

UCSF Office of Career & Professional Development's  
Professional & Academic Success Skills series

Presents...

## Writing Effective Grant Proposals



### EXAMPLES & RESOURCES

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## I. EXAMPLES

### ❖ SPECIFIC AIMS (SOURCE: NIH DATABASE)

#### Example 1:

Our main analysis is designed to achieve 3 specific aims: **1) to investigate** the extent of differences in use of NICUs and high volume facilities by race and ethnicity, and examine the correlates of differences in utilization rates; **2) to construct** new outcome-based indicators of the quality of hospital care for newborns, and examine variations in the quality of hospitals at which newborns of different races and ethnicities are born or to which they are transferred, and to examine the correlates of differences; and **3) to examine** the effect of differences in access to NICUs, high volume facilities, and high quality hospitals on disparities in health outcomes for newborns by race and ethnicity.

#### Example 2:

The **specific** outcome aims of the proposal are to improve graduating students' (1) knowledge of core end-of-life tasks, (2) attitudes toward end-of-life care, (3) emotional comfort with dying patients, (4) satisfaction with their end-of-life instruction, and (5) feeling of preparedness to provide end-of-life care at the level of a medical intern.

#### Example 3:

Measurements of antihypertensive drug responses and stored DNA from GERA will be used to accomplish the following specific aims: **Aim 1:** Use genome-wide association analyses of single nucleotide polymorphisms to identify novel genes influencing BP response to a thiazide diuretic in hypertensive African-Americans (n = 200) and non-Hispanic whites (n = 200) previously enrolled in GERA protocol 1. **Aim 2:** Use genome-wide association analyses of single nucleotide polymorphisms to identify novel genes influencing BP response to an angiotensin II receptor blocker in hypertensive African-Americans (n = 200) and non-Hispanic whites (n = 200) enrolled in GERA protocol 2.

### ❖ SPECIFIC AIMS SECTION--BASIC SCIENCE RESEARCH

Include 3 general sections:

- 1) **"Set-up" sentence or paragraph**, illuminates the relationship between a pressing problem in biomedicine and the research theme of your laboratory.
- 2) **"Hypothesis" sentence or paragraph**, points to a specific problem or area and culminates in the statement of the hypothesis.
- 3) **"Specific Aims" sentence or paragraph**, lists the aims and alludes to the techniques used in order to achieve each one.

#### 1) **Set-up Paragraph** (Source: NIAID)

##### Example 4:

**Staphylococcus aureus is a well-armed opportunistic pathogen that produces a diverse array of virulence factors and causes a correspondingly diverse array of infections.** The pathogenesis of *S.aureus* infections depends on the coordinately-regulated expression of two groups of virulence factors, one of which (surface proteins) allows the bacterium to evade phagocytes and colonize host tissues while the other (extracellular toxins and enzymes) promotes survival and multiplication at a localized site of infection. **Our long term goal** is to elucidate the regulatory mechanisms controlling expression of these virulence factors as a prerequisite to the development of therapeutic protocols that can be used to attenuate the disease process.

#### 2) **Hypothesis Paragraph:**

##### Example 4 cont'd:

**The specific hypothesis behind the proposed research is that the staphylococcal accessory regulator (*sar*) is a major regulatory switch controlling expression of *S. aureus* virulence factors.** That hypothesis is based on the following observations. **First**, ... (refs) **Second**... (refs) **Third**.... (refs) **Moreover**... (refs).

### 3) Specific Aims Paragraph

Start with an introduction.

Example 4 cont'd:

Based on these observations, the experimental focus of this proposal is on the *sar* regulatory locus. The specific aims are designed to provide a comprehensive assessment of the *agr*-independent regulatory functions of *sar*.

Then list each Aim. Be as brief and specific as possible (one sentence per aim), using a short paragraph under each aim if detail is needed.

Example 4 cont'd:

**Specific Aim 1. Correlate the production of each *sar* transcript with the production of functional SarA.** The only recognized protein product of the *sar* locus is the SarA DNA-binding protein. However, Northern blot analysis reveals.... The functional significance of this differential regulation will be assessed by correlating the production of each transcript with the production and activity of SarA.

**A.** The temporal production of SarA will be assessed by Western blot of *S. aureus* whole cell extracts with an affinity-purified anti-SarA antibody.

Consider including a conclusion for the Specific Aims Section.

