome measure for efficacy: describe the 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. State if the proposed asset has been evaluated for addiction potential. If so, provide information on specific findings. For biomarkers, explain what biomarkers are currently available 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, i.e. 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.