Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE):

Grant Application Proposal (GAP) Guidelines 6/2016

Using CANDLE for Grant Applications

CANDLE encourages individuals and teams who have worked with the CANDLE study and its data to submit grant applications for research funding. Applications from outside investigators will also be considered. Review of applications requires consideration of many factors, including the effort of CANDLE staff in helping to prepare grant applications, as well as work on the study that will require participation of staff and faculty should the grant be funded.

Investigators are also encouraged to submit proposals to CANDLE to obtain permission to use their own funds (e.g. start-up funds, endowments, flexible grant funds) to conduct research using CANDLE data and the cohort. For this type of application, follow the procedures outlined for Grant Application Proposals. On the Grant Application Proposal Cover Form, please indicate that the support for the proposal has already been secured and provide an estimate of this support.

In order to protect the integrity of the CANDLE study and the scientific interests of its investigators, a Letter of Intent (LOI) and Grant Application Proposal (GAP) Cover Form and Grant Application Proposal (GAP) must be *submitted and approved prior to initiating* a grant proposal using CANDLE data.

1) Grant Applications using CANDLE data fall into one of four categories:
    a. **Cohort Continuation or Expansion**: Uses CANDLE for preliminary data that if funded, will contribute financial or personnel resources to the CANDLE Study to support the follow-up or expansion of the cohort and acquisition of new data or samples. Examples include the recruitment of other family members, or an additional wave of data collection on the existing cohort.
    b. **Augmenting Existing Data Resources**: Uses CANDLE for preliminary data and will contribute financial or personnel resources to a project that will enhance CANDLE's existing data. For example, an NIH grant that funds assays of existing biospecimens or a set of analyses related to CANDLE's primary aims.
    c. **Ancillary Study:** Proposes specific additional data collection on the CANDLE cohort. These proposals may involve the entire cohort or a specific subpopulation within the cohort (although priority will be given to grants attempting to utilize the value of the full cohort). This grant will contribute financial or personnel resources to the collection of new information from CANDLE participants or their environment. For example, an investigator may propose to collect an additional behavioral measure from a subsample of the cohort. Note that investigators may already have funds to conduct the proposed work, but they will still need to complete a GAP and indicate that resources are already available.
    d. **Support for Secondary Data Analysis**: Uses CANDLE information for preliminary data or meta-analysis with human or model organism cohorts, but will not produce any new data for CANDLE and will not contribute any financial or personnel resources to CANDLE. For example, an NIH grant to fund an investigator to conduct secondary data analyses or to compare neurocognitive development in CANDLE with rodent or non-human primate models. Proposals that address CANDLE priority research areas will be given strong preference.

Letter of Intent (LOI)
In an effort to protect investigator and administrator time, we request that you make an initial inquiry about the appropriateness of a grant or ancillary study idea. If you are interested in submitting a GAP, please first submit the following electronically via the CANDLE website:

1. A **Grant Application Proposal (GAP) Cover Form:** This is a brief cover form with specific checklists and details about the proposed support mechanism or grant application and its timeline. It requires a signature of the submitting investigator and a statement that you have read the guidelines for collaboration with CANDLE.

   A Letter of Intent: This document should be no longer than one page and should include clearly articulated specific aims and hypotheses. Also include a short summary of how the CANDLE cohort will be used to meet your sample or data requirements (e.g. will new data be collected, what additional burden will subjects experience, etc.). If you are requesting preliminary data for your grant submission, please provide a brief description of data requested and proposed analyses in your LOI (you may put this on a second page if more space is needed). The LOI will be reviewed by the Emerging Science Coordinator to assess overlap with existing projects, and the extent to which the project addresses priority research areas. CANDLE leadership and study personnel will review the LOI for availability of specimen(s) in the bio-repository; and the availability/feasibility of using CANDLE data/participants. The LOI will be reviewed by the CANDLE Oversight Committee for review of compliance with the Institutional Review Board.

