

COLUMBIA UNIVERSITY
DEPARTMENT OF NEUROLOGY

RESEARCH RESOURCES GUIDE

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RESIDENT & FELLOW ORIENTATION

Research is an important part of the educational experience in neurology. According to the Residency Review Committee in Neurology, "Graduate medical education must take place in an environment of inquiry and scholarship in which residents participate in the development of new knowledge, learn to evaluate research findings, and develop habits of inquiry as a continuing professional responsibility"

The resources at Columbia for those interested in research as part of their training or career are outstanding. The opportunities for both basic science and clinical research are unparalleled, and include the Howard Hughes Institute for Neuroscience, the Genome Center, the New York State Psychiatric Institute, the Taub Institute for the Study of Alzheimer's Disease, the Sergievsky Center for Neuroepidemiology, the Clinical Research Center and numerous other opportunities.

The purpose of this document is to provide information about resources in research, funding, and career planning both at Columbia and elsewhere. While the information is primarily intended to be of use to residents in Neurology, fellows and junior faculty in Neurology will also find this information of value.

I) Courses in Clinical Research Methodology

A) Protection of Human Participants in Biomedical and Behavioral Research (Good Clinical Practices (GCP) course).

For information and registration for this course or the exam, see <http://cpmcnet.columbia.edu/research/gcp.htm>. The Columbia University Health Sciences Division requirement is the demonstration of knowledge of the protection of human research participants, as evidenced by either attending these lectures or studying the materials for the indicated course and passing an examination on that material with a score of at least 80%. This is required for submission of IRB protocols and sponsored project applications (involving human research participants).

The syllabi and slide presentation for the two courses can be viewed on the web at <http://www.research.hs.columbia.edu/gcp.htm>.

All certification exams are administered via Rascal, Columbia University's Electronic Research Administration system. Log-in to Rascal's Testing Center with your UNI ID (university ID) and Password. The "Testing Center" can be found under "Compliance" on the Rascal homepage.

B) Responsible Conduct of Research and Related Policy Issues.

This course explores a variety of ethical and policy issues that arise during the conduct of basic and clinical scientific research. The course is sponsored by the office of Grants and Contracts and is directed by Dr. Jaime Rubin. It meets weekly in the spring term. **This course is required by those involved in NIH sponsored training grants such as the Neuroscience Training Grant and the Neuroepidemiology Fellowship.** Please contact Dr. Rubin for information about the course: jsr9@columbia.edu or go to the website at <http://cpmcnet.columbia.edu/research/rcr-crse.htm>

C) Funding for Research Activities: Basic Issues in Obtaining Support

This course is also offered by Dr. Rubin, usually in the spring on Thursday afternoons, and covers issues related to obtaining funding for research. It is an excellent course, and goes through all of the various funding mechanisms.

(<http://cpmcnet.columbia.edu/research/funf-crs.htm>)

D) Clinical Research Seminar Series

The Irving Center for Clinical Research, in collaboration with the Division of Biostatistics, School of Public Health, offers this non-credit seminar series on clinical research. The series is designed for new investigators, particularly postdoctoral clinical fellows and residents embarking on careers in clinical research. Classes are held in the Milstein Building Clark Conference Center on Mondays from 5-6 p.m., usually beginning in late November. Seminars provide basic training relevant to epidemiology, biostatistics, computing, human investigation, and the development of clinical research grant applications. Topics generally include: Study Design, Mechanics of Conducting a Trial, Sample Size, Power, and Statistical Analysis, Kaplan-Meier Method of Estimation, Cox or Proportional Hazards Regression, Introduction to Genetic Epidemiology, and NIH Funding for Clinical Investigation. **This is really an excellent overview without a huge time commitment and would be appropriate for a senior resident interested in considering a career in clinical research.** For information try:

(http://cpmcnet.Columbia.edu/dept/irving_center/announce.html)

E) Responsible Animal Use in Research

This course offered by the Institute of Comparative medicine is required of all research personnel before gaining access to the animal facility or participating in animal related research. For information contact 305-2404.

F) Neuroepidemiology

This course reviews the epidemiology of neurologic diseases as well as the techniques employed in neuroepidemiologic research. It is offered in the spring every other year.

This course is required of those participating in the Neuroepidemiology fellowship. For information, contact Dr. Ralph Sacco or Dr. Allen Hauser.

G) Other Clinical Research Methods Courses

Some courses at the School of Public Health may be available to residents. Information on course schedules can be obtained from the school of Public Health, and further information can be obtained from Drs. Richard Mayeux, Allen Hauser and Ralph Sacco.

