Clinical Management of Hepatitis C Infection

Applicant Town Hall
April 8, 2015
Agenda

Programmatic Overview

Administrative Overview

Merit Review Criteria

Questions and Answers

Submitting Questions:
Submit questions via the chat function in Meeting Bridge.

Ask a question via phone (an operator will standby to take your questions).
Today’s Presenters

David Hickam, MD, MPH
Program Director
Clinical Effectiveness Research

Danielle Whicher, PhD, MHS
Program Officer
Clinical Effectiveness Research

Carolyn Mohan, DrPH, MPH, MIA
Merit Review Officer

Maricon Gardner, CRA
Contracts Associate,
Contracts Management and Administration
Programmatic Overview

David Hickam, MD, MPH
Program Director
Clinical Effectiveness Research

Danielle Whicher, PhD, MHS
Program Officer
Clinical Effectiveness Research
The Model of Patient-Centered Outcomes Research

• Helps people and their caregivers communicate and make better-informed healthcare decisions

• Actively engages patients and key stakeholders throughout the research process.

• Compares the effectiveness of important clinical management options.

• Evaluates the outcomes that are the most important to patients.

• Addresses implementation of findings in clinical care environments.
PFA Overview: Clinical Management of Hepatitis C Infection

Objective of this PFA:

• Address *critical* clinical and healthcare delivery choices faced by hepatitis C patients, their caregivers, clinicians and/or delivery systems.

In this PFA we seek to fund:

• Pragmatic clinical trials
• Comparative observational studies
Letter of Intent and Application

You were invited to submit a full application based on the information provided in the LOI. Changes after the LOI require PCORI approval.

Show stoppers include:

- Changes of PI
- Changes to the Institutions
- Changes to the Study Design or Budget
Programmatic Requirements
Essential Characteristics of Studies

- Compare the effectiveness of two or more alternative approaches to management of HCV
- Have strong endorsement and participation by stakeholders
- Take place within typical clinical care and community settings
- Have a sufficiently large study population to enable precise estimates of effect sizes and to support evaluation of potential differences in intervention effectiveness in patient subgroups
Responsive Applications

• Investigators must propose projects that address at least one of the four priority research questions

• Investigators should consider the feasibility of measuring outcomes of interest identified by PCORI in this funding announcement

• Given the significant treatment costs associated with many of the newly available therapies, investigators must address the support from payers, health plans, industry sponsors, or others in covering the study drugs and non-study protocol-related clinical costs and services rendered in the care processes
PCORI Methodology Standards

- 47 standards in 11 groups
- The Methodology Standards do not address all issues related to study designs and methods
- Note that PCORI is not using a specific set of methodological standards for “pragmatic studies.”
  - Consider design tradeoffs (e.g., blinding vs not blinding)
  - Refer to other respected sources for additional guidance.
  - View report and standards here:
    http://www.pcori.org/research-we-support/research-methodology-standards/
PCORI Methodology Standard* RQ1 – Identifying Gaps in Evidence

“Gap analysis and systematic reviews should be used to support the need for a proposed study. If a systematic review is not available, a systematic review should be performed using accepted standards in the field (see standard SR-1), or a strong rationale should be presented for proceeding without a systematic review. In the case where a systematic review is not possible, the methods used to review the literature should be explained and justified.”

Justification for the Design Elements of a Large Pragmatic Study

• Suggest reviewing pragmatic–explanatory continuum indicator summary (PRECIS) tool

• Consider tradeoffs
  – Eligibility criteria
  – Flexibility of intervention
  – Range and types of outcomes
  – Follow up intensity
  – Adherence
  – Etc.

Recruitment

• Discuss past experiences with recruitment
• Provide preliminary evidence of the potential for successful recruitment
• Consider barriers to recruitment – and how you plan to overcome them
• Strategies for successful recruitment
  – Engaged clinical sites
  – Clinician advocates for the study
  – Proactive, experienced research coordinator
  – Protocol flexibility, within reason
  – Alignment and integration of recruitment activities with clinical workflow
Use of Electronic Health Records and Other Computerized Data Sources

• Pragmatic, systems-based studies should take advantage of previously captured electronic clinical and demographic data whenever possible.

