Writing Your R25 Protocol

- Think about the next step—the grant application that will come from this
- Plan the R25 Protocol like an NIH grant
- It is essentially like an R03 or a developmental grant in P30 or P50 Center
What will be the next step

- Will the project lead to....
  - An efficacy-type trial (R01)?
  - A pilot intervention (R34)?
  - A large explanatory study (R01)?
  - A larger exploratory study (R21)?
  - Mentored training to broaden your focus (K-award)?
Considerations for Intervention R01s

- Efficacy trials of interventions (R01)
  - Interventions should have a strong empirical and theoretical base
  - The project should have a well integrated conceptual framework
    - Potential mediators and moderators should be addressed
  - Clinical or public health implications should be clear
  - The R01 intervention should be substantially similar to the pilot project
    - Substantial changes or adaptations to a new setting, population or mode of delivery would make an R34 more appropriate

- Preliminary research should provide:
  - Bases for estimating power & sample size
  - Evidence of acceptability, feasibility, & indications of behavior change
Considerations for R34s

- Pilot trials of interventions (R34)
  - Interventions should have a strong empirical and theoretical base
    - R34s do not need preliminary data, but formative findings or a small pilot will help
  - The project should have a well integrated conceptual framework
    - You won’t have power to test the complete model, but you should be able to look at gross, univariate outcomes
    - Substantial changes or adaptations to a new setting, population or mode of delivery would make an R34 more appropriate

- Preliminary research should provide:
  - Provide a rationale for moving to an intervention
  - Work should be done in the population, setting, or modality of interest unless the R34 is used for as an adaptation/implementation step
Considerations for Non-intervention R01s

- Large explanatory study (R01)
  - The aims and hypotheses should have a strong empirical and theoretical base
    - The project should address novel research questions in terms of content or methods
    - The aims should be aligned with important clinical or public health questions
  - The project should have a well integrated conceptual framework
    - Potential mediators and moderators should be addressed
  - The R01 investigation should be substantially similar to the pilot project in terms of population
  - Preliminary research should provide:
    - Bases for estimating power & sample size
    - Evidence supporting the importance of the question and the associated variables of interest
Considerations for R21s

- Further exploratory research (R21)
  - The aims and hypotheses should have a strong empirical and theoretical base
    - The project should address novel research questions in terms of content or methods
    - The aims should be aligned with important clinical or public health questions
  - The project should have a well integrated conceptual framework
    - Potential mediators and moderators should be addressed
  - Preliminary research should provide:
    - Evidence supporting the importance of the question and the associated variables of interest
    - A rationale for continuing exploratory research
      - Going from analogue to real world;
      - Going from secondary analysis, meta-analysis or thematic review to empirical study
Considerations for Ks

- Mentored training to broaden your focus (K-award)?
- This should support a new direction
  - Something not part of the R25 or your prior training
  - The experience should plausibly lead to a program of research
- Preliminary research should provide:
  - A building block for the proposed research and a complement to the mentored training
Plan the R25 Protocol like an NIH Grant

- Questions should be novel for the field or for HIV/AIDS
- Adequate attention to prior work
- Clear conceptual framework
  - Integration of aims/hypotheses/analyses
- Alignment with clinical, public health or other programmatic concerns
  - Remedies and explanation rather than documenting deficits and complaints
  - Real world populations rather than simulations
  - Outcomes/surrogates over intentions and attitudes
Questions should be novel for the field or for HIV/AIDS

- Well developed areas should be approached with novel methods or new perspectives
  - Informed consent
  - Knowledge, attitudes, etc. among research stakeholders
  - Acceptability/willingness to participate
- Areas new for HIV/AIDS may have a history in other areas
  - Well developed disease areas like cancer, diabetes
  - Competence issues in mental health, neuroscience
  - Genetics
Attention to Prior Work

- Look over a long period of time
  - Ethics research goes through peaks, valleys, & periods of intense interest in particular topics
  - Use NIH Report to identify recently funded work
- Look at a variety of fields and topics
  - Chronic disease issues may already have significant attention in cancer, diabetes, etc.
  - Issues with minors or other special populations may have been considered in other contexts
  - Questions recur in new contexts: Vaccine, micorobicide, PrEP
- More work has been done in treatment & assessment than prevention
  - Treatment and assessment procedure considerations may be difficult to translate into prevention
Clear Conceptual Framework