- 1) Introduction to Biostatistical Methods**
- 2) Principles of Epidemiology**
- 3) Applied Regression Analysis**
- 4) Analysis of Categorical Data**
- 5) Randomized Clinical Trials**

H) Biology of Neurologic and Psychiatric Disorders

This course is offered Saturday mornings during the fall and winter, and reviews basic and clinical science of neurological diseases. This course is directed by Dr. Arnold Kriegstein and is free to all residents. Lectures are presented by faculty in the Department of Neurology and selected basic science faculty in other departments.

II) Mentors

Several faculty members have offered to mentor residents in research design, methodology, and conduct. The resident will meet with the faculty member to design a specific research program. Appropriate projects include basic science investigations, clinical studies, case reports, case series based on a retrospective review of patient material from the service, or an evidence-based review of the literature on a particular topic, among others. Research mentorships will generally begin during the second year of residency. At the end of this training, the resident will be expected to produce an abstract, a book chapter or a case study. For information about, contact Dr. Sacco, Dr. Elkind, or Minu Chaudhuri (mc1431@columbia.edu).

III) Important Information Regarding Funding

You cannot simply submit a grant on your own!

It is important to be aware that all grants at Columbia are awarded to the institution, not to the individual. Therefore all grants must be approved by departmental and university administrators, and thus must have an institutional signature. Offices that might be involved in your submission include:

A) Grants & Contracts

B) Office of Clinical Trials

C) Columbia Innovation Enterprises (Industry sponsored research other than clinical trials)

Because of this, you must often meet internal deadlines ahead of the external deadlines imposed by the granting institutions (such as NIH, etc.). Generally, your budget should be ready **10 days** before the final grant is due, and any other administrative matters should be taken care of at least **5 days** before the grant is due. Therefore, seek help early from your mentor, as well as your Departmental Grants Manager or Divisional Administrator.

There are several internal documents that must be prepared, in addition to the grant itself. These include the following required forms:

A) RASCAL – internal coversheet for grant application. A RASCAL coversheet must be prepared for all grants being submitted, otherwise Grants & Contracts will not issue an account #. After filling out RASCAL, the PI must approve and finalize the proposal and Department approver (Minu Chaudhuri) must approve proposal.

B) Documentation of Required Education on the Protection of Human Research Participants (see above)

C) Conflict of Interest

D) IRB approval (final or pending)

E) Animal Care (IACUC forms) when appropriate

IV) Columbia Funding Resources

- 1) **The Office of Clinical Trials** sponsors a pilot grant program, which is generally a one year grant for up to \$50,000 to sponsor a pilot clinical investigation or clinical trial. The goal is to provide the investigator with pilot data to allow later submission of an NIH or other grant. Several awards are given annually. This is appropriate for those with (or about to receive) junior faculty appointments. For information, contact the office of Clinical Trials (PH 15), or discuss with Drs. Elkind or Sacco.
- 2) Our **Departmental Grants Office** (mc1431@columbia.edu) can help with administrative aspects of grants and interacting with the University Grants & Contracts Office, as well as assisting with identifying sources of funding.
- 3) University Research webpage <http://cpmcnet@columbia.edu/research/> This is an excellent resource and includes Columbia's internal information about funding, as well as links to external databases of funding sources. There is also an email listserv that allows you to receive email notification of research information. Information transmitted includes: (1) announcements of research funding opportunities; (2) the Table of Contents of the weekly NIH *Guide to Grants and Contracts* (which includes RFAs, program notices, policy changes); (3) communications on national biomedical research funding issues; and (4) information related to University/Campus research matters.
 - To subscribe to this email listserv, email: listserv@cuvmc.ais.columbia.edu and enter SUBSCRIBE hsd-resadm Firstname Lastname.
- 4) The **Funding for Research Activities: Basic Issues in Obtaining Support** course by Dr. Rubin (see 1.3 above).

V) External Funding Resources

There are several research funding databases available, many of which are accessible from the University Research webpage: <http://cpmcnet.columbia.edu/research/>

1) Sponsored Programs Information Network (SPIN) Database

This commercial database from Infoed Inc. is updated daily and contains information on approximately 10,000 different funding opportunities from more than 1,200 different agencies which sponsor research projects. Over half are in health-related or biomedical fields. Access is limited to Columbia University faculty, staff, and students.

2) GrantsNet

Searchable database of biomedical funding opportunities from non-profit organizations and federal agencies. Database focuses on training support **programs specifically for graduate students, postdocs, and junior faculty members in the biological and medical sciences**. Created by AAAS and the HHMI.