• Discuss any proposed uses of existing electronic data in the approach section:
  – Cohort identification and recruitment
  – Collection of covariate and outcome data

• Provide evidence of the validity and completeness of available data (e.g., that all follow-up and outcomes of interest are captured)
  – PCORI Standards on Data Networks and Registries
Administrative Overview

Maricon Gardner, CRA
Contracts Associate - Pre Awards
PCORI Online: Application

► PI and Contact Information
► Project Information
► Key Personnel
► Milestones
► Templates and Uploads
► Save
Key Personnel

Key Personnel

- To add key personnel: click on the plus sign, enter key personnel information, and click "Update Key Personnel."
- To remove key personnel: click on the minus sign that appears when you scroll the cursor over a name.
- Note: After you click "Update Key Personnel" you cannot go back to edit any information. If there is an error, you must remove the entry and create a new one.

Add a Key Personnel

- Project Role
- Required information is in **bold**

- For the purposes of this project, which one of the following patient or stakeholder communities reflects this person's primary affiliation?

- Degrees
  - AAS
  - AB
  - APRN
  - BA
  - BC

- Phone
- Email

Click "Update Key Personnel"
PCORI Monitors Projects Against Milestones & Deliverables

**Milestones:**
Significant events or accomplishments within the project; may have deliverables associated with them

**Deliverables:**
Measurable and verifiable outcomes or objects that a project team must create and deliver according to the contract terms
### Example of Milestone Schedule

<table>
<thead>
<tr>
<th>Milestone Name</th>
<th>Description</th>
<th>Projected Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Project Start Date</td>
<td>11/1/2014</td>
</tr>
<tr>
<td>B1</td>
<td>IRB approval</td>
<td>12/1/2014</td>
</tr>
<tr>
<td>B2</td>
<td>Registration at clinicaltrials.gov</td>
<td>12/05/2014</td>
</tr>
<tr>
<td>B3</td>
<td>DSMB meeting minutes</td>
<td>12/10/2014</td>
</tr>
<tr>
<td>B4</td>
<td>Advisory Board meeting</td>
<td>12/15/2014</td>
</tr>
<tr>
<td>B5</td>
<td>Advisory Board meeting</td>
<td>03/15/2015</td>
</tr>
<tr>
<td>B</td>
<td>Report Submission</td>
<td>04/30/2015</td>
</tr>
<tr>
<td>C1</td>
<td>Advisory Board meeting</td>
<td>06/15/2015</td>
</tr>
<tr>
<td>C2</td>
<td>Completion of Preparatory Steps prior to enrollment</td>
<td>06/15/2015</td>
</tr>
<tr>
<td>C3</td>
<td>Begin patient enrollment</td>
<td>06/15/2015</td>
</tr>
<tr>
<td>C4</td>
<td>Report of Patient Enrollment Activities Directly Provided by the PAGs</td>
<td>09/15/2015</td>
</tr>
<tr>
<td>C5</td>
<td>Completion of 25 percent of recruitment</td>
<td>10/30/2015</td>
</tr>
<tr>
<td>C</td>
<td>Report Submission</td>
<td>10/31/2015</td>
</tr>
</tbody>
</table>
Milestones

Enter milestone information, including: milestone name, description, and projected completion date. You can delete milestones by clicking on the minus sign in the top right corner, which will appear as you scroll the cursor over the entry. **You cannot edit your entry; you must delete and start over.**

![Milestone Entry Form]

- **Enter milestone information. All fields are required.**
- **Click “Update Milestones” after entering your information.**
Templates and Uploads
Research Plan Template

- Research Strategy
- Dissemination & Implementation Potential
- Replication & Reproducibility of Research and Data Sharing
- Protection of Human Subjects
- Consortium Contractual Arrangements
- References Cited
- Appendix
Research Plan Template—Research Strategy

A. Background
B. Significance
C. Patient Population
D. Study Design or Approach
E. Engagement Plan
F. Project Milestone and Timeline
G. Research Team and Environment