The LOI will be reviewed by the Emerging Science Coordinator to assess overlap with existing projects, and the extent to which the project addresses priority research areas. If the content area described in the LOI is found to be unique and within CANDLE research priorities, the investigator will be asked to submit a full GAP. Investigators will receive a response to their LOI and Cover Form within two weeks of submission.

Grant Application Proposal (GAP) Guidelines
Once the proposal within a Letter of Intent and its accompanying GAP Cover Form has been determined appropriate for further inquiry, investigators will then be invited to submit a GAP. The GAP should include the following:

1. **Title of the Project**: Please provide a title that clearly identifies the primary predictors and outcomes in your grant or funded research.
2. **Investigator List:** Please include all investigators listed as key personnel on the grant application. Investigators must demonstrate expertise in the proposed research area. Collaboration is encouraged and often expected, and it is appropriate for applicants to articulate an area of needed expertise within the grant and inquire about available CANDLE investigators who might fill a niche of required expertise.
3. **Background and Significance:** Please provide a brief review of the literature pertaining to your topic to demonstrate the need for the proposed study, the novelty of your grant proposal, and its potential contribution to your area of research. Also summarize why CANDLE provides a suitable cohort for your study. Please note that grants capitalizing on the unique characteristics of the full cohort will be given priority.
4. **Study Aims and Hypotheses:** In addition to general aims, please provide clearly articulated hypotheses. It is essential to minimize concurrent overlap of projects using CANDLE and we request that you be as specific as possible to help us evaluate your goals. Similarly, proposals must demonstrate appropriate scope (i.e. a defined research question within a single, larger outcome area), and plans may be returned

to the investigator if they are too broad in scope. In some cases, exploratory aims without specific hypotheses will be considered if appropriate for the investigator's discipline and state of the field.

5. **Approach:** Please provide a brief description of the methodological approach you will use to test your hypotheses, including any additional measures or assays planned. Please make clear your primary dependent, independent, and potential confounding variables, as well as a justification for why those variables or additional data elements were selected.
6. **Subject Burden and Cohort Resource Use:** Please describe in detail the added subject burden expected, if any. Include the number of subjects who will be assessed, and describe any additional study visits. This should include a description of 1) the time commitment required by each participant, the measures that will be collected on each participant (e.g. biological samples, behavioral measures, cognitive testing), and the time commitment from CANDLE staff (e.g. recruitment, subject visits, etc.). If existing CANDLE biospecimens will be assayed as part of your grant, please list the number, type, and volume of samples requested, as well as a list of the specific assays you plan to complete.
7. **Details on Any Preliminary Data Required for Your Submission:** If needed, describe preliminary data requested to support this grant submission (e.g. descriptive data on the sample, evidence for variability in a particular measure, etc.), and list variables needed and what analyses will be conducted. Please remember that any analyses intended for publication must be approved via the "Manuscript Analysis Plan Proposal" (MAPP) process, which is separate from this "grant" process. PIs will be granted "first rights" to future analyses proposed within their grant proposals, but once funding is acquired and prior to commencing analyses, investigators must submit a MAPP in order for his or her analyses to be tracked.
8. **Details on Your Data Sharing Plan:** CANDLE is eager to ensure that all relevant primary data on the cohort be error-checked, databased, and ultimately, be made accessible broadly to the research community via CANDLE databases. We therefore request a short data sharing plan similar to that now required for many NIH and NSF grant applications. Please provide details on procedures you will use to return primary data to CANDLE upon completion of the data processing so the data can be assembled within CANDLE databases. In some instances, investigators will be encouraged to use NIH standards for data sharing, for example, dbGaP for genotype and phenotype data sets. Upon approval of your GAP and prior to receiving specimen or data, you will be required to sign a Data Use Agreement form which confirms your understanding of your rights and responsibilities with CANDLE data.
9. **CVs** of lead author and investigators with substantive expertise in topic area.