Example 4 cont'd:

We believe the *sar* regulatory locus may be an appropriate target in that disruption of *sar*-mediated regulation has the potential to attenuate the bacterium to the point that it is more susceptible to clearance either by the normal host defense systems or existing antimicrobial agents. **Accomplishing the specific aims outlined in this proposal will provide the foundation required to assess that possibility** by establishing the correlation between *sar* transcription and SarA production and activity (**Specific Aim #1**), elucidating the mechanism by which *sar* controls expression of a specific target gene (*cna*) (**Specific Aim #2**) and identifying additional SarA targets within the *S. aureus* genome (**Specific Aim #3**).

### ❖ SPECIFIC AIMS SECTION--CLINICAL RESEARCH

Begin with a concise, accurate synopsis of the research. Then describe primary and secondary aims and related hypotheses.

Example 5: (Source: AN EVIDENCE-BASED GUIDE TO WRITING GRANT PROPOSALS FOR CLINICAL RESEARCH. See resources)

The Insulin Resistance Intervention after Stroke Trial (IRIS) is a randomized, double-blind, placebo-controlled trial that will test the hypothesis that reducing insulin resistance and its sequelae with thiazolidinedione therapy will prevent stroke and myocardial infarction among patients with a recent ischemic stroke. Eligible subjects are men and women over 44 years of age without diabetes mellitus who have insulin resistance and a non-disabling ischemic stroke. During 3 years of recruitment, 3136 patients will be randomly assigned to pioglitazone, a thiazolidinedione, or placebo.

The specific aims are as follows. 1. Primary Aim. To determine if pioglitazone, compared to placebo, will reduce the overall risk for fatal or non-fatal stroke or fatal or non-fatal MI among non-diabetic men and women over age 44 years with insulin resistance and a recent ischemic stroke.

Among diabetics with insulin resistance, we hypothesize that pioglitazone will reduce the occurrence of any primary endpoint (fatal or non-fatal stroke or MI) within four years from 27% to 22%. The basis of this hypothesis is research showing... (*details about studies associating insulin resistance with increased risk for stroke, MI, etc.*)...By these and other mechanisms, we hypothesize that pioglitazone will protect patients with ischemic stroke and insulin resistance against recurrent vascular events.

Example 6. A complete Specific Aims Section (Kindly provided by Dr. Hobart Harris, Department of Surgery, UCSF)

## **SPECIFIC AIMS**

Exposure to pathogenic microbial lipids, like lipopolysaccharide (LPS), triggers a complex and coordinated protective response by the immune system. A growing body of evidence indicates that triglyceride-rich lipoproteins and apolipoprotein E (apoE) play an integral role in host defense against bacterial infection. Yet, how these non-traditional elements of the immune system contribute to host immunocompetence is unclear. Published data indicate that apoE is protective against bacterial infection and injury. Accordingly, infusion of apoE has been shown to decrease LPS-induced morbidity and mortality in rodents. [2, 3] Also, apoE-deficient mice have an increased susceptibility to lethal infection when injected with live bacteria. [4, 5] But, unexpectedly, our laboratory has recently discovered that infusion of apoE *increased* rather than decreased mortality after cecal ligation and puncture, an *in vivo* model of polymicrobial sepsis. [1] We believe that this discordant observation highlights a novel activity for apoE in regulating the host response to pathogenic microbial lipid antigens through activation of thymus-derived lymphocytes (T cells). Consequently, uncovering the role that triglyceride-rich lipoproteins, apoE and T cells play in the mammalian response to infection simultaneously assigns important new biological functions to plasma lipoproteins, further blurs the boundary separating innate and adaptive immunity, and provides unique insights into the host response to infection that could yield innovative therapies for sepsis. This proposal will investigate how apoE and natural killer T (NKT) cells, a sub-population of T lymphocytes, contribute to the host response to severe sepsis following cecal ligation and puncture in mice. Furthermore, we will test the hypothesis that modifying the expression or activity of apoE can protect against sepsis.

Our working hypothesis that triglyceride-rich lipoproteins are integral components of the immune system is supported by the following observations. First, the synthesis and secretion of triglyceride-rich lipoproteins is dramatically increased during clinically significant infections, an observation termed “lipemia of sepsis.” Second, triglyceride-rich lipoproteins bind various microbial lipids and thus protect against shock and death in rodent models of sepsis. [6-9] Third, triglyceride-rich lipoproteins clear LPS from the circulation and deliver it to the liver [7, 10], where lipoprotein-LPS complexes subsequently modulate the hepatic immune response to infection. [11-14] And, fourth, apoE has recently been shown to bind and deliver microbial lipids to antigen-presenting cells, a critical step in activating NKT cells and the immune system. [15]

**The specific hypothesis driving the proposed research is that apoE, a key constituent of triglyceride-rich lipoproteins, regulates the host response to severe infection through its effects on NKT cell activation and cytokine production.** By examining the effect of apoE on an *in vivo* model of polymicrobial sepsis in mice, we aim to uncover the regulatory impact of apoE on the immune response to infection. **Our long term goal** is to identify how plasma lipoproteins contribute to host immunocompetence and apply this knowledge to the development of novel and effective treatments for severe bacterial infections.

