## Step 1: Development of a Protocol or Data Analysis Concept Capsule

1. The proposing investigator(s) develops a Concept Capsule, a brief description of the proposed study or data analysis. The capsule should be no longer than four single-spaced typewritten pages and includes the following:

- Study title
- Lead investigator
- Basic study objectives
- Significance
- Study population and/or data set required
- Outcome measures
- Analysis plan and approximation of sample size, e.g., <20, >100 (formal sample size calculation not required)
- Resources required
- Collaborating networks if appropriate

2. The proposing investigator(s) submits the capsule to the chair of the Scientific Leadership Group (SLG) in electronic form through the PHACS Coordinating Center (CC). For a capsule to move forward for Concept Sheet (CS) development, it must relate to the current scientific research agenda of the PHACS protocols. The chair of the SLG receives the capsule and after preliminary review may 1) reject the capsule for further development, or 2) may request a review and vote by the Scientific Leadership Group for approval or disapproval for further development. If the capsule is consistent with the scientific agenda, but there are feasibility concerns regarding the number of subjects, statistical input may be requested by the SLG.

3. If the capsule is approved for further development by a two-thirds vote of the SLG, the chair of the SLG will:

- Notify the proposing investigator(s) of the decision
- Request that the capsule receive a Concept Sheet number (CS_#_) by the Coordinating Center.
- If the proposing investigator is external to the PHACS network, assign a member of the SLG to serve as a liaison to work with the investigator.

4. If a capsule is rejected by the chair of the SLG, the proposing investigator can request review by the SLG. Any questions, concerns, or disputes regarding the initial review of a capsule that cannot be resolved by the SLG will be brought to the PHACS Executive Committee (EC) for discussion and resolution.

5. A capsule approved by the SLG is submitted to the PHACS Clinical Investigator Group (CIG) for review and comment, including feasibility and site logistics, as it moves to concept sheet development. No vote or formal approval is required. The capsule is included on the agenda of the next conference call of the CIG and the lead investigator joins this call to present the capsule and answer any questions/concerns. The CIG provides written comments on the capsule to the SLG and the proposing investigator.

6. The EC members are informed monthly of decisions concerning any capsules that have been reviewed (via E-mail or conference call). All approved capsules are posted on the PHACS web site so that all PHACS members are aware of all approved capsules.

**Step 2: Development of a Protocol Concept Sheet (PCS) or Data Analysis Concept Sheet (DACS)**

1. Following approval of a capsule, the proposing investigator(s) develop(s) a Concept Sheet (CS) that includes the following components (in page/line numbering format):

- Study title
- Proposing investigator(s)
    - Lead investigator
    - Team members
- Study objectives and aims

    - Brief study overview and objective
    - Aims and/or hypotheses
- Study rationale/background
- Study design
- Study population with inclusion and exclusion criteria and data set required if applicable ( for a DACS)
- Interventions or evaluations, if applicable
- Analytic section
    - Analysis plan
    - Sample size estimate
- Feasibility section detailing required PHACS resources and collaboration with other networks if applicable.
- Proposed assessment measures (in an appendix) if developed in a pilot study or if the measures have limited use in children or youth f applicable.
- Training needs/capacity (for intervention, data collection, procedure) if applicable
- Budget (on PHS 398 forms) with budget justification
- Accrual timeframe or timeframe for completion of analysis for a DACS.

If the proposed study will be using a subset of the PHACS clinical sites, the CS should include:

- Site selection criteria (obligatory and desirable)

  Attach an appendix describing criteria necessary or desirable for site selection and external constraints (e.g., school program, specialty clinic, detention center). Minimum and maximum number of subjects per site; minimum and maximum number of sites. Rationale/basis for site restriction that may include but not be restricted to: Staffing (existing staff expertise and availability, space, capacity, funding needs for additional staff), existing site partnerships or facilities, locale, etc.

  If a team has specific site preferences, in addition to the above, the appendix must include: 1) their request in writing with a justification addressed to the Executive Committee and 2) statements from the PHACS site PIs at those preferred sites stating their interest, availability of staff, and immediate availability of the populations required for the proposed study. Final site selection will occur once the protocol is completed.

If needed, a CS team may request a consultation review with members of the SLG to discuss issues related to development of the proposed concept before the full CS is submitted to the SLG for formal review and vote.

2. Proposing investigators should submit the CS to the CC in electronic form within eight weeks of the CS number being assigned. If the CS is not submitted within eight weeks, the CS team is responsible for setting a timeline for submission of the CS and discussing reasons for delay with the SLG chair. The SLG chair notifies the EC of any delays.

