

Example 1**INSTRUCTIONS PERTAINING TO NON-EXEMPT HUMAN SUBJECTS RESEARCH**

In your application narrative, create a section entitled “E. Human Subjects Research” immediately following the last entry in the Research Design and Methods section. Although no specific page limitation applies to this section of the application, be succinct. Scientific Review Groups will assess each application as being “acceptable” or “unacceptable” with regard to the protection of human subjects.

As the first entry, create a heading entitled “**Protection of Human Subjects.**” Use subheadings to address the issues listed under items 1-4 below.

If your research includes a clinical trial, **address item 5**, "Data and Safety Monitoring Plan."

Protection of Human Subjects**1. RISKS TO THE SUBJECTS****a. Human Subjects Involvement and Characteristics**

- Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status.
- Identify the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special classes of subjects, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. Note that 'prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites in performing the proposed research.

b. Sources of Materials

- Describe the research material obtained from living human subjects in the form of specimens, records, or data.
- Describe any data that will be recorded on the human subjects involved in the project.
- Describe the linkages to subjects, and indicate who will have access to subject identities.
- Provide information about how the specimens, records, or data are collected and whether material or data will be collected specifically for your proposed research project.

c. Potential Risks

- Describe the potential risks to subjects (physical, psychological, social, legal, or other), and assess their likelihood and seriousness to the subjects.
- Where appropriate, describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research.

2. ADEQUACY OF PROTECTION AGAINST RISKS**a. Recruitment and Informed Consent**

- Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.

- Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. Informed consent document(s) need not be submitted to the PHS agencies unless requested.
- b. Protection Against Risk
- Describe planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness.
 - Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (biomedical and behavioral intervention studies) must include a description of the plan for data and safety monitoring of the research and adverse event reporting to ensure the safety of subjects.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

- Discuss the potential benefits of the research to the subjects and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

- Discuss the importance of the knowledge gained or to be gained as a result of the proposed research.
- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

NOTE: Test articles (investigational new drugs, devices, or biologicals) including test articles that will be used for purposes or administered by routes that have not been approved for general use by the Food and Drug Administration (FDA) must be named. State whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the Food and Drug Administration, and/or the status of requests for an IND or IDE covering the proposed use of the test article in the research plan.

5. DATA AND SAFETY MONITORING PLAN

- If your research includes a clinical trial, create a heading entitled "Data and Safety Monitoring Plan."
- Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the funding I/C, the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations. Be succinct. Contact the FDA (<http://www.fda.gov/>) and also see the following websites for more information related to IND and IDE requirements:
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr312_01.html (IND)
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr812_01.html (IDE)
- The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:
 - Principal Investigator (required)
 - Independent individual/Safety Officer
 - Designated medical monitor
 - Internal Committee or Board with explicit guidelines

Data and Safety Monitoring Board (DSMB). NIH specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for *multi-site* clinical trials involving interventions that entail potential *risk* to the participants, and generally for Phase III clinical trials. Although Phase I and Phase II clinical trials may also use DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.

Institutional Review Board (IRB - required)

- A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>). For additional guidance on creating this Plan, see the above reference.

Example 2

Principal Investigator/Program Director (Last, first, middle): Cattamanchi, Adithya

**BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY**

BUDGET CATEGORY TOTALS		INITIAL BUDGET PERIOD <i>(from Form Page 4)</i>	ADDITIONAL YEARS OF SUPPORT REQUESTED			
			2nd	3rd	4th	5th
PERSONNEL: <i>Salary and fringe benefits. Applicant organization only.</i>						
CONSULTANT COSTS						
EQUIPMENT						
SUPPLIES						
TRAVEL						
PATIENT CARE COSTS	INPATIENT					
	OUTPATIENT					
ALTERATIONS AND RENOVATIONS						
OTHER EXPENSES						
SUBTOTAL DIRECT COSTS						
CONSORTIUM/ CONTRACTUAL COSTS	DIRECT					
	F&A					
TOTAL DIRECT COSTS		\$112,750	\$112,750	\$112,750	\$112,750	\$112,750
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD <i>(Item 8a, Face Page)</i> _____						\$ 563,750
<u>SBIR/STTR Only</u> <u>Fixed Fee Requested</u>						
SBIR/STTR Only: Total Fixed Fee Requested for Entire Proposed Phase II Period <small>(Add Total Fixed Fee amount to "Total direct costs for entire proposed project period" above and Total F&A/indirect costs from Checklist Form Page, and enter these as "Costs Requested for Proposed Period of Support on Face Page, Item 8b.)</small>						\$

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

Pursuant to University of California policy, salaries in the initial budget are based on current published UC salary scales and include University mandated range adjustments and merit increases scheduled to occur before the proposed project start date. Merit increases for faculty, other academic appointments and staff on step-based pay plans are included at the time they are due according to UC guidelines for normal length of time at each step.