Grant Analysis Plan ID Number

Once a complete application is received, each GAP will be given a GAP ID#. Please reference this number in email subject lines and in all future verbal communication with CANDLE staff.

GAP Application Review Process

All submitted GAPs will undergo the review process described below. Investigators will receive feedback on Grant LOIs within two weeks of submission and on their full GAP within six weeks of their submission, although efforts will be made to provide feedback more quickly. We are unfortunately not able to expedite proposal reviews, so please plan accordingly.

1. Review by the CANDLE Emerging Science Coordinator to assess completeness of the application. Plans may be rejected at this stage if they deviate sufficiently from the plan articulated in the LOI, overlap significantly with an existing project, or are incomplete. Otherwise plans will be forwarded to the Publication and Presentation (P&P) Committee.
2. Review by the Publication and Presentation (P&P) Committee

a. Two members of the CANDLE P&P Committee (one of which will be a UTHSC faculty member) with substantive expertise in the area of the proposed project will be assigned by the CANDLE PI. This team will review the grant proposal for significance, innovation, methodological approach, and the qualifications of the investigators. Comments and recommendations regarding approval will be provided. If specific CANDLE investigators have made significant scientific contributions to the CANDLE study or possess required expertise for the execution of the proposed work, submitting authors may be asked to include these investigators as co-investigators.

3. Review by the CANDLE Oversight Committee
    a. Decisions on GAP reviews will be available to the CANDLE Oversight Committee which will include:
        i. Title of the MAPP, the authors (with affiliation) and abstract,
        ii. Copies of Reviews
    a. CANDLE Oversight Committee will vote electronically for approval within 1 week of receiving the recommendations from the reviewer based on the leading principles.
4. Investigators will be contacted with one of the following outcomes:
    a. The GAP is approved.
    b. The GAP is pending and requires investigators to respond to issues raised by the P&P committee and resubmit their proposal.
    c. The GAP is rejected due to significant lack of expertise on investigative team, or limitations in the research proposed.

Preliminary Data Analyses

If required for the proposed submission, preliminary data analyses will be completed by CANDLE analytic staff. Please note that preliminary data analyses required for grant submissions will not be approved until a GAP has been submitted and approved. This includes requests for undocumented or unpublished descriptive statistics on the CANDLE population or measures. Depending upon the level of detail required and the focus of the grant, preliminary data analyses may be conducted by a CANDLE biostatistician, or in some circumstances may be conducted by the investigator. Please contact the CANDLE PI for more information about this situation if appropriate.

Responsibilities of the Submitting PI

The principal investigator who submits the final grant application is responsible for submitting a full copy of the application to the Emerging Science Coordinator as well as notifying the Emerging Science Coordinator of the status of the grant submission (i.e. if the submission is scored and/or funded).
Given that most grant applications will have several co-investigators, we strongly suggest that you establish a publication plan with all co-investigators and the CANDLE Leadership prior to beginning data collection.

Amendments to the Proposed Grant Including Requests for Additional Preliminary Data Analyses

If, in the process of writing the grant application, additional preliminary analyses are required and/or the main objectives deviate from the original plan (e.g. new primary aims, new focus, changes to the proposed sample or subject burden), the first author is responsible for submitting a GAP Amendment Form and revised GAP. These documents should be sent to the Emerging Science Coordinator prior to submitting the grant and include:

1. GAP Amendment Form
2. A revised GAP that accurately reflect new aims, hypotheses, required variables and appropriate literature review to match the new focus of inquiry. See details for formatting in the GAP Amendment Form.

Amendments will be reviewed as quickly as possible to expedite the grant-writing process. If the P&P committee decides that the amendment is too great a departure from the original plan, this will be discussed with the investigator to find a resolution.