Page Limit 20
Dissemination & Implementation

- Describe the potential for disseminating and implementing the results of this research in other settings.
- Describe possible barriers to disseminating and implementing the results of this research in other settings.
- Describe how you will make study results available to study participants after you complete your analyses.
Replication & Reproducibility of Research and Data Sharing

- Describe the ability to reproduce potentially important findings from this research in other data sets and populations.
- Describe how you will make a complete, cleaned, de-identified copy of the final data set used in conducting the final analyses available within 90 days of the end of the final year of funding, or your data-sharing plan, including the method by which you will make this data set available, if requested.
- Propose a budget to cover costs of your data-sharing plan, if requested.
Protection of Human Subjects

• Describe the protection of human subjects who will be involved in your research.
• Refer to NIH standards for research involving human subjects
Consortium Contractual Arrangement

- Describe the proposed research projects that will be performed by subcontracted organizations; explain the strengths that these partners bring to the overall project.
References Cited

• Following scholarly citation practice, list the source material cited in this Research Plan
Appendix

► PCORI applications may include an appendix for additional materials the investigators think may be useful
  ► Survey instruments
  ► Papers and publications from members of the research team; however, reviewers will not be required to include the appendices in the review and assessment of the project
People and Places Template

Biosketch

- You may use the NIH biosketch or PCORI’s format
- Biosketches are required for all key personnel
- List all partners within the Key Personnel section
- Patient/Stakeholder Biosketch

**NOTE:**

New page limit: Biosketches may now be 5 Pages per person.
People and Places Template

**Project/Performance Site**
- Demonstrate that the proposed facilities have the appropriate resources required to conduct the project to plan, within budget, and on time
- Provide a description of the facilities that will be used during the project, including capacity, capability, characteristics, proximity, and availability to the project

NOTE: Follow PCORI’s required naming conventions when uploading PDF files!
Budget Templates: Overview

Three budget sections must be submitted as part of the online application process:

- Detailed Budget
- Budget Summary
- Budget Justification

**NOTE:** A detailed budget is needed for each year of the program. Complete each budget section for the prime applicant and any/each subcontractor.
Costs of Interventions

- PCORI will not cover costs for clinical care alternatives that are being compared in the project.
- PCORI will consider covering costs for ancillary tasks necessary in the implementation or monitoring of a clinical intervention or strategy as part of the research program.
  - Examples include costs for obtaining consent, collecting data, or monitoring that would not normally be performed in routine care.
- Support for the study by the involved healthcare delivery systems must be documented.
Detailed Budget

- Personnel
- Consultant
- Equipment
- Supplies
- Travel
- Other Expenses
- Consortium/Contractual Direct Costs
- Consortium/Contractual Indirect Costs
- Prime Indirect Costs
Budget Justification

• Narrative that fully supports and explains the basis for the information in the Budget Detail
  – Provide sufficient detail to understand the basis for costs, the reason that the costs are necessary, and an explanation for major cost variances
  – Use the budget template to tell PCORI why the costs are reasonable for the work to be performed
• Breakdown of costs proposed for each consortia or contractor
• Must specify any other sources of funding that are anticipated to support the proposed research project
• Provide quotes, indirect cost rate letter, fringe benefit policy
Common Application Errors

- Using the wrong browser, access PCORI Online via Chrome or Safari browsers
- Not entering information into all required fields in the system
- Not clicking the ‘Save and Review’ button on the Save and Review page and on the side navigation pane
- Having multiple people working on the application at the same time
- Having the incorrect file extension, only PDF files can be uploaded
- Not choosing the correct document type from the drop-down menu
- AO is unable to view the application
Resources

Refer to the Pragmatic Studies page in our Funding Center (http://www.pcori.org/announcement/clinical-management-hepatitis-c-infection) for the following resources:

- PFA and Application Guidelines
- PCORI Online User Manuals
- Sample Engagement Plans
- Hepatitis C Applicant FAQs: http://www.pcori.org/content/hepatitis-c-applicant-faqs
- PCORI Online: https://pcori.fluxx.io/
- Research Methodology: http://www.pcori.org/node/4020
Merit Review Criteria

Carolyn Mohan, DrPH, MPH, MIA
Merit Review Officer
The Goal of PCORI Merit Review