3) The [Illinois Researcher Information Service \(IRIS\) database](#)

This database, from the University of Illinois Library at Urbana-Champaign, is updated daily and contains information from 2,000 different agencies on 7,700 different funding opportunities. The University also subscribes to the IRIS Alert and Expertise Services, the former of which allows users to create personal IRIS search profiles and receive funding information automatically via e-mail. Access to the database and these services are limited to Columbia University faculty, staff, and students.

4) Other Useful websites:

(a) NIH website <http://grants.nih.gov/>

(b) AAN compendium of clinical research training programs:
<http://www.aan.com/resources.html>

(c) AAN clinical research funding database: <http://www.aan.com/resources.html>

(d) Tips for successful grant writing
<http://www.ninds.nih.gov/funding/grantwriting.htm>

VI) Suggested Reading

- Batchelor T, Cudkovicz ME. Principles of Neuroepidemiology. Boston: Butterworth-Heinemann, 2001.
- Gordis L. *Epidemiology*, 2nd edition. Philadelphia: W.B. Saunders, 2000.
- Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical Epidemiology: A Basic Science for Clinical Medicine*, 2nd edition. Boston: Little Brown and Company, 1991.
- Rothman KJ. *Modern Epidemiology*. Boston: Little Brown and Company, 1986.
- Kelsey JL, Thompson WD, Evans AS. *Monographs in Epidemiology and Biostatistics: Volume 10: Methods in Observational Epidemiology*. Lilienfeld AM, editor. New York: Oxford University Press, 1986.

VII) Administrative Information Required For Grants & Contracts Applications

<http://cpmcnet.columbia.edu/research/ogc-info.htm>

(Periodically updated)

Institution's Legal Name:	The Trustees of Columbia University in the City of New York
Name of individual to be notified if award is made:	<u>Your Departmental Project Officer</u> Office of Grants and Contracts Health Sciences Division Columbia University Box 49 630 West 168th Street New York, New York 10032-3702 tel: (212) 305-4191 fax: (212) 305-3697
If awarded, check should be drawn to:	The Trustees of Columbia University in the City of New York
Checks should be mailed to:	The Trustees of Columbia University CU Grants and Contracts P.O. Box 29789 General Post Office New York, NY 10087-9789
Electronic Transfer of Funds:	<u>Bank, Routing, and Checking Account Information</u>
Type of Organization:	Private, Non-Profit, 501(c)(3)
University Fiscal Officer:	Ms. Patricia Francy Treasurer/Controller
Entity Identification # (Federal Tax):	13-5598093
Entity Identification # (for NIH awards):	13-5598093A7
e-mail Address for Receipt of Electronic Notice of Grant Awards (for NIH awards):	nihhs@cuvmc.ais.columbia.edu
Institutional Profile No.	1833205

(Box 9 on NIH grant face page):	
Congressional District:	15 th
Human Subjects Federal-Wide Assurance #:	FWA00002636
Approval Date:	June 4, 2002
Expiration Date:	December 17, 2005
Laboratory Animals Animal Welfare Assurance #:	A3007-01
Expiration Date:	August 31, 2005
Continuously accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) since:	June 16, 1989
Animal Care Per Diem Rates:	<u>Institute of Comparative Medicine's Rates</u>
Travel Policy:	<u>Columbia University's Travel & Business Expense Policies & Procedures</u>
Federal Travel Per Diem Rates:	
Contiguous U.S.:	
Noncontiguous U.S. and Overseas Non- Foreign:	<u>U.S. General Services Administration Department of Defense</u>
Foreign:	<u>Department of State</u>
Misconduct in Science Assurance Date:	February 7, 2000
Radioisotopes NRC License #:	74-2878-03
Fringe Benefits Rate on Sponsored Projects:	
Government Agencies:	26.0%, effective 1 July 2002
Future Years:	
7/1/03-6/30/04	26.2%
7/1/04-6/30/05	26.4%
7/1/05-6/30/06	26.6%
7/1/06-6/30/07	26.8%
Non-Government Agencies:	26.0%, effective 1 July 2002
Future Years:	
7/1/03-6/30/04	26.2%