The specific aims of the proposal are therefore:

- 1. To demonstrate that serum apolipoprotein E (apoE) concentrations correlate with morbidity and mortality in a murine model of polymicrobial sepsis.**
  - A. show that apoE increases mortality following cecal ligation and puncture (CLP) sepsis in mice in a dose-dependent manner;
  - B. show that apoE increases CLP-induced morbidity via changes in Th1 cytokine secretion, liver injury and bacterial clearance;
- 2. To demonstrate that apoE promotes the activation of natural killer T (NKT) cells during CLP-induced sepsis.**
  - A. delineate the effect of apoE on NKT cell frequency, proliferation, cytokine expression and cytotoxic effector functions in the liver, spleen and thymus following CLP in mice;
  - B. show that apoE-mediated immune regulation during sepsis is dependent on NKT cell activation using immunodeficient mice;
- 3. To test the hypothesis that inhibition of apoE activity protects against the morbidity and mortality of sepsis.**
  - A. show that the biochemical, immunologic or genetic inhibition of apoE activity protects against sepsis;
  - B. examine the effect of modifying apoE activity during the early versus late phase of sepsis.

## ❖ BACKGROUND AND SIGNIFICANCE SECTIONS

*Example 7:* (Background at the beginning & significance last; see how the researcher's aims are woven into the narrative):

### ***Why Study Square Cell Disease in the Kidney?***

Renal dysfunction commonly complicates square cell disease and is a major cause of morbidity and mortality. Acute Renal Syndrome is the leading cause of death in square cell disease and commonly leads to acute renal failure (58), while chronic uremia, filtration insufficiency, and renal vascular disease occur in 20-60% of adults with square cell disease (46, 54). Despite its clinical importance, the kidney has rarely been the focus of basic research in square cell disease. Current understanding of square cell pathophysiology derives from studies performed in other organs or in vitro. **Because mechanisms of vaso-occlusion and inflammation in the kidney are likely to be different from those in other organs, there is a critical need for basic research on square cell disease that focuses on the kidney.**

### ***Physiological Determinants of Vaso-occlusion in the Kidney***

Research on renal vaso-occlusion is limited to two studies that suggest severe medullary hypertonia causes sequestration of SQ RBCs in the kidney (3, 17). These studies did not adequately assess effects of modest tubular hypertonia and no study has evaluated the importance of mixed arterial hypertonia or inflammation to renal vaso-occlusion. In **Specific Aim 1**, we adapt the isolated rat kidney model used in these original studies (3, 17) to determine effects of tubular hypertonia, and mixed arteriolar hypertonia and renal inflammation on kidney micro vaso-occlusion...etc.

### ***Summary and Clinical Significance***

Studies performed in vitro and in other organs have given important insights into the pathophysiology of square cell disease, but have not yet defined the important pathophysiology in the kidney. The studies we propose will attack the problem directly using sensitive and specific techniques. These studies will lay the experimental foundation for understanding square cell disease crises in the kidney. The importance of these studies to the affected population cannot be exaggerated.

## ❖ PRELIMINARY STUDIES SECTION—BASIC SCIENCE

EXAMPLE 8: (Excerpt; note the introduction, informative subheadings, reference to figures. source: NIAID)

### **Preliminary Studies**

Pharmacodynamics is the area of science that links drug exposure to response. A key element of pharmacodynamics investigation is to identify the true pharmacodynamically (PD)-linked variable. This idea operates under the hypothesis that the shape of the drug concentration-time curve may impact drug effectiveness (76). For example, the time that free drug concentrations remain above the measure of potency of the drug for the virus in question (EC<sub>50</sub>, EC<sub>95</sub>) may be most closely linked to the effect. In this case, relatively short dosing intervals lead to maximal effects. Alternatively, peak concentrations relative to the measure of potency (Peak/EC<sub>50</sub> ratio) may be linked to outcome. Here, infrequent dosing with high peak concentrations result in the best effect. There are times when the mode of administration does not alter the effect produced. Here, the Area Under the concentration time Curve (AUC) relative to the measure of potency (AUC/EC<sub>50</sub> ratio) is linked to effect. We will use the in vitro hollow fiber infection model (HFIM) pharmacodynamic system to determine the pharmacodynamically-linked variables of compounds active against influenza A and B viruses. We have used the HFIM pharmacodynamic system to prospectively predict the optimal dose and schedule of administration for a number of antibacterial, antifungal and antiviral compounds required to positively affect the outcome in patients infected with these agents (7-16). Clinical validation of the HFIM system exists for the predictions that the HFIM produces. In the HIV arena there have been a number of prospective validations that are listed in **Table 1**. ...