To identify quality applications that have the strongest potential to improve patient outcomes.
Reviewer Roles

Patients

Stakeholders

Scientists
Review Criteria

**Criterion #1:** Impact and importance of research aims, interventions, comparators, and outcomes

**Criterion #2:** Potential for the study results to be incorporated into clinical practice

**Criterion #3:** Technical merit

**Criterion #4:** Patient-centeredness

**Criterion #5:** Patient and stakeholder engagement
#1: Impact and importance of the research aims, interventions, comparators, and outcomes on individuals with hepatitis C and their caregivers, clinicians, employers, insurers, and policy makers

- Does the research study address an evidence gap that systematic reviews, guideline development efforts, or previous research prioritizations have noted as being of high importance for validating policies for screening, diagnosis, treatment, and/or management of hepatitis C?

- Does the proposal provide an adequate case that the proposed intervention and comparators will fill the evidence gap?

- Does the application make a convincing case that currently there are wide variations in practice patterns that can be addressed with new evidence?
#2: Potential for the study results to be incorporated into clinical practice

- Will the proposed study provide sufficient data about important patient subgroups, so that the data about comparative effectiveness can be applied to particular clinical settings?

- Have the investigators established connections with key organizations responsible for the dissemination or implementation of research results and the development of professional standards of care?

- Have the investigators addressed the implementation and long-term sustainability of successful interventions(s) in the chosen settings?

- Does the application identify facilitators and barriers to implementation, as well as how to surmount the identified barriers?
#3: Technical Merit

- Is there a clear research plan with rigorous methods that adhere to PCORI’s Methodology Standards and accepted best practices?
- Is there a clear justification for the study design?
- Is there a carefully constructed and realistic timeline that includes specific scientific and engagement milestones?
- Does the research team have documented appropriate expertise and experience - and is there a rational organizational structure?
- Does the research environment include the appropriate delivery system(s) to host the study, adequate resources, and strong support of the proposed research?
Human Subjects Protection

• PCORI requires that research involving human subjects include adequate safeguards.

• Institutional Review Boards selected by awardees have authority for ensuring the protection of human subjects.

• Reviewers will identify issues with protection of human subjects that PCORI staff should review with potential funding awardees.
#4: Patient-Centeredness

- Is the research focused on questions that affect outcomes of interest to patient and their caregivers?
  - *Does the research question address choices that are important to - and faced frequently by - patients, their caregivers, or clinicians?*
  - *Is the study powered on outcomes that are important to patients?*
- Does the research address one or more of the key questions mentioned in PCORI’s definition of patient-centered outcomes research?
#5: Patient and Stakeholder Engagement

- Evidence that patients, caregivers, patient and caregiver organizations, clinician organizations, and other stakeholders have been and will be engaged in:
  - Formulating the research questions
  - Defining the characteristics of study participants, comparators and outcomes
  - Selecting the important outcomes to be assessed
  - Monitoring study conduct and progress
  - Designing plans for dissemination of study results
- Clear statement of the roles and the decision-making authority of all patient and stakeholder research partners
- Demonstration of the principles of reciprocal relationships, co-learning, partnership, trust, transparency, and honesty
Patient-Centeredness vs. Patient Engagement

- **Patient-Centeredness** concerns answering questions that affect outcomes of importance to patients
  - Does the project aim to answer questions or examine outcomes that matter to patients within the context of patient preferences?
  - Research questions and outcomes should reflect what is important to patients and caregivers

- **Patient engagement** includes patients as partners in research as opposed to merely subjects
  - Active engagement between scientists, patients, and stakeholders
  - Community, patient, and caregiver involvement already in existence or a well-thought out plan
Addressing Engagement

• Several approaches to engagement can succeed
• PCORI provides many engagement resources:
  – PCORI’s “The Patient and Family Engagement Rubric”
  – Sample Engagement Plans
  – Engagement in Research website page
    • [http://www.pcori.org/content/engagement-research](http://www.pcori.org/content/engagement-research)
  – PCORI’s Methodology Standards PC-1 to PC-4
Overarching Engagement Rubric Principles

