HEAL Partnership Committee – Teleconference Meeting

April 15, 2019, 2:00–3:30 pm ET

Attendees

Chris Austin, National Center for Advancing Translational Science (NCATS); Rebecca Baker, National Institutes of Health/Office of the Director, (NIH/OD); Christine Colvis, NCATS; Stephanie Cush, Foundation for the National Institutes of Health (FNIH); Chris Flores, Johnson and Johnson (J&J); Danielle Friend, Biotechnology Innovation Organization (BIO); Steven Joffe, University of Pennsylvania (UPenn); Samantha Jonson, NCATS; Barbara Karp, National Institute of Neurological Disorders and Stroke (NINDS); Walter Koroshetz, NINDS; Joseph Menetski, FNIH; Mark Mintun, Lilly; Emily Morgan, FNIH; Richard Moscicki, Pharmaceutical Research and Manufacturers of America, (PhRMA); Judith Paice, Northwestern University; Linda Porter, NINDS; Kurt Rasmussen, National Institute on Drug Abuse (NIDA); Bill Schmidt, FNIH; Erin Spaniol, NIH/OD; Amir Tamiz, NINDS; David Wholley, FNIH; Ashley Wittorf, AdvaMed; Clifford Woolf, Harvard; Clinton Wright, NINDS

Agenda

1. Welcome and Review of Agenda
2. Review of Revised Asset Template and Information Dossier for EPPIC-Net
3. Communications Plan for the Request and Solicitation Process for EPPIC-Net
4. Scope and Potential Agenda Items for Next Meeting
5. Next Steps and Closing

Action Items

Action Item Description	Owner
All HPC members must complete a conflict of interest form and return it to Rebecca Baker for each HPC meeting	Rebecca Baker NIH/OD
The Conflict of Interest and Confidentiality for Working Group Participants forms will be recirculated to HPC members.	Rebecca Baker NIH/OD
Update the asset-entry template based on the feedback received during this teleconference.	Amir Tamiz NINDS
Update the asset dossier based on the feedback received during this teleconference.	Amir Tamiz NINDS
Circulate an updated flow chart to HPC members outlining the process for asset submission to EPPIC-Net.	Rebecca Baker NIH/OD & Amir Tamiz NINDS

Set a date to begin the solicitation process for EPPIC-Net and communicate timelines to the HPC, so they can communicate with their stakeholders	Rebecca Baker NIH/OD
Solicit feedback from HPC members on the next topic to address with the HPC and timing of next meeting	Rebecca Baker NIH/OD

Meeting Minutes

1. Welcome and Review of Agenda

Rebecca Baker, Director, HEAL Initiative, NIH/OD

The HEAL Partnership Committee (HPC) is a subgroup within the larger HEAL Multi-Disciplinary Working Group (MDWG), which is tied to the NIH advisory councils. Therefore, this teleconference was publicly accessible via a listen-only line, and this summary will be available online. HPC members must provide Dr. Baker with a completed conflict of interest form for every meeting. As a courtesy, Dr. Baker will recirculate the Conflict of Interest and Confidentiality Information for Working Group Participants forms to all HPC members.

The HPC was formed to provide expertise to the MDWG regarding HEAL research activities aimed at developing and testing new treatments (i.e., medications and devices, referred to here as “assets”) for pain and addiction via the Early Phase Pain Investigation Clinical-Network (EPPIC-Net).

Participants at the HPC face-to-face meeting in March began to determine the information that will be needed in order for the NIH to evaluate assets, including by providing feedback for the asset-entry templates and the more comprehensive asset dossiers, which have since been updated and circulated for HPC review. Additionally, participants at the March meeting specified the information that partners would need to disseminate to stakeholders. This discussion culminated in a draft EPICC-Net handout, which was also circulated to participants for review.

2. Review of Revised Asset Template and Information Dossier for EPPIC-Net

Amir Tamiz, NINDS; Clinton Wright, NINDS

EPPIC-Net is a clinical trials network designed as a hub-and-spoke system. This means that the network consists of a clinical coordinating center and a data coordinating center which are each connected to numerous specialized clinical sites. These sites provide access to patients with specific conditions, creating a network to run early-phase exploratory trials investigating a broad spectrum of treatment modalities (i.e., drugs, biologics, devices, natural products, and surgical interventions) for acute and chronic pain. EPPIC-Net will also support biomarker validation, proof of mechanism, and deep phenotyping studies. A repository will contain all data generated by EPPIC-Net, as well as by select studies related to HEAL.