### **The *in vitro* Hollow Fiber Infection Model (HFIM) Pharmacodynamic System.**

**Figure 1** illustrates the workings of the HFIM system. For our studies, we use 4300-C2011 cartridges (FiberCell Systems, Inc, Frederick, MD) containing high molecular weight cut off (20 kd) polysulfone hollow fibers (HF) with a surface area of 2100 cm<sup>2</sup> and a 15 ml extracapillary space (ECS) giving a surface area to volume ratio of 140. The

high surface area to volume ratio guarantees that the drug exposures in the ECS and the central reservoir rapidly come to equilibrium....[etc.]

#### **The HFIM pharmacodynamic system for amantadine and oseltamivir carboxylate for influenza viruses.**

The long term goal of these investigations is to clearly identify the pharmacodynamically (PD)-linked variable for amantadine and the oseltamivir carboxylate for influenza viruses. To identify the PD-linked variable, we first perform a dose range study in the HFIM system using a continuous infusion profile. This identifies a daily AUC that will have a known effect...[etc.]

#### **Growth of virus stocks.**

Flasks containing one day old confluent MDCK cell monolayers were washed 2X with virus growth medium (MEM + 0.2% BSA + 2 µg/ml of TPCK-treated trypsin + pen/strep) and influenza viruses obtained from the ATCC or other sources were diluted 1:1000 in virus growth medium and 0.5 ml of diluted virus was added to the monolayer...[etc.]

### **❖ RESEARCH DESIGN AND METHODS SECTION—BASIC SCIENCE**

EXAMPLE 9: (Excerpt from Research Design and Methods section for Basic Science, Source: NIAID)

#### **Research Design and Methods:**

The first specific aim of this grant application is to use the HFIM system to show that monotherapy with amantadine or oseltamivir carboxylate will lead to the emergence of resistance in influenza virusinfected cells and to demonstrate that the resistant viruses produced in the HFIM system under these conditions have the same mutations as those that emerge when people are treated with these drugs. In the second specific aim, we will use the HFIM system to optimize the dose and schedule of administration of current antiviral compounds effective against influenza viruses, delivered as monotherapy, to minimize the emergence of resistance. Finally, in the third specific aim we will determine the optimal dose and administration schedule of these anti-influenza virus drugs administered in combination therapy to prevent virus infection and the emergence of resistance.

**Specific Aim #1.** Validate the HFIM as a model experimental system for influenza virus infection and the generation of drug resistant mutants.

#### **A. Introduction.**

Treatment of patients infected with type A influenza viruses with amantadine/rimantadine is known to lead to the rapid emergence of resistant viruses in the treated population (1-3). Treatment of patients with influenza with the neuraminidase inhibitors, oseltamivir carboxylate or zanamivir, usually does not lead to the emergence of resistant viruses (48). However, recent data have shown that treatment of children with influenza with oseltamivir carboxylate has led to the emergence of neuraminidase inhibitor-resistant influenza viruses (4-6). Data presented in the **preliminary results section** of this grant application showed that treatment of MDCK cells infected with a clinical isolate of influenza A virus in the HFIM system with amantadine can lead to the emergence of resistant viruses within two to three days of initiation of treatment. Phenotypic, but not genotypic, resistance was demonstrated when influenza virus-infected MDCK cells were treated with the D-tartrate salt of oseltamivir carboxylate in the HFIM system. The purpose of this portion of the grant application is to confirm these observations with A/Albany/1/98 influenza virus and to expand that observation for amantadine to additional influenza A viruses and for oseltamivir carboxylate to additional influenza A and B viruses.

#### **B. Experimental Design.**

We will examine the effect of amantadine and oseltamivir carboxylate on the replication of wild type rgA/Vietnam/1203/2004xA/PR/8/34 (a surrogate for avian H5N1 influenza virus), A/Texas/36/91(H1N1), A/Sydney/5/97(H3N2), and A/Victoria/3/75(H3N2) in the HFIM system. For comparison, we will also include our original clinical isolate, A/Albany/1/98(H3N2), to be certain that our original observations are reproducible for amantadine and oseltamivir carboxylate. Oseltamivir carboxylate will be tested against B/Lee/40 and B/Memphis/20/96