7/1/04-6/30/05	30.5%
7/1/05-6/30/06	30.7%
7/1/06-6/30/07	30.9%
Copy of Verification of Tax Exempt Status Letter:	<u>PDF Document (200kb)</u>
Copy of Charitable Organization Exempt Status Letter:	<u>PDF Document (300kb)</u>
Dun & Bradstreet (DUN) #:	621889815
Commercial and Government Entity (CAGE) Code #:	1B053
Federal Interagency Committee on Education (FICE) Institution Code #:	0027078
Standard Industrial Code #:	8821
Cost Accounting Standards Board Disclosure Date:	December 12, 1996
Cognizant Agency:	Mr. Robert Aaronson Director Division of Cost Allocation Department of Health and Human Services 26 Federal Plaza New York, N.Y. 10278
Indirect Costs (IC):	
Established with:	Department of Health and Human Services (DHHS)
Date of IC Agreement:	May 1, 2002
Copy of IC Agreement:	<u>PDF Document (200kb)</u>
Type of IC Agreement:	Predetermined (PRED)
Base of IC Agreement:	Modified Total Direct Cost (MTDC)
IC Rates:	63.5% on campus 28.9% off campus (<50 miles) 26.0% off-campus (>50 miles)

VIII) Clinical Grant Writing¹

Ralph L. Sacco, MD
Columbia University, New York, NY

Clinical Research Funding Opportunities

Familiarize yourself with the NIH Grant Process

NIH Grants: K awards, R01

Websites:

NIH <http://www.nih.gov/>

Center for Scientific Review <http://www.csr.nih.gov/>

Requests For Applications (RFA)

Requests For Proposals (RFP)

Program Announcements (PA)

Speak to Program Staff

Seek advice from NIH personnel

Check Out Other Organizations

AAN Clinical Research Funding Database

The Successful Grant Application

Novel, interesting experiments

Advances knowledge in the area of study

Hypothesis driven

Specific aims well defined

Experimental design well detailed

Preliminary data support hypothesis

Studies are well focused

Expertise is appropriate and documented

Budget is reasonable and justified

Outline of a NIH Grant Proposal

Research Plan: 25 pages

When Preparing An Application

Read Instructions

Never assume that Reviewers "will know what you mean"

Refer to literature thoroughly and thoughtfully

Explicitly state the rationale of proposed investigation

Include well-designed, well labeled tables and figures

Present an organized, lucid write-up

¹ AAN 53rd Annual Meeting, Education Program Syllabus, May 7, 2001

I) Specific Aims (1 page)

- What are the specific objectives of the study?
 - State them clearly and succinctly.
 - Primary and Secondary aims
- What are the hypotheses? Null or alternative

Examples:

- **Primary Aims:** To determine the relationship between ischemic stroke and alcohol use after adjusting for age, gender, socioeconomic status, and other conventional risk factors and define the dose-response relationship with respect to recent exposure in the last year, as well as lifetime exposures.
- **Secondary Aims:** 1. To evaluate separately in each age, gender and race-ethnic subgroup the prevalence, relative risk and attributable risk for alcohol, physical activity, HDL, and homocysteine.
- The aims of this prospective cohort study are to evaluate the following hypotheses: Occasional to mild alcohol use independently reduces the risk of ischemic stroke and the relative protection is similar in the three race-ethnic groups with a J-shaped dose-response curve.

II) Background and Significance (2-3 pages)

- What is the significance of the problem?
- What have others found out about the problem: refer to literature thoroughly and thoughtfully.
- Identify gaps in knowledge that your project will help fill
- What will your study add?

Example:

There are still significant gaps in our knowledge of the epidemiology of stroke in blacks and Hispanics. Incidence and case-control studies have demonstrated that the excess stroke mortality among blacks and Hispanics in the US reflects an increased stroke incidence possibly resulting from differences in socio-economic status and the prevalence and impact of risk factors. Population-based, prospective epidemiologic investigations in ethnically-mixed regions are the next step to confirm and explain these reported differences in stroke incidence, determine the importance of environmental and genetic stroke risk factors, and plan effective stroke prevention programs. Few areas have tri-ethnic populations such as Northern Manhattan which make it an ideal region to study this problem. This study will be an important resource in evaluating the determinants of stroke in our rapidly expanding black and Hispanic populations.

III) Preliminary Studies

- What have you and your colleagues done to prepare for the study?
- Describe any pilot data.
- Include well-designed, carefully labeled tables and figures

- How have you been preparing to carry out the aims of the study?
- What organizational structures are in place to help you succeed?

Example:

Alcohol has been shown to be a risk factor for ischemic stroke, but the dose-response relationship has not been clarified. Our case-control analysis regarding alcohol was just recently completed and presented at the AHA Stroke Meeting in February, 1997. A manuscript is being prepared at this time. Heavy alcohol use of 5 or more drinks/day was clearly an independent risk factor for ischemic stroke. Occasional to light alcohol consumption of up to 2 drinks/day is protective. The J-shaped curve was found in whites, blacks and Hispanics (Figures 2-3 App A). We hope to verify these observations in a cohort study and evaluate for the relationship of alcohol use to other factors such as homocysteine and HDL.