Assets will enter the network through a multistage review process. First, asset holders will complete a preliminary asset entry application template, providing limited information to facilitate initial asset review. If EPPIC-Net’s objective review panelists are interested in pursuing the asset, the asset holder will produce a detailed dossier with help from a contractor provided by EPPIC-Net. After a dossier is reviewed and approved by the objective review panel, EPPIC-Net

will design a Phase 2 clinical trial to test the selected asset. Once approved, the protocol will enroll patients from EPPIC-Net sites.

Template Feedback and Revisions

Participants at the March face-to-face meeting suggested making the template review process more feedback-oriented so that it is useful even for applicants whose assets are not yet ready for clinical trials. This would provide EPPIC-Net with a broader picture of the assets that are in development while helping holders of less mature assets. Participants also discussed incorporating the FDA Target Product Profile (TPP) into the dossier and advocated more robust collaboration with the FDA when preparing for clinical trials. The latest versions of both the template and the dossier incorporate recommendations from these discussions. The template is currently in version 9. The template draft was presented as an Excel sheet that will be integrated into a drop-down menu web form. The application template is two pages and should take asset owners approximately 1 to 2 hours to complete.

Since the March meeting, the HPC has resolved issues related to asset ownership, target populations, and safety/liability, in addition to other concerns. The template now contains two additional asset ownership questions. Applicants will also have space to answer high-level questions about ownership, such as whether the application comes from industry or academia. Applicants will also report whether they have the authority to propose the application, and if they do not, they will provide evidence that the asset owner is aware of the application and that an agreement between the applicant and the asset owner is in place.

The template contains separate sections for devices and biologics. Since the March meeting, fields have been added to record site and population information for any previous clinical trials. A space was added for applicants to report safety and liability concerns.

Offering further feedback on the version 9 document, participants recommended better aligning the device section with FDA standards by adding line items for expected FDA device class, expected product code, and device classification name. Participants also recommended tying device type to the ISO 10993 form. Dr. Tamiz will update the template to reflect these suggestions.

Dossier Feedback and Revisions

Application review will begin once a large enough batch of template applications have been received. Top applications will move forward to the dossier stage. The dossier will then provide the EPPIC-Net team with access to all the asset information that would be included in an IND or IDE. A completed dossier will be approximately 10 to 15 pages and will include any information from from preclinical safety studies, IND or IDE, investigator brochures, and additional pharmacology studies.

After review, the dossiers will be assigned to one of three categories: (1) those ready for efficacy trials, (2) those that are of interest but not ready for efficacy trials, and (3) those that will not advance. For assets in category (2), the team will communicate to the asset owner what steps are required to advance the asset. Participants suggested that all applicants receive some level of feedback regarding their dossiers. The HPC will need a clear outline of how these communications will occur so that everyone understands the process and so that applicants can facilitate advancement of their assets in EPPIC-Net.

The dossier was also updated following suggestions at the face-to-face meeting and subsequent feedback:

- **Section 3** of the dossier now contains shortened TPP documentation to better harmonize applications for assets at varying stages of development.
- **Section 4**, which focuses on preclinical data, now requests more details regarding efficacy studies (e.g., replication information). This will allow the review panel to provide feedback regarding additional studies that may be needed to confirm or support the indication or population before conducting a clinical trial.
- **Section 5** has added more information about safety and whether decisions of go/no go were based around safety. This is consistent with the updates made to the template document.
- **Section 7** allows the objective review panel to learn more about the non-scientific decisions that contributed to development and current status of an asset (e.g., reasons for discontinuation, plans beyond phase 2 trials, conflicts of interest).

Additional feedback was provided during this teleconference. The dossier will be updated to reflect the following points:

- **Section 2d** refers to pharmacokinetics and pharmacodynamics but specifies only pharmacokinetics. The reference to pharmacodynamics should be dropped.
- **Section 4** should include a question about pediatric preclinical data and about any known or expected gender-based differences.
- **Section 5** should specify the applicant's envisioned comparators for a randomized trial or historic control data for a non-randomized trial.
- **Section 5** should contain, under "safety," a question regarding dependence or addiction.

Participants also suggested reviewing the document for potential duplications; Dr. Tamiz noted that some duplications were intentionally included.

Participants commented that the "conflict of interest" field is too broadly framed. Dr. Tamiz presented a hypothetical situation in which an academic investigator submits an asset held by a company. In this situation, the dossier should include an agreement between the academic and the asset-holder confirming that the asset-holder is aware of the application and is prepared to provide materials as needed. HPC members noted that this should be explained more clearly in the dossier. Examples will be added to specify the information that is being requested.