viruses. **First**, we will determine the EC50/EC95 values of amantadine HCl and oseltamivir carboxylate for these viruses in monolayers of MDCK cells grown in flasks as described below in **Experimental Methods\***. **Second**, we will perform dose ranging studies with these viruses in the HFIM system to test the system for emergence of resistance. To this end, 108 uninfected MDCK cells will be mixed with 102 virus-infected cells. The cell mixtures will be added to six 50 ml centrifuge tubes, the cells pelleted by centrifugation at 1500 rpm for 5 min to remove the cell growth medium, and the pelleted cells will be suspended in 30 ml of virus growth medium supplemented with various concentrations of amantadine or oseltamivir carboxylate. The suspended cells will be added to six different HF units and infused continuously with different concentrations of amantadine or oseltamivir carboxylate for seven days. At various times post infection, the medium containing virus-infected cells and released virus in the extracapillary space (ECS) will be sampled from each port on the HF unit, the cells in each sample will be removed by pelleting the sample at 1500 rpm for 10 min, the supernatant will be collected into a fresh tube, mixed well, dispensed into several tubes, and frozen at -80oC until assayed for infectious virus by plaque assay or TCID50 assay. A separate sample of the supernatant will be mixed with AVL extraction buffer (Qiagen, Inc.) containing carrier RNA for analysis of genomic equivalents by quantitative real-time PCR (see **Experimental Methods below**). Both ECS and ICS will be sampled for determination of drug concentrations by LC/MS/MS to insure that the intended drug concentrations were present during the virus infection. The results of the plaque assay, the TCID50 assay and the qPCR assay will determine the effect of amantadine or oseltamivir carboxylate on the production of virus. Once the plaque assay results have been determined, one of the two frozen tubes containing those ECS samples will be thawed and plated on MDCK cell monolayers to form plaques. Then 10 plaques will be picked from each time point at each drug concentration, suspended in AVL buffer containing carrier RNA and shipped to TGen for Sanger sequencing of the M2, HA and NA genes to determine the genotype of the viruses produced at each time point under each drug concentration. A similar approach will be taken for cells infected with B/Lee/40 or B/Memphis/20/96 except that only oseltamivir carboxylate will be used since amantadine does not inhibit influenza B viruses.

### **C. Expected results.**

Resistance will emerge under monotherapy. Amantadine resistant strains will have mutations in the M2 gene (residues 26, 27, 30, 31); neuraminidase inhibitor resistant strains will have mutations in the NA gene (residues 274 and 292) and/or HA genes (multiple residues).

### **D. Potential problems.**

It is often difficult to generate mutations in vitro in the neuraminidase genes in the presence of neuraminidase inhibitors that resemble the mutations identified in the clinic. This may be due to the use of MDCK cells which have inappropriate cell surface receptors for influenza viruses. To address this potential problem, we will use a variety of other cell lines which more closely reflect the surface characteristic of lung epithelial cells such as A549 pulmonary alveolar epithelial cells (82), St Jude porcine lung (SJPL) cells (83), ST6Gal I cells (84) or SIAT1 cells (85) which express cell surface receptors with more terminal sialic acid, and Mink lung cells (86) to perform these dose ranging studies aimed at producing resistant viruses in the HFIM system. It is expected that by using the appropriate cell lines, resistant strains will be produced that more accurately reflect the neuraminidase inhibitor-resistant strains that have been identified in the clinic.

### **E. Time frame.**

If this grant application is funded we will be able to purchase 4 additional duet pumps for the hollow fiber experiments thus doubling our capacity to perform these experiments. We plan to perform dose ranging experiments for amantadine and oseltamivir carboxylate on A/Victoria/3/75, A/Texas/36/91, rgA/Vietnam/1203/2004xA/PR/8/34, and A/Albany/1/98 and oseltamivir carboxylate for B/Lee/40 and B/Memphis/20/96 in the HFIM system. Each experiment will be repeated at least 1 time. One hollow fiber experiment takes approximately two weeks to perform from setup to take down. Analysis of virus yield (plaque assay, TCID50 assay and real time quantitative PCR) will take an additional two weeks. Therefore, each experiment, including a repeat, will take approximately 2 months. We plan to study at least the four type A and two type B viruses listed above for two drugs for a total of 24 hollow fiber experiments. Since we can study two viruses at a time for one drug or one virus for two drugs, Specific Aim 1 will take at least one year to complete.

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\* Not provided here.