IV) Methods

- How will you test the primary hypothesis?
 - Discuss in detail the experimental designs and procedures
 - State specifically what will be studied and precisely how.
 - Provide an “Overall Plan”
- Identify the patient population
- Define the inclusion-exclusion criteria.

Example: D.2.a. Eligibility Criteria

The eligibility criteria for this prospective cohort study are: (1) white, black or Hispanic resident of at least 3-months of Northern Manhattan defined by zip-codes 10031, 10032, 10033, 10034, & 10040; (2) randomly derived from a household with a telephone; (3) age 55 or older at the time of first in-person assessment; and (4) no baseline history of stroke.

- Recruitment procedures
 - Describe what and how you will collect the data.
- Data collection instruments
 - Plans for standardization of training of personnel across centers
 - Issues of reliability and validity

Example: D.3. Baseline Data Collection

Baseline data collection will be done through in-person interviews, measurements of anthropometric indices and systolic and diastolic blood pressures, neurological examination, cardiac testing, and phlebotomy. Subjects will be evaluated in-person with an interview to enumerate demographics, psychosocial and socioeconomic factors (education, occupational attainment, insurance status), medical history and use of medications, vascular risk factors, family history and other health-related information. All assessments are conducted in English or Spanish depending upon the primary language of the subject. Data is obtained directly from study subjects using the standardized data collection instruments. When the subject is unable to answer questions, a proxy who is knowledgeable about the subject’s history is interviewed (so far, data obtained from a proxy in only 1% of stroke-free subjects).

D.3.c. Alcohol Assessment

Alcohol use is assessed through a structured in-person interview using questions adapted from the NCI Food Frequency questionnaire developed by Block. The questions have been modified by providing a defined frequency response set, making the instrument similar to the alcohol assessment in the food frequency questionnaire of Willett. The questionnaire inquires about a subject's consumption of three different forms of alcohol--wine, beer, and liquor--during the past year, and the defined responses regarding frequency allow nine possibilities ranging from never to greater than six drinks per day. Both the Block and Willett questionnaires have been validated in studies such as the Women's Health Trial Feasibility Study, the Health Professionals Follow-Up Study, and the Nurses' Health Study. Efforts are underway to validate the Block questionnaire with regard to alcohol consumption among multi-ethnic cohorts including non-Hispanic blacks, non-Hispanic whites, and Hispanics in the NIH/NHLBI-funded Insulin Resistance and Atherosclerosis Study.

In our stroke-free sample, test-retest reliability among 37 subjects showed a high correlation (Pearson's $R=0.62$; $p=.0001$). Among 16 stroke cases, we also found that the reliability of proxy respondents was quite good (Pearson's $R=0.81$; $p=.0001$). To further assess the validity of our questionnaire we will prospectively interview a subsample of 30 subjects at baseline, every 3 months for one year to evaluate 1-week alcohol consumption, and at one year to assess alcohol use over the preceding year.

- Follow-up Methods
 - Duration, frequency, and mechanism
 - Ways to insure low loss to follow-up.
 - Define outcomes clearly - use of committees, issues of blinding
- Database methods - collation and storage of the data, back-ups, security, quality assurance, accuracy of the data
- Clear descriptions of how data will be managed.
- Study Timetables
 - Precisely identify when data will be collected.
 - Identify when various aspects of the study will be performed.

Example:

D.6. Timetable

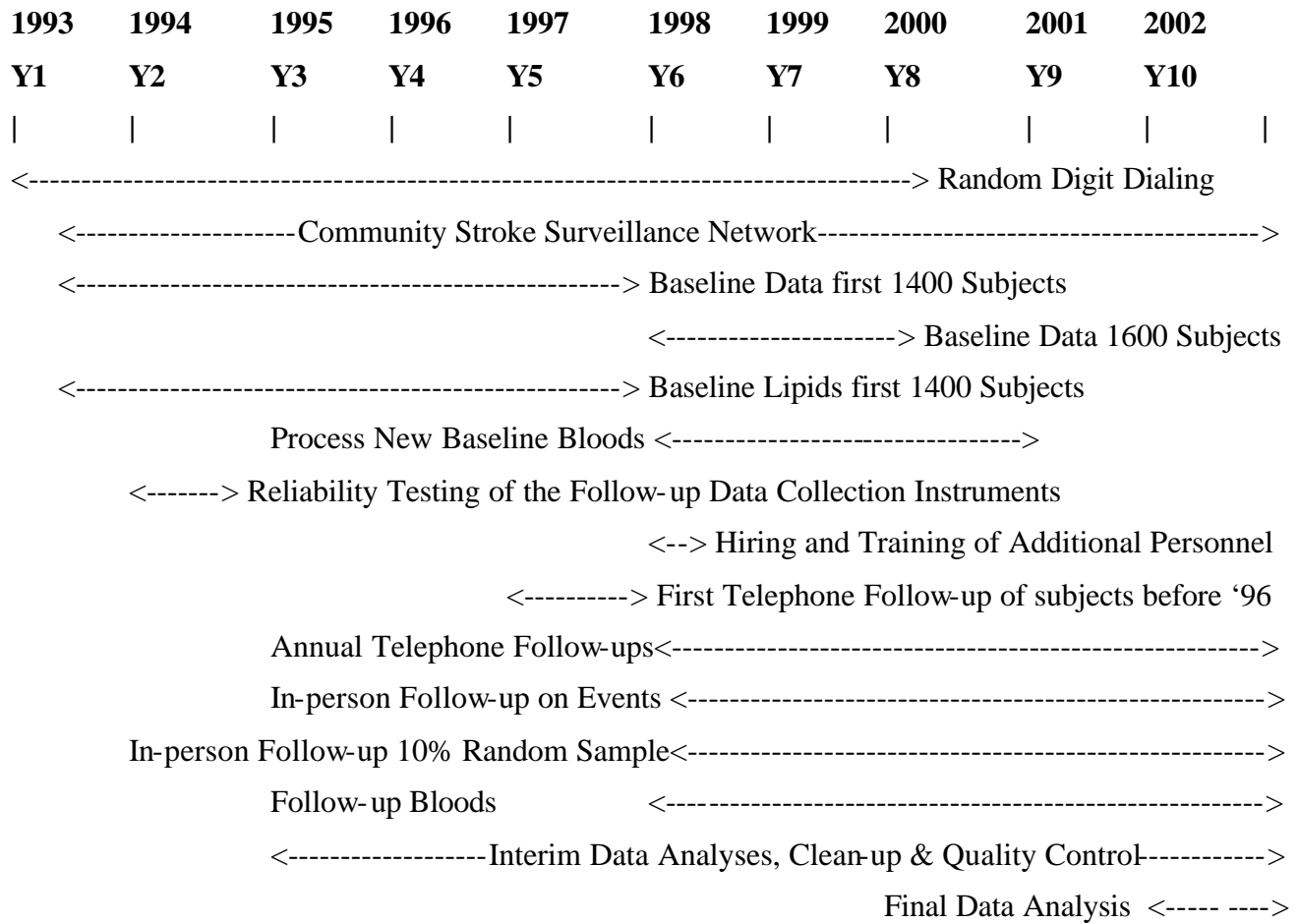
D.6.a. Timing of Data Collection

	Time (years) From Baseline								
<u>Follow-up Data Subgroups</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>
Follow-up (FUF Form)	X	X	X	X	X	X	X	X	X
Functional (FCT & QWB Form)	X	X	X	X	X	X	X	X	X

This follow-up data is collected by telephone interview. All subjects who have affirmative answers to any of the questions on neurological or cardiovascular symptoms or events or have a reduction from the prior Barthel ADL score will be scheduled for an in-person visit. A 10% random sample stratified by race-ethnicity will have annual in-person follow-up visits.

D.6.b. Study Timetable

This proposal covers Years 6-10. Pertinent prior work is shown in Years 1-5 regarding the stroke-free cohort already enrolled in the study.



- Statistical Analyses
 - Clearly state how you will analyze the data to assess each of the primary aims of the study.
 - Choice of the appropriate statistic.
 - Get statistical advice.
 - Evidence that appropriate biostatistical expertise is available and has been consulted.

Example:

We will estimate the rate of ischemic stroke and survivor functions stratified by the baseline exposure. Whether the two survivor functions with and without the exposure of interest are the same will be tested using log rank tests. Cox proportional hazards model will be used to estimate the relative risk of each exposure variable of interest adjusting for other covariates. Exposure variables of interest will be first examined as categorical variables in the Cox model,

then if a linearity is suggested, will be used as continuous covariates. Categorization will be based on our preliminary findings, for example, four categories for alcohol; never, occasional to light (1/month to <2 drinks/day), moderate (3-5 drinks/day), and heavy (5+drinks/day).

- Sample Size and Power calculations
 - Will you have a sufficient sample size to avoid a type 1 and type 2 errors?
 - State the power of the study and justify the number of subjects.
 - Detailed descriptions of the number of patients.
 - Document that the numbers will be available through collaborative efforts with other institutions or hospitals.
 - Describe how patient drop-out will be handled.