Fringe Benefit rates effective July 1, 2007 through June 30, 2009:

Academic Personnel increase from 17.0% to 20.0%. Staff personnel-career increase from 22.0% to 25.0%

Effective July 1, 2009 and thereafter:

Academic Personnel increase from 20.0% to 22.0%. Staff personnel-career increase from 25.0% to 27.0%

A Mentored Patient-Oriented Research Career Development Award (K23) can include up to \$75,000/year in salary support + fringe benefits for the candidate, plus \$25,000/year for other expenses. Per PHS 398 instructions for K awards, we include only a narrative justification for major budget items (other than personnel) that are requested for the conduct of the proposed research, and no specific costs for items or categories are shown.

A. Personnel:

1. Adithya Cattamanchi, MD (Candidate, 90% effort in Year 1 (10.8 cal mos) and 80% effort in Years 2 - 5 (9.6 cal mos): Funds are requested in the amount of \$75,000/year in salary support plus fringe benefits for Dr. Cattamanchi.

2. Philip Hopewell, MD (Sponsor and Primary Mentor): Dr Hopewell is a Professor of Medicine at UCSF. He is an attending physician in the Department of Medicine at San Francisco General Hospital (SFGH) and a member of the Division of Pulmonary and Critical Care Medicine. Dr. Hopewell will serve as sponsor and primary mentor for Dr. Cattamanchi. Dr. Hopewell is an internationally recognized expert in the molecular epidemiology of tuberculosis and in HIV-associated pulmonary diseases, and he has mentored numerous highly successful patient-oriented clinical researchers. Dr. Hopewell will provide primary supervision of the studies proposed herein and will also provide career mentoring and guidance. Dr. Hopewell will provide effort as needed, without salary.

3. Laurence Huang, MD, MAS (Co-Mentor): Dr. Huang is a Professor of Medicine at UCSF. He is an attending physician in the Department of Medicine at SFGH where he holds dual appointments in the Division of Pulmonary and Critical Care Medicine and the HIV/AIDS Division and where he is Chief of the HIV/AIDS Chest Clinic. Dr. Huang is an internationally recognized expert in HIV-associated pulmonary diseases. He is the principal investigator of the IHOP study, the parent study for this proposal, and has been involved in the design of this proposal. Drs. Huang and Cattamanchi will continue their already established weekly meetings to discuss patient recruitment, patient enrollment, and retention of study subjects in the IHOP cohort. In addition, Dr. Huang will review study protocols and data collection instruments specific to this proposal. Dr. Huang will provide effort as needed, without salary.

4. Dennis Osmond, PhD (Co-Mentor): Dr. Osmond is a Professor Emeritus of Epidemiology and Biostatistics at UCSF. Dr. Osmond has a proven track record of highly successful patient-oriented clinical research studies and has mentored several highly successful patient-oriented clinical researchers. Dr. Osmond has guided Dr. Cattamanchi in the design of this research proposal and will continue to serve as a resource for epidemiologic methods, data management, and data analysis. Dr. Osmond will provide effort as needed, without salary.

5. Huyen Cao, PhD (Co-Mentor): Dr. Cao is an Assistant Professor of Medicine at UCSF. She is also the Director of Cellular Immunology at the California Department of Public Health and Director of the HIV Vaccine Trial Network Central Immunology Laboratory. Dr. Cao's expertise was critical in selecting and field-testing the T-SPOT.TB assay in Kampala. She will continue to provide technical expertise to troubleshoot problems with processing and testing of clinical samples from the proposed study. Dr. Cao will also assist with data interpretation and manuscript preparation. Lastly, in her capacity as an immunological collaborator for the IHOP study, Dr. Cao will be responsible for supervising the proposed laboratory training. Dr. Cao will provide effort as needed, without salary.

6. David Lewinsohn, MD, PhD: Dr. Lewinsohn is an Associate Professor, Pulmonary and Critical Care Medicine and an Adjunct Associate Professor of Molecular Biology and Immunology at the Oregon Health Sciences University. Dr Lewinsohn is uniquely qualified to serve as a scientific advisor for this proposal due to his expertise in applied TB immunology and extensive experience with ELISPOT technology. Dr. Lewinsohn will provide a structured tutorial on current concepts in TB immunology focused on important and sophisticated

data-management. During the planned laboratory training in Year 3, his expertise in M. TB immunology will be tapped to review experimental data and to plan additional studies. Dr. Lewinsohn will provide effort as needed, without salary.