- Framework should reflect theory and prior research
  - Program models can be used instead of theory but require a clear rationale
- Aims, hypotheses, concepts & data analyses should clearly be linked
  - The framework should underlie concepts and how they are used
- Use of operational language
  - Write for people outside your discipline
  - Clearly operationalize the components of the framework
Implications Need to be Clear

- Align aims with clinical, public health, or other programmatic concerns
  - Work toward remedies & explanation rather than documenting deficits & complaints
    - There already is much documentation of concerns in many areas
  - Real world populations rather than simulations
    - Vignette studies, lab analogues, etc. have limited validity & are not used optimally
  - Outcomes or reasonable surrogates over intentions or attitudes
NIH Ethics Funding Announcements

• Current Announcements
  • Research on Ethical Issues in Biomedical, Social, and Behavioral Research (R03, R21, R01)
    • PA11-180, PA11-181, PA11-182
    • Topics vary by Institute
    • NIDA Topics include:
      • Novel approaches to consent; improving comprehension
      • Addressing limitations in capacity; substance use & mh pops
      • Increasing participation of under-represented populations
      • Ethical issues in resource constrained environments
      • Consent & safeguards in vulnerable pops; use of surrogates
      • Issues related to biobanking
      • Electronic health info systems

• Keep an eye open for additional FOAs
**NIH Grant Review Criteria**

- **Overall Impact**
  - Likelihood for exerting a sustained, powerful influence on the field, considering the following:

- **Scored Review Criteria**
  - Significance
    - Does it address an important question, does it make maximal use of the resources involved?
  - Investigator(s)
    - Are they well suited to the project?
  - Innovation
    - Does it challenge or seek to shift current thinking?
  - Approach
    - Does the strategy accomplish the specific aims of the project?
  - Environment
    - Will the environment contribute to the success of the project?
10 Fatal Flaws of Grant Submission

- Waiting until the Last Minute/Not Enough Eyes
  - Make sure everyone involved with the project has read the proposal

- Missing or Problematic Hypotheses
  - Research questions need to be testable
  - The aims, hypotheses, framework & analyses all should be consistent

- Poorly Organized Proposal
  - Emphasis should be on methods rather than background

- Lack of a Back-up Plan
  - Prepare for alternative conditions/outcomes
  - Aims should be separable

- Gaps in Expertise
10 Fatal Flaws of Grant Submission (Cont’d)

- Lack of Significance/Innovation
  - Questions and/or approach should be novel
- Under Powered
  - Less of an issue for pilot proposal, but will be an issue in publication
- Overly Ambitious
  - Too many aims for available resources
- Weak Analytic Plan
  - Should tie together aims, hypotheses & framework
- Human Subjects Concerns
NIDA AIDS Research Priorities: Domestic

- Understanding HIV transmission among drug users (injection & non-injection) and their networks
- Research on substance abuse, risky decision-making, and impulsivity and HIV transmission among adolescents and adults
- Research on structural interventions to prevent HIV/AIDS transmission and/or to enhance access/utilization of treatment and services
- Seek, test, treat, and retain—expanding HIV testing, linkage, and retention in care for hard-to-reach populations
  - Reducing racial/ethnic disparities in these areas
  - Interventions for drug users involved in the criminal justice system
  - Improve treatment & services for HIV, drug abuse, & co-occurring conditions (e.g., HCV)
- Drug treatment as HIV prevention
- Improving effectiveness of HIV therapy for substance abusers
  - Enhancing adherence to treatment for HIV and co-morbid conditions
- Drug abuse, HIV, and the brain
- Genetics, epigenetics, proteomics, and systems biology studies in drug abusers and/or animal models of HIV
NIDA AIDS Research Priorities: International

- Develop new methods for HIV epidemiology
- Assess role of immigration and migration on HIV transmission
- Develop prevention strategies addressing non-injection drug use such as stimulants (e.g. methamphetamine, cocaine, crack) in vulnerable populations (e.g., MSM, young women) where prevalence is high (e.g., Latin America, Asia, Africa)
- Develop prevention strategies addressing IDU/HIV epidemics in different geographic areas (Russia, China, SE Asia, India, Eastern/Central Europe)
- Drug treatment as HIV prevention, including development of long-acting, sustainable therapies
- Assessment of HIV/AIDS treatment as HIV prevention
- Implementation research to guide scale-up of cost-effective interventions
- Develop regional research networks
- HIV and co-infections (e.g., HCV, TB)