3. The CC distributes the CS to the SLG for review.

4. The SLG chair assigns two reviewers from the SLG within 3 days of receipt of the CS; reviewers are assigned on a rotating basis. Occasionally outside reviewers may be consulted at the discretion of the SLG. Reviewers provide a written review of the CS to the CC within 10 working days. A CS is reviewed on the basis of scientific merit, feasibility, priority relative to the core protocol objectives (AMP or SMARTT), and placement within the PHACS Network's scientific agenda. The written review should include major and minor points (if any) and comments on each of the CS content areas listed above as appropriate. All specific recommendations and comments should refer to a specific page and line number when applicable. Reviews are sent to the CC for distribution to the investigators and the SLG.

5. When reviews are completed, the CS is included on the agenda of the next monthly SLG conference call. SLG members will review the CS and the evaluations prior to the call.

6. The proposing investigator(s) present(s) a brief overview of the CS on the SLG conference call, and the two SLG reviewers present their evaluations, and other SLG members may offer additional comments or feedback. Discussion with the SLG may ensue, and the proposing investigator(s) will have an opportunity to clarify and discuss issues and answer queries and concerns.

7. The proposing investigator(s) then leave the conference call and the SLG may further discuss the CS if needed. Following the call, the CC distributes an e-mail ballot for SLG voting members to vote to 1) approve or disapprove the CS to move forward to be developed into a protocol, and, if approved, to 2) approve or disapprove a recommendation to the EC for requested PHACS resources, including site selection if appropriate. An approval vote of two-

thirds of eligible voters is required to approve a CS and to approve a recommendation to the EC concerning the requested resources. SLG members are not eligible to vote if they are a proposing investigator or collaborator on the CS under review.

If approved and no revisions are required, the CS moves forward to the next step in the review process. If the CS is approved but revisions are requested by the SLG, the SLG will specify if the reviewers alone can approve the revised CS (for minor modifications), or if full SLG review is required (for major modifications). If the latter occurs, revisions are made and the CS is re-submitted to the CC within three weeks of notification of the results of the review. The CS is then submitted to the SLG for full re-review and an approval vote as above.

8. When a CS is approved by the SLG, it is distributed the CIG for feedback on feasibility, subject issues and site selection, and logistical issues. The CS is included on the agenda of the next CIG conference call, and the lead investigator or a designee joins the call to present an overview of the CS, receive the CIG evaluations, and answer any questions and/or address concerns. Written comments on the CS may be submitted by the CIG to the CS team and the SLG through the CC. No vote or formal approval is required.

9. When a CS is approved by the SLG, it is also distributed the PHACS NIH Steering Committee for review. If written comments are deemed appropriate, they are sent to the coordinating center for distribution to the SLG and EC. No vote or formal approval is required.

10. The CC forwards the approved CS and written comments from the SLG (including recommendation on use of resources and participating sites), CIG, and NIH Steering Committee, to the EC for approval. The CS is included on the agenda of the next EC conference call. The EC chair presents the CS, reviews, and SLG recommendation. Following the call the CC distributes an e-mail ballot to voting EC members to approve or disapprove the CS resource recommendation. A simple majority vote is required for approval.

11. Once a concept sheet proposing a sub-study or nested study is approved by the SLG and EC, the protocol team is formed and protocol development is initiated. Once a Data Analysis Concept Sheet (DACS) is approved, the analysis/writing team is formed and the analysis initiated.

**Step 3: Full Protocol Development**

1. In general, the protocol chair will be the person proposing an approved CS.

2. When the CS is approved for protocol development, a protocol team is organized which will generally include the proposing investigators, a SLG liaison if the proposing investigators are from outside the PHACS Network, a Protocol Specialist from the DOC, a PHACS site PI, and a Study Coordinator. Other investigators including site PIs, Study Coordinators who desire to devote time and effort to the development of the protocol may contact the protocol team directly regarding their involvement through a written communication outlining their proposed contribution. CAB input on developing protocols is solicited as appropriate.

3. Procedures for protocol development depend upon whether the protocol is to be developed within the PHACS Network or within a collaborating network:

a. If protocol development is to be within the PHACS Network, a Protocol Specialist will be assigned to assist in full protocol development including full detailing of study procedures, visit schedules, timelines, IRB materials, and data monitoring safety issues. Please refer to the PHACS Procedure for Protocol Development, Approval, and Implementation for details of this process.
b. If protocol development is to be within a collaborating network, issues of logistical support will be negotiated with the appropriate network. A Memorandum of Understanding (MOU) will be signed by the PIs of both Networks and by the protocol chair.

4. The PHACS Network is committed to the most efficient development of the studies that it endorses and therefore, the performance of the protocol team is monitored closely by the EC. Reassignment of a protocol chair could be considered by the EC if there is lack of leadership or an inattention to timelines during protocol development, protocol implementation, or manuscript production.

Records will be kept on how protocol concept plan development proceeds and what precedents are set each year of the study. These will be reviewed and the policy amended as needed annually.

## Capsule & Concept Sheet Development Process