7. Moses Kamya, M.Med, MPH: Dr. Kamya is a key person in AIDS care at Mulago hospital and a founding member of the Infectious Diseases Institute, a major public-private partnership established by physician scientists from Uganda and North America with the support of Pfizer Inc. Dr. Kamya will serve as an on-site mentor when I am in Kampala and we will meet at least weekly. His expertise and experience in clinical research will be heavily relied upon during the implementation phase of the study. He will provide specific guidance around regulatory and ethical issues and management of the study team. Dr. Kamya will provide effort as needed, without salary.

8. James G. Kahn, MD, MPH: Dr. Kahn is a Professor of Clinical Epidemiology at UCSF. His work focuses on the use of cost-effectiveness analysis to inform decision-making in public health and medicine. He has developed computer models to assess the health and economic outcomes of HIV prevention (particularly in injecting drug users) and care (including the effects of expanded health insurance). He also assesses strategies for family planning (contraception and abortion) and sexually transmitted disease control, as well as other medical interventions. Dr. Kahn will provide mentorship for learning how to perform cost-effectiveness analyses of new diagnostics. Dr. Kahn will provide effort as needed, without salary.

B. Other Expenses:

1. Equipment – A laptop computer will be purchased for use by Dr. Cattamanchi in coursework, data management, data analysis, and manuscript preparation. An additional desktop computer will be purchased and shipped to Uganda for data entry purposes. Licenses will be purchased for data analysis software (Stata Version 10, Stat Transfer, etc.) needed for the proposed research.

2. Supplies –

- a. Specimen collection materials - 50 ml conical tubes, N95 respirator masks, 0.9% normal saline, cell preparation tubes, paper towels
- b. Specimen processing materials – 50 ml conical tubes, 15 ml conical tubes, 70 micron nylon mesh filters, diethiothreitol (mucolyse), AIM V culture medium, RPMI culture medium
- c. Specimen storage materials – cryovials, cryovial boxes
- d. Reagents/Supplies for Laboratory training – Luminex cytokine assay kits, monoclonal antibodies (for immunophenotyping)

3. Travel –

- a. Travel to Kampala – Dr. Cattamanchi will make 4 trips per year in Years 1-2 and 4 additional trips in Years 3-5 to implement the proposed study, develop experience with patient enrollment, and to plan a future R01 grant. The expenses for each trip include airfare and lodging.
- b. Travel to OHSU – Dr. Cattamanchi will make 4 trips to Portland Oregon in Year 3 to meet with Dr. David Lewinsohn for laboratory training. The expenses for each trip include airfare and lodging.
- c. Travel to Conferences – Dr. Cattamanchi will attend at 1-2 conferences per year. The expenses for each conference include airfare and lodging.

4. Coursework –

- a. Master's Degree in Clinical Research – This is 2-year degree offered by the UCSF Department of Epidemiology and Biostatistics.
- b. Immunology Coursework – Dr. Cattamanchi will take two separate week-long courses offered by the American Association of Immunologists.
- c. WHO TB Consultant Courses – Dr. Cattamanchi will take two separate week-long courses typically offered in a developing country setting.

5. Other Expenses –:

- a. Specimen Shipping – Specimens will be shipped frozen in batches from Kampala to UCSF every 4 months during Years 1-3.
- b. Bank Charges – Monthly charges to handle international wire transfers for MU-UCSF sub-contract expenses (see below).

6. MU-UCSF sub-contract: A sub contract with MU-UCSF Research Collaboration will be established to handle the following expenses in Kampala, Uganda.

- a. Personnel – A part time (50%) laboratory technician and part time (50%) data entry person will be hired.
- b. Patient care costs – Patient care costs will be covered by the IHOP study. We will pay for daily transport of patient specimens to the JCRC laboratory for T-SPOT.TB testing.
- c. UNCST certification – Annual certification to conduct patient related research in Uganda is required by the Uganda National Council of Science and Technology.
- d. Indirect costs – 8% indirect costs are assessed on all MU-UCSF sub-contracts. In exchange for this fee, administrative services including accounting, purchasing, telephone/fax and photocopying services are provided.