• The rubric contains a collection of examples, intended to provide guidance to applicants, merit reviewers, awardees, and engagement/program officers
  – It is not intended to be comprehensive or prescriptive
  – Applicants can choose to include some (but not all) activities illustrated, and they can include additional innovative approaches not included
  – The examples provided are from real PCORI-funded projects

• The rubric also describes PCORI’s PCOR Engagement Principles:
  – Reciprocal Relationships
  – Co-Learning
  – Partnership
  – Trust, transparency, and honesty
Elements of the Engagement Rubric

Planning the Study

Conducting the Study

Disseminating the Study Results

PCOR Engagement Principles
B. Engagement Plan

PCORI Funded Projects: Sample Engagement Plans

October 31, 2013

- Provides examples of engagement plans taken from actual funded projects.
- Do not reflect all engagement and stakeholder plan models.
- Do not reflect PCORI’s endorsement.
C. Engagement – website page

What We Mean by Engagement

By “engagement in research,” we refer to the meaningful involvement of patients, caregivers, clinicians, and other healthcare stakeholders throughout the research process—from topic selection through design and conduct of research to dissemination of results. We believe that such engagement can influence research to be more patient centered, useful, and trustworthy and ultimately lead to greater use and uptake of research results by the patient and broader healthcare community.

Effective engagement of patients and other stakeholders in research requires a well thought-out plan. So, all applications for PCORI funding must include an Engagement Plan, and we evaluate that plan in our review process. Because we recognize that engagement can take many shapes, and it varies with the nature of the research, we don’t require specific activities. Instead, we encourage applicants to bring their most creative engagement ideas forward.

Who are Healthcare Stakeholders?

A broad range of communities have a stake in the effectiveness of our healthcare system. In the term patient partners, we include patients who are representative of the population of interest in a particular study, as well as their family members, caregivers, and the organizations that represent them. Other stakeholder partners include members of constituencies based on professional, rather than personal, experience. These can include clinicians, healthcare purchasers, payers, industry, hospitals and other health systems, policy makers, training institutions, and researchers. Some individuals may fit into several categories.

How Can Researchers Engage Stakeholders in Research?

We seek to support research that includes authentic involvement of patients and other stakeholders. Our Methodology Standards include requirements associated with patient-centeredness and engagement.

Engagement can take many forms, so we ask teams to come up with their own, appropriate blueprints for partnership. Because many researchers have not had experience engaging patients and other stakeholders in the planning, conduct, and dissemination of research, our Engagement Program offers guidance tools. These include the PCORI Engagement Rubric and sample Engagement Plans from our funded research portfolio, including our methods portfolio.
D. Methodology Standards for Patient-Centeredness

- Are patients and other stakeholders engaged in (PC-1):
  - Formulating research questions
  - Defining essential characteristics of study participants, comparators, and outcomes
  - Identifying and selecting outcomes that the population of interest notices and cares about (e.g., survival, function, symptoms, health-related quality of life) and that inform decision making relevant to the research topic
  - Monitoring study conduct and progress
  - Designing/suggesting plans for dissemination and implementation activities
This proposal demonstrates patient-centeredness at every stage of the research. It addresses the following questions:

- Is the proposed research focused on questions that affect outcomes of specific interest to patients and their caregivers? \(\text{(PC-3)}\)
- Does the research address one or more of the key questions mentioned in PCORI’s definition of patient-centered outcomes research?
# Submission and Key Dates

<table>
<thead>
<tr>
<th>What</th>
<th>When</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Deadline</td>
<td>May 5, 2015 by 5:00pm ET</td>
</tr>
<tr>
<td>Merit Review Dates</td>
<td>August 6-7, 2015</td>
</tr>
<tr>
<td>Awards Announced</td>
<td>September 30, 2015</td>
</tr>
<tr>
<td>Earliest Start Date</td>
<td>November 2015</td>
</tr>
</tbody>
</table>
Questions?

For Programmatic Inquiries…
Phone: 202.627.1884
Email: sciencequestions@pcori.org

For Administrative/Technical Inquiries…
Phone: 202.627.1885
Email: pfa@pcori.org