Guidelines for "Rights to Data" for Grant Proposals and Funded Grants

In general, CANDLE's approach to biospecimen allocation and protecting the rights to data collected from funded grants is as follows:

1. If your full GAP proposal is approved and includes the use of CANDLE biospecimen, the biospecimen required to complete your study will be reserved while your grant is under review. If your grant is funded, those biospecimens will remain allocated to your study. If your grant is not funded, the biospecimens allocated to your study during the review process will not necessarily be available for additional grant submissions. Continued support of your proposed biospecimen usage for a subsequent grant submission/resubmission will depend on a number of factors including the score on the prior submission, competing requests for biospecimen by CANDLE investigators, and relevance of your project to CANDLE study goals. Upon receiving CANDLE biospecimen, you will be given 6 months to complete the proposed assays, return any remaining samples to the CANDLE study team, and provide a cleaned database with all assay values for integration with the larger CANDLE database.
2. If you obtain funding to augment CANDLE either through biospecimen assay or additional data collection (see Using CANDLE data for Grant Applications types a-c above), you will be entitled to the data and the exclusive right to develop manuscripts addressing the primary aims articulated in your grant for 3 years after data collection or biological specimen assay is completed.
3. Also during this 3-year embargo period, funded investigators must make the collected data available to other investigators interested in using the data for research questions outside the aims of the funded grant. What constitutes non-overlapping research projects will be determined collaboratively with the funded investigators and CANDLE leadership. The funded investigator will be entitled to authorship on these additional manuscripts if they meet criteria for authorship.
4. Funded investigators are strongly encouraged to make partial datasets available to investigators requiring pilot data for grant applications that do not overlap with the specific aims of the funded grant. If occurring within the 3-year embargo period and prior to the completion of data collection, data will be used only as pilot data in the grant application and will not be published without the involvement and consent of the funded investigator.
5. After the 3-year embargo period, the data collected as part of the funded grant will be considered part of the larger CANDLE dataset and made available to all investigators regardless of their research question. Please note that funded investigators are welcome to submit additional Manuscript Analysis Plan Proposals (MAPPs) to complete research projects outside the aims of their original grant.
6. We acknowledge that longitudinal data collection efforts may involve several waves of data collection. In this case, the 3-year embargo will apply to each wave of data collection such that funded investigators will still have a 3-year embargo period during which to address the aims of their grant once the final wave of data is collected.

Rights to Biospecimens and Assay Results:

In cases where biospecimens are collected or assayed, "data" refers to results from the specific assay generated by the grant (e.g. hormone levels in maternal blood)-see above section for data rights. These results (i.e. a primary data file with assay values and other relevant covariates and identifiers for all subjects in the study sample) must be submitted to the Emerging Science Coordinator to be included in the master database as soon as assays have been completed. The primary investigator is not entitled to biospecimens for additional assays beyond those articulated in the proposal, and must return any additional specimens to the CANDLE biobank. Investigators may not dictate how and by whom additional specimens may be used.

<u>Ancillary Studies</u>

Ancillary Studies Without Funding: Studies requiring additional data collection that are not funded by the investigator will not be considered. In other words, CANDLE staff and research scientists are not available to collect data that was not part of the original study. However, with prior approval via this GAP process,

investigators may apply for funds to support the personnel and administrative costs associated with additional data collection.

Ancillary Studies Using Existing Funds: In some cases, primary investigators my elect to use their own funds (e.g. start-up funds, flexible grant funds) to conduct an ancillary study. For this type of application, a cover form, letter of intent and GAP must still be completed. Follow the procedures outlined for Grant Application Proposals. On the Grant Application Proposal Cover Form, please indicate that the funds have already been obtained and the amount available.

Institutional Review Board
All approved and funded grants must have their procedures approved by The University of Tennessee Health Science Center's IRB prior to the commencement of the activities described within the GAP.

A NOTE ABOUT USE OF BIOREPOSITORY SAMPLES
At this point in time, the CANDLE biorepository is under inventory and reorganization. Thus, proposals to use the biospecimens for new assay or discoveries are not being accepted until this process is complete and the new infrastructure is in place. Please check with the Emerging Science Coordinator or the Principal Investigator updates on the status of the biorepository.