Example:D.8.b. Aim 2: Alcohol

We project that among the 3000 subjects over age 55, we will detect a minimum of 3.8% [n=114] total strokes or 2.9% [n=87] ischemic strokes based on a total annual stroke rate of .007. With 3000 subjects followed for a mean of 5.4 years, we calculated the power to detect a relative stroke risk of 2.0 for annual stroke rates ranging from .005 to .009 in the reference group and prevalence rates of the exposure of interest ranging from 25% to 50%. For occasional to mild alcohol use which has a prevalence of 41%, we will have at least 97% power to detect a relative risk of 0.50.

- Include a section on **limitations** of the study at the end of the Methods.
- Identify where you think problems may occur and how you may handle them.
- Think of potential pitfalls and alternative approaches.

V. Human Subjects

Assurance of Compliance form (596) and IRB review certification.

1) Subjects

The projected sample sizes are:

Gender	White, NH	Black, NH	Hispanic	Total
Women	450	630	720	1800
Men	300	420	480	1200
Total	750	1050	1200	3000

2) Sources of Research Material

3) Recruitment Procedures

4) Potential Risks

5) Procedures to Minimize Risks

6) Risks vs. Benefits

Gender and Minority

It is the policy of NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research

projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. For studies using human subjects or identified human materials (e.g. blood, cells, organs, autopsy materials) the investigator must describe and justify the minority and gender composition in the study population and if the distribution does not reflect the distribution in the general population, an explanation must be provided.

Research Involving Children

NIH policy is that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are clear and compelling reasons not to include them. This policy applies to all NIH conducted or supported research involving human subjects, including research that is otherwise "exempt" in accord with Section 401 (b) of 45 CFR 46 Subpart A - Federal Policy for the Protection of Human Subjects. The inclusion of children as subjects in research must be in compliance with all applicable subparts of 45 CFR 46 as well as with other pertinent federal laws and regulations.

Therefore, proposals for research involving human subjects must include a description of plans for including children. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion.

In the research plan, the investigator should create a section titled "Participation of Children." This section should provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. When children are included, the plan must also include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study. Scientific review groups at the NIH will assess each application as being "acceptable" or "unacceptable" in regard to the age-appropriate inclusion or exclusion of children in the research project.

Justifications for Exclusions

It is expected that children will be included in all research involving human subjects unless one or more of the following exclusionary circumstances can be fully justified:

- 1) The research topic to be studied is irrelevant to children.
- 2) There are laws or regulations barring the inclusion of children in the research.
- 3) The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
- 4) A separate, age-specific study in children is warranted and preferable.
- 5) Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). While children usually should not be the initial group to be involved

- in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
- 6) Study designs aimed at collecting additional data on pre-enrolled adult study participants (e.g., longitudinal follow-up studies that did not include data on children).
 - 7) Other special cases justified by the investigator and found acceptable to the review group and the Institute Director.

Literature Citations

Relevant and current
Not exhaustive, and not out-of-date

Budgets

Modular budget process for <\$250,000 per year
Need permission if over \$500,000 per year
Justify the budget
Describe the role of all personnel, professional and non-professional
Justify each section carefully-equipment, travel, supplies.
Prepare a realistic budget.

Appendix

Data collection instruments
Published papers or draft manuscripts
Useful for photographs, oversized documents, and other materials that don't reproduce well

General Tips

- Develop a clear, concise, coherent writing style. Use the active voice whenever possible. It is more direct, less wordy and less confusing than the passive voice. Keep related ideas and information together; put clauses and phrases close to the words they modify. Simplify and shorten overly long and involved sentences and paragraphs. Eliminate redundant and awkward words, phrases, and sentences.
- Proofread very carefully. Reviewers are quite likely to think that one who writes sloppily also thinks and does research sloppily.
- Ask a colleague to critically review your application.
- Administrative matters would be appropriately handled; IRB and minority and gender issues clearly addressed.
- Page limitations-DRG will send back your application if you exceed them.

Addendums

Briefly provide any new data or an update for the reviewers since the application was submitted

Revised Applications

If you're submitting a revised proposal, clearly respond to all criticisms raised in previous review in the introduction section. Be sure to make all changes in the body of the proposal clearly marked.