## ❖ ABSTRACTS

Example 10 (kindly provided by Dr. Hobart Harris, Department of Surgery, UCSF)

### ABSTRACT

Exposure to pathogenic microbial lipids, like lipopolysaccharide (LPS), triggers a complex and coordinated protective response by the immune system. Our laboratory investigates the novel postulate that triglyceride-rich lipoproteins and apolipoprotein E (apoE) have been co-opted to play an important role in host defense against bacterial infection, in addition to their well-established roles in lipid metabolism. Yet, precisely how these non-traditional elements of the immune system contribute to host immunocompetence is unclear. Published data indicate that apoE is protective against bacterial infection and injury as injection of this apolipoprotein has been shown to decrease LPS-induced morbidity and mortality in rodents. Also, apoE-deficient mice have an increased susceptibility to lethal infection when injected with live bacteria. But, unexpectedly, our laboratory has recently discovered that infusion of apoE *increased* rather than decreased mortality after cecal ligation and puncture, an *in vivo* model of polymicrobial sepsis. We believe that this apparent dichotomy highlights the existence of a novel activity for apoE in the sequestration and delivery of pathogenic microbial lipid antigens to thymus-derived lymphocytes (T cells). **Specifically, we hypothesize that apoE, a key constituent of triglyceride-rich lipoproteins, regulates the host response to pathogenic bacterial lipids through its effects on natural killer T (NKT) cell activation and cytokine production.** Through three specific aims, this proposal will investigate how apoE and NKT cells contribute to host defense against toxic bacterial lipids after cecal ligation and puncture in mice. **In Aim 1**, we will demonstrate that serum apoE concentrations correlate with morbidity and mortality in a murine model of polymicrobial sepsis. **In Aim 2**, we will demonstrate that apoE promotes the activation of NKT cells during sepsis. Lastly, **in Aim 3**, we will test the hypothesis that inhibition of apoE activity protects against the morbidity and mortality of sepsis. Results of our studies will yield considerable insight into the role of triglyceride-rich lipoproteins, apoE and T cells in the mammalian response to microbial infection. Moreover, our studies will simultaneously assign important new biological functions to plasma lipoproteins, further blur the boundary separating innate and adaptive immunity, and provide unique insights into the host response to infection that could yield innovative therapies for sepsis.

Example 11 (Source: AHSP Foundation)

### **Development of a Continuity of Care Record: Bridging the Medication Use Gap from Hospital to Home**

Principal Investigator: Kim C. Coley, Pharm.D., FCCP

#### **Abstract**

The U.S. health care system is multifaceted and complex with patients commonly receiving care from several providers in various locations. Despite efforts to emphasize care driven by a primary care provider and a focus on medication safety, little attention has been given to the problems faced by patients and providers as patients transition across settings. It is recognized that problems with medication reconciliation and adverse drug events after discharge from the inpatient setting occur commonly. Community-based pharmacists frequently don't have the information or tools necessary to ensure appropriate medication use and follow-up monitoring for patients recently discharged from the hospital. In 2003, the ASHP House of Delegates approved the Continuity of Care Policy Statement which aims to strongly encourage pharmacists to assume responsibility for ensuring the continuity of pharmaceutical care as patients move from one setting to another. With this goal in mind, the purpose of this study is to develop a consensus-based Medication Continuity of Care (MCOC) Record to communicate medication-related clinical information from the point of hospital discharge to the point of community-based pharmaceutical care. Furthermore, we seek to determine the effects of the MCOC Record under different provision of pharmaceutical care practices, including community-based medication therapy management (MTM), in high risk patients following hospital discharge compared to usual care.

## II. SUGGESTIONS FOR HOW TO STRUCTURE A TWO-PAGE PROPOSAL

All of the necessary elements need to be clear and easy to find within 2 pages of packed text: overall goal, hypotheses, specific aims, rationale/background/prelim data for each aim, innovation, research/health implications.

One key trick is to explicitly state each specific aim, and then build out a detailed paragraph for each aim. Each of these paragraphs would describe the important background, preliminary studies, hypothesis, rationale, and methodological approach. Thus, the same elements are there, but they're combined into a single paragraph per aim.

**Paragraph 1:** 4-5 sentences that cover: 1) background, 2) importance, 3) proposal goal (underlined), 4) general approach. **Innovation** can be highlighted here or, depending on the proposal guidelines, in its own separate paragraph, as shown in Paragraph 5, below. **Potential Health/Research Impact** can also be highlighted here, or, depending on the proposal guidelines, in its own paragraph, as shown in Paragraph 6, below.

**Paragraph 2:** *Specific aim 1* (indent 2 spaces, and state it *in italics*), followed by a description of your approach and the rationale (not in italics). You can weave preliminary results here insofar as they lead to the specific gap in knowledge addressed in the current proposal, provide rationale for the approach, or both. Make it clear you are referring to your preliminary results by saying, "Our preliminary studies have identified..." Be sure to state the hypothesis being tested. You can do that by saying "We hypothesize...", or something like "The novel concept that X mediates Y and Z that are commonly observed in patients with *disease A*, and is responsible for the established effects of B on C and D, will be examined by studies of ....[this allows you to include some methodological details, but remember to do so in broad strokes, not fine detail].