Example 3

PERSONAL STATEMENT

Dr. DuBois is an Assistant Professor of Pediatrics at UCSF School of Medicine, and he is the principal investigator for this proposed career development award. Dr. DuBois is developing a research program focused on developmental therapeutics and novel biomarkers in pediatric solid tumors, with an emphasis on Ewing sarcoma. During his fellowship at Dana-Farber and Children's Hospital Boston, he gained both practical and didactic training in the conduct of early phase clinical trials in children. He has continued that training as a junior faculty member at UCSF, taking advantage of the opportunities afforded by the UCSF CTSI KL2 program. During this same time, Dr. DuBois developed a novel flow cytometry-based approach for detecting rare Ewing sarcoma cells in the bone marrow. He successfully obtained foundation grants to develop this assay and then test the assay in a pilot study. With the preliminary data generated from those studies, he now plans to evaluate bone marrow micrometastatic disease at diagnosis and over time, which is the focus of this K23 award. This award will enable him to obtain the additional training needed to solidify his background in flow cytometry and biomarker development.

Example 4**Facilities and Other Resources**

The University of California, San Francisco (UCSF) is one of the preeminent health sciences universities in the country. As a recipient of an NIH Clinical and Translational Science Award, UCSF has a well-developed network of core laboratory resources available to investigators across the university. Dr. DuBois will conduct his research in the UCSF Core Flow Cytometry Laboratory. Additional laboratory resources are available to support future directions that follow from the proposed research. Potentially relevant other resources include: the UCSF Core Tissue Culture Laboratory; the UCSF Cancer Center Preclinical Therapeutics Core Laboratory; and the Genomics Core Laboratory. Each of these facilities is equipped with state of the art equipment.

Dr. DuBois will utilize his private office to complete his work. This office is adjacent to the UCSF CTSI Pediatric Clinical Research Center, allowing Dr. DuBois to be immediately available to meet with subjects participating in his research studies. Dr. DuBois has access to a research nurse practitioner and to a team of clinical research assistants, including one focused exclusively on his research studies.

The UCST CTSI also provides biostatistical resources. Dr. DuBois will have the ability to consult with a PhD-level biostatistician to plan his studies. He will also be able to utilize the UCSF CTSI biostatisticians to execute his planned analyses.

Equipment

The UCSF Core Flow Cytometry Laboratory utilizes state of the art flow cytometers. Most of the proposed flow cytometry studies will be performed either on the LSRII flow cytometer or FACS Aria flow cytometer, both from BD Biosciences. The laboratory also includes computer hardware, FlowJo software (Treehouse), and computational support to handle the large amounts of data collected as part of flow cytometry experiments. Standard equipment for tissue culture, isolation of mononuclear cells, and antibody staining for flow cytometry are available.

Example 5

Abstract

This is an application for a K23 award for Dr. Neera Gupta, a pediatric gastroenterologist at the University of California, San Francisco. Dr. Gupta is establishing herself as a young investigator in patient-oriented clinical research of pediatric inflammatory bowel disease. This K23 award will provide Dr. Gupta with the support necessary to accomplish the following goals: (1) to become expert at patient-oriented clinical research in pediatric Crohn's disease; (2) to conduct clinical investigations of endocrinologic aspects of growth in pediatric patients with IBD; (3) to implement advanced biostatistical methods in clinical studies; (4) to develop and maintain a relational database containing data from multiple sites; and (5) to develop an independent clinical research career. To achieve these goals, Dr. Gupta has assembled a mentoring team comprised of a primary mentor, Dr. Melvin Heyman, Director of the Training Program in Pediatric Gastroenterology at UCSF, who conducts clinical investigations in pediatric IBD, and three co-mentors: Dr. Robert Lustig, an endocrinologist who focuses on hypothalamic function and its regulation of growth and energy balance; Dr. Eric Vittinghoff, and expert in study design and current state-of-the-art biostatistical analysis; and Dr. Michael Kohn, who has expertise in database development and management.

Growth impairment is a well-recognized complication of Crohn's disease. Dr. Gupta's research will focus on the relative influence of gender and age at disease presentation and diagnosis on height and growth velocity z scores in newly diagnosed pediatric patients with Crohn's disease (**Aim 1**) and the relative effects of gender, pubertal development (Tanner stage) and disease activity on growth hormone/insulin-like growth factor I levels and height z scores in pediatric patients with Crohn's disease (**Aim 2**). In Aim 1, Dr. Gupta will use the existing infrastructure of the Pediatric IBD Consortium (composed of centers in 6 geographically distinct US regions) to enroll and follow 200 newly-diagnosed pediatric patients with Crohn's disease to determine the independent effects of gender and age at disease presentation and diagnosis on growth. In Aim 2, Dr. Gupta will conduct a single-center cross-sectional pilot study to generate preliminary data on the effects of gender, pubertal status, and disease severity on growth in children with Crohn's disease. Both studies will utilize advanced multivariate statistical analyses. This research will form the basis for a multicenter longitudinal study in newly diagnosed childhood Crohn's disease, to be proposed in an R01 grant application before the end of the K award.