Other Next Steps

An updated process flow chart capturing the process of asset application from template to clinical trial is needed. Dr. Baker has created multiple flow charts capturing various stages of this process. Drs. Tamiz and Baker will work together to provide a finalized flow chart to the HPC.

Once experience is gained throughout the EPPIC-Net process, a frequently asked questions (FAQ) page will be added to the website to further assist applicants. The HPC will be asked to provide feedback once the FAQs have been drafted.

3. Communications Plan for the Request and Solicitation Process for EPPIC-Net

Rebecca Baker, Director, HEAL Initiative, NIH/OD

In response to previous HPC member suggestions to develop EPPIC-Net outreach materials, a communications document was drafted. The 2-page document incorporates feedback from the March face-to-face meeting as well as comments received afterward. The first page contains a description of EPPIC-Net and the network's priorities. The second page concisely describes the entire process, starting with template submission and culminating in a clinical trial.

Dr. Baker noted that EPPIC-Net will be open to assets from foreign-based companies, as pain management and addiction are global issues. This information could be added in the proposed outline or handled as part of ancillary materials.

Participants suggested providing a broader outline of the HEAL initiative as part of the outreach materials. Dr. Baker remains open to suggestions regarding what asset owners may be interested in knowing.

Participants requested additional information regarding the forthcoming EPPIC-Net requests for proposals (RFPs). Currently there are several RFPs to build the infrastructure for EPPIC-Net and a review section to evaluate the applications. EPPIC-Net has developed a non-grant/non-contract process to review assets and launch trials. This is a unique approach that will not require a full proposal. NIH hopes this approach will reduce the time between template submission and clinical trial execution.

Possible EPPIC-Net Dissemination Methods

EPPIC-Net should leverage multiple dissemination methods to increase awareness of EPPIC-Net. This will include EPPIC-Net presentations at large conferences that present opportunities for interaction with potential asset holders. One such opportunity is the June BIO Convention, which features a planned session about NIH being a catalyst for opioid crisis research. There will be four sessions focused on addiction and pain. It would be possible to mention EPPIC-Net and to distribute handouts or other additional information for those who are interested.

Dr. Baker asked that the partners on the HPC assist in outreach efforts to member organizations within industry groups to promote interest among companies who might otherwise be unaware of EPPIC-Net.

Ms. Wittorf noted also the possibility of gaining information through the trans-agency memorandum of understanding for the FDA, which held an innovation challenge that received more than 250 applications. Only 10 of these were granted, so the 240 others may be eligible and available to join EPPIC-Net. Applicant information may be obtainable through FDA. The FDA website might also be used to promote awareness of EPPIC-Net. Industry publications could also be leveraged.

The HPC may also promote awareness of EPPIC-Net by responding to press requests.

4. Scope and Potential Agenda Items for Next Face-to-Face Meeting

Rebecca Baker, Director, HEAL Initiative, NIH/OD

Looking beyond EPPIC-Net, the HPC should consider (1) its potential value for the wider HEAL Initiative and (2) potential ideas for research activities and translational models for testing pain treatment.

Dr. Austin presented a brief use case for his system which allows for the mechanistic investigation of novel compounds. Through HEAL, his team is developing novel human cell-based platforms using induced pluripotent stem cells (iPSCs) from pain patients and healthy controls and is developing 3D printed tissue models of various levels of nerve access that mediate pain and addiction. Dr. Austin's team is also interested in partnering with companies to continue development of deprioritized compounds.

Dr. Joffe suggested that the EPPIC-Net infrastructure might offer the ability to set the design standards for pain trials (e.g., by establishing endpoints and biological correlatives).

Participants recognized the potential for expansion into three key areas: (1) preclinical screening and innovative technology, (2) animal models and associated preclinical testing, and (3) biomarkers and endpoints. Participants agreed to wait to pursue these areas until several anticipated relevant grants are awarded.

Mr. Schmidt suggested that EPPIC-Net ensure some interaction with the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) public-private partnership. EPPIC-Net already includes some representatives from ACTTION.

NIH expects the first EPPIC-Net trials to begin in 2020 and hopes to begin the asset submission and review process as soon as possible, to allow for 6-8 months between the first template submission and initiation of the first resulting clinical trial. There is no set time for the availability of the template and other documentation. Dr. Baker noted that a date does need to be set. She will speak with the communications offices to determine a date by which to begin the solicitation process.

5. Next Steps and Closing

Rebecca Baker, Director, HEAL Initiative, NIH/OD

Topics for the next meeting will be obtained vie email.

Participants are reminded to complete their conflict of interest forms.