**Paragraphs 3 & 4:** *Specific aims 2 & 3*, as above

**Paragraph 5:** Use bold face and italic font to make the following clear within the paragraph:

**Innovation.** *Conceptual innovations* include: (1)...(2)...(3)... Enumerate and describe them—these often relate to your hypotheses... *Technological innovations* include: ...(1)...(2)...(3) [enumerating them is helpful for readers]

**Paragraph 6:** Use bold face and italic font to make the following clear within the paragraph:

**Potential Health/Research Impact.** *Health related implications* include...(1)... (2), etc [as above, enumerating them is helpful]

**Paragraph 7:** Use bold face and italic font to make the following clear:

**Applicant's Expertise and Capacity to Implement Proposed Research...**

**Reference List:** should be minimal

### III. RESOURCES AND TIPS FOR WRITING GRANT PROPOSALS

Good science is *essential*, but it is only part of the package:

Never forget that your proposal is a work of persuasion and not a collection of disparate facts. It isn't merely a description of the work you want to do; you are making an argument that it is work that needs to be done and that you are the right person to do it. Make your argument convincingly.

~ Science NextWave 2001

#### A. NIH Grant Proposals

**New NIH Proposal Format:** NIH grant applications submitted for due dates on or after January 25, 2010 (i.e., for funding in FY11 and beyond) now have [shorter page limits](#) and a restructured format, with changes to the research plan, biosketch, resources, and select agent components. Unfortunately, that coverage doesn't yet include "good examples" of what the NIH is looking for.

The most detailed NIH instructions I could find about the new review system & format are available here:

[http://enhancing-peer-review.nih.gov/docs/application\\_changes.pdf](http://enhancing-peer-review.nih.gov/docs/application_changes.pdf)

[http://enhancing-peer-review.nih.gov/page\\_limits.html](http://enhancing-peer-review.nih.gov/page_limits.html)

<http://www.niaid.nih.gov/ncn/newsletters/2009/0923.htm#n01>

Writing tips "in sync" with the new NIH Format; Scroll down the page to the "in sync" section.

<http://funding.niaid.nih.gov/ncn/grants/app/default.htm>

**Helpful for preparing a new NIH proposal:** *The Grant Application Writer's Workbook: Guide to A Successful Proposal*, National Institutes of Health.

[http://www.grantcentral.com/workbook\\_nih\\_sf424\\_shortened.html](http://www.grantcentral.com/workbook_nih_sf424_shortened.html)

**Essential Overview of the Review Process and How to Improve Your Chances of Being Funded (NIH-specific but much will be true for other agencies):** [ora.stanford.edu/ora/ratd/nih\\_04.asp](http://ora.stanford.edu/ora/ratd/nih_04.asp)

This is a video link to a recent workshop on *NIH Funding Opportunities, Peer Review and Grant Writing*, which was presented by Anthony Coelho, Ph.D. Review Policy Officer, NIH National Institutes of Health on December 14, 2004, at Stanford University.

**UCSF's Office of Career & Professional Development provides several useful resources:**

In particular, download Keith Yamamoto's **presentation** from the 2010 PASS workshop on "Funding Your Research, Part A". It gives an overview of the NIH and new review policies, plus great advice about writing each section of the research plan (using examples from the "old" NIH format). From Keith Yamamoto PhD, UCSF's Executive Vice Dean for Research:

<http://career.ucsf.edu/lifesci/samples.grants.html>

**UCSF's Clinical and Translational Science Institute provides several useful resources:**

- **Examples** of K08, K23 and K24 grant applications: <http://ctsi.ucsf.edu/training/grants-library>

**More from NIH:**

<http://www.niaid.nih.gov/ncn/grants/cycle/part00.htm>. The NIH grant cycle

<http://www.drug.nih.gov/Video/Video.asp>. The Center for Scientific Review (the portal for NIH grant applications and their review for scientific merit) has produced a video of a mock study section meeting to provide an inside look at how NIH grant applications are reviewed for scientific and technical merit. The video shows how outside experts assess applications and how review meetings are conducted to ensure fairness. The video also includes information on what applicants can do to improve the chances their applications will receive a positive review.

[www.training.nih.gov/careers/careercenter/grants.html#prop](http://www.training.nih.gov/careers/careercenter/grants.html#prop) Provides links to the **best** resources available on proposal writing. Many links will be useful for non-NIH proposals as well.