Project Narrative/Public health relevance: Improved understanding of the etiology and gender-associated differences in growth impairment in pediatric patients with Crohn's disease is critical to effective medical management and may clarify the underlying mechanisms for gender differences in this chronic disorder.

Example 6

January 22, 2010

Center for Scientific Review
National Institutes of Health
Suite 1040
6701 Rockledge Drive MSC 7710
Bethesda, MD 20892-7710

Re: Assignment of "Bone Marrow Micrometastatic Disease in Ewing Sarcoma"

Dear Sir or Madam:

Enclosed is a grant application for a Mentored Patient-Oriented Research Career Development Award (K23), which is being submitted in response to **PA-09-043**.

My long-term research goal is to improve the outcome for children and young adults with solid tumors, particularly Ewing sarcoma. Therefore, I am requesting assignment of this grant application to the **National Cancer Institute**.

My letters of reference are from:

Holcombe Grier, MD
Professor of Pediatrics
Harvard Medical

Stephen Lessnick, MD, PhD
Associate Professor of Pediatrics
University of Utah

Neyssa Marina, MD
Professor of Pediatrics
Stanford University School of Medicine

Should you have any questions, I can be reached at (415) 476-4764 or by email at duboiss@peds.ucsf.edu.

Sincerely,

Steven DuBois, MD
Assistant Professor of Pediatrics
University of California, San Francisco

Example 7

Investigator: Wendy Katzman, PT, DPTSc
Funding Agency: NIA
Title: Hyperkyphosis, Physical Frailty, and Adverse Outcomes
Type of Grant: K23 (PA-09-043)
RSA: Research Support Analyst
Due dates:
 Agency: February 12, 2010
 C&G: February 8, 2010

Whose Task Done? UCSF forms

- RSA 1. UCSF OSR approval form
- RSA 2. Financial disclosure UCSF key personnel only
 - a. Declaration: PI's list of participants who must file disclosures
- RSA 3. Human subjects protection training certification letter (optional)
- RSA 4. Investigator human subjects training certifications (optional)
 - Wendy Katzman, PT, DPTSc (Candidate)
 - Deborah Grady, MD (Sponsor and Primary Mentor)
 - Kenneth Covinsky, MD (Co-Mentor)
 - Dennis Black, PhD (Co-Mentor)
- RSA/WK 5. Detailed budget and budget justification

NIH grant forms (SF 424 and PHS 398)

- RSA 1. Face page
- RSA 2. Table of contents
- RSA 3. Research and Related Project/Performance Site Location(s)
- RSA 4. Research and Related Project/Other Project Information
- WK/TM 5. Project Summary/Abstract
- WK/TM 6. Public Health Relevance Statement
- WK/TM 7. Facilities & Other Resources
- WK/TM 8. Equipment
- RSA 9. Biographical sketches
 - Wendy Katzman, PT, DPTSc (Candidate)
 - Deborah Grady, MD (Sponsor and Primary Mentor)
 - Kenneth Covinsky, MD (Co-Mentor)
 - Dennis Black, PhD (Co-Mentor)
 - Deborah Kado, MD (Scientific Advisor; UCLA)
- RSA 10. Additional Current and Pending Support (Mentors only)
 - Deborah Grady, MD (Sponsor and Primary Mentor)
 - Kenneth Covinsky, MD (Co-Mentor)
 - Dennis Black, PhD (Co-Mentor)
- RSA/WK 11. PHS 398 Specific Modular Budget
- WK/TM 12. K Award Training and Research Plan (Sections 2 – 22)
- WK/TM 13. Letters from Mentors and Advisors
 - Deborah Grady, MD (Sponsor and Primary Mentor)
 - Kenneth Covinsky, MD (Co-Mentor)
 - Dennis Black, PhD (Co-Mentor)
 - Deborah Kado, MD (Scientific Advisor; UCLA)
- 14. Letter of Institutional Commitment
- 15. Letters of Reference
 - Jeanette Brown, MD

Deborah Sellmeyer, MD
Kim Topp, PT, PhD

RSA
RSA
RSA

- 16. Checklist
- 17. Personal Data Form
- 18. Appendices