**Some Sites with Real Examples of Funded Proposals (these won't be the new NIH format yet):**

[www.neurosurgeon.org/education/cenr.asp](http://www.neurosurgeon.org/education/cenr.asp)

[www.niaid.nih.gov/ncn/grants/app/default.htm](http://www.niaid.nih.gov/ncn/grants/app/default.htm)

<http://www.nhlbi.nih.gov/funding/training/redbook/newintro.htm>

**Essential Article for Writing Clinical Proposals:** (includes several real examples):

[Evidence-Based Grant Writing for Clinical Research](#)

Inouye SK and Fiellin F. An evidence-based guide to writing grant proposals for clinical research. *Ann Intern Med* 2005;142:274-282

**Useful for Writing Clinical Proposals:**

<http://www.niaid.nih.gov/ncn/grants/charts/checklistshs.htm#hsplan>

## B. Beyond the NIH but Good for NIH Proposals Too

**From the American Association for the Advancement of Science:**

[http://sciencecareers.sciencemag.org/career\\_magazine](http://sciencecareers.sciencemag.org/career_magazine)

A weekly on-line publication of the AAAS devoted to scientific training and career development. Provides global news, profiles of emerging careers, and advice on a variety of topics from experts and role models drawn from the international scientific community. Some specific links are listed below for grant writing.

[http://sciencecareers.sciencemag.org/career\\_development/tools\\_resources/how\\_to\\_guides/how\\_to\\_get\\_funding](http://sciencecareers.sciencemag.org/career_development/tools_resources/how_to_guides/how_to_get_funding)

Tips on how to find grants, and "work the process".

[http://sciencecareers.sciencemag.org/career\\_development/previous\\_issues/articles/0210/grants\\_and\\_grant\\_writing\\_index](http://sciencecareers.sciencemag.org/career_development/previous_issues/articles/0210/grants_and_grant_writing_index)

Index of **all resources** from the AAAS on grant writing. Be sure to read the series of short articles entitled "How not to kill a grant application".

<http://sciencecareers.sciencemag.org/funding>

Funding opportunities for training in the sciences (Grantsnet).

**Essential Article Describing Grantsmanship Process from Beginning to End:** (includes information of specific interest to pharmacists, but is a great resource for everyone else):

Devine, EB. The art of obtaining grants. *Am J Health-Syst Pharm* 2009;66:580-587.

**Statistics:**

Excellent series in Critical Care Medicine. Edited by Jonathan Ball, Viv Bewick and Liz Cheek. Available at:

[http://ccforum.com/series/CC\\_Medical](http://ccforum.com/series/CC_Medical)

Excellent series in the *Canadian Medical Association Journal*. Available online at: <http://www.cmaj.ca/>

Guyatt G, Jaeschke R, Heddle N, Cook D, Shannon H, Walter S. *Basic statistics for clinicians. 1. Hypothesis testing*. *Can Med Assoc J* 1995;152:27-52.

Guyatt G, Jaeschke R, Heddle N, Cook D, Shannon H, Walter S. *Basic statistics for clinicians. 2. Interpreting study results: confidence intervals*. *Can Med Assoc J* 1995;152:169-173.

Jaeschke R, Guyatt G, Shannon H, Walter S, Cook D, Heddle N. *Basic statistics for clinicians. 3. Assessing the effects of treatment: measurements of association*. *Can Med Assoc J* 1995;152:351-357.

Guyatt G, Walter S, Shannon H, Cook D, Jaeschke R, Heddle N. *Basic statistics for clinicians. 4. Correlation and regression*. *Can Med Assoc J* 1995;152:497-504.

Very handy, user-friendly statistical analysis software. Available online at:

<http://faculty.vassar.edu/lowry/VassarStats.html>

## Overviews of "Grantspersonship":

**From the University of Pittsburgh's "academic survival" series:**

<http://www.survival.pitt.edu/library/documents.asp>

Clear, concise and complete. You can download it as an adobe file.

**From the Burroughs Wellcome Fund/ Howard Hughes Medical Institute:**

<http://www.hhmi.org/grants/pdf/labmgmt/ch9.pdf>

This chapter on funding comes from the BWF/HHMI book, *Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty*, which is based on presentations and discussions from a course developed by HHMI and the Burroughs Wellcome Fund. This downloadable book is a collection of practical advice, experiences, and opinions from seasoned biomedical investigators and other professionals.

**Summary of Recommendations for First-Time Grant Writers, from the American College of Surgeons (includes key contacts at the NIH):**

<http://www.facs.org/cqi/src/youngbroch.html>

Good advice and not for surgeons only!