Quick Guide for the Preparation of Grant Applications

Excerpted from

<http://nccam.nih.gov/nccam/fi/research/guidelines/firsttimers/quick-guide.html#prepare>

Submission and Review of Your Application

Applications should be submitted to the Center for Scientific Review (CSR), at the NIH, on the appropriate application form (usually PHS Form 398), which is available at your institution's Office of Sponsored Research or you may download it from the World Wide Web at

<http://grants.nih.gov/grants/funding/funding.htm>

The CSR assigns your application to an Institute (for example, NHLBI) or Center (for example, NCRR) and to an Initial Review Group (IRG) such as Health Promotion and Disease Prevention.

Note: You may request, in a cover letter, the assignment of your application to a particular Institute and/or IRG. (The CSR usually honors such requests and consider them helpful).

If you have been in contact with program staff in the process of developing your application, mention this by providing the person's name and telephone number. You should also indicate on the face page of the application that it is in response to a particular program announcement or an RFA when this is appropriate. The assignment to an Institute and an IRG is the first official step in the nine-month review process. You can obtain preliminary feedback about four to five months after the submission of your application by contacting program staff. In addition, a summary of critiques of your application will be routinely sent to you as soon as it is available.

The IRGs are the main evaluating groups for your application and form the core of the peer review system. A secondary review is conducted by the respective Institute's Advisory Council. IRGs review applications for scientific merits in terms of: novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigators; the adequacy of the research design; the suitability of the facilities; and the appropriateness of the requested budget to the proposed work. For those applications they judge to be competitive, they assign a priority score ranging from 100 to 500, which is converted into percentile scores based upon the voting pattern of the IRG. (The lower the number, the better the percentile). In addition to assigning a score, the IRGs prepare the written critique. This summary statement consists of a synopsis of the review as well as the verbatim evaluations prepared by each of the reviewers.

Commencing October 1994, the IRGs employed a procedure in which the applications are subjected to a streamlining process. Reviewers are asked to identify applications that they judge noncompetitive and to designate these applications as "non-scored." This means that with limited funds available, applications so designated are not competitive for funding when compared to other applications. While a summary statement is still prepared, it is only a compilation of reviewers' comments without significant modification or editing on the part of NIH staff, and without budget recommendations. There is no further review at the level of Advisory Council. Applicants are free to revise and resubmit their application after taking into account the reviewers' comments.

Only applications that are deemed to be competitive are discussed by the review group and assigned priority scores. These applications will be percentiled against all of the applications assigned to the review group, not just ones actually reviewed. The Institutes' decision to fund or not to fund an application is based primarily on the evaluations of the scientific merit made by the IRGs.

Planning Your Application

Some key points to consider prior to, during, and after your application is prepared:

1. The standard deadlines for new NIH grant applications are February 1, June 1, and October 1; the deadlines for Request for Applications (RFAs) may differ. The review and award process of applications submitted to NIH takes, in general, about nine months.
2. Read the program announcement or RFA in detail. Before you start writing your grant application, read the pertinent instructions (for example, PHS 398) carefully and become thoroughly familiar with all the requirements and certifications necessary. If needed, find someone who can assist you, based on his/her experience, in understanding and completing the requirements. Incomplete applications are returned without review.
3. Establish investigators' own deadlines for the preparation of the grant application, particularly when collaborating investigators are involved. Be aware of institutional deadlines that could delay your application. Allow time for equipment failures, support personnel shortages, etc.
4. Do not hesitate to request technical assistance from the funding agency or your institution. Contact the scientific review administrator who will coordinate the peer review process or the program officer who will manage your award for advice on scientific and technical issues. Seek advice from the NIH grants management specialist on administrative issues.
5. Reread your application. Have someone else read and comment on it. Proofread it. Make sure someone has final editing responsibilities.
6. If available, have senior scientists (for example, successful grantees, objective experts) review your application. Professional colleagues or close associates may not be as critical as the scientific reviewers at NIH.
7. Inquire about funding priorities of funding agencies, and ascertain from the program officer whether your application falls within the scope of set priorities.
8. When submitting a revised application that originally responded to an RFA, keep in mind that the application will need to provide all scientific rationale, significance, potential contribution, etc., because it will go to a different review group than the one that originally reviewed the application. Some aspects of the original RFA may not be acceptable to the new review group.
9. Feel free to consult NIH staff with specific questions.

Preparation of Your Grant Application

Remember that you are writing primarily to an IRG when you submit a grant application. Given this fact, what can you do to improve your chances of a favorable review? While there are no substitutes for good ideas and well-planned studies, IRGs are obviously influenced by how these ideas and plans are presented. Much of the following advice may appear to be self-evident, but it is astounding how many applications run into difficulties because they do not follow these simple principles:

Contact institute program staff. They can help in the proposal phase. They should be your first and primary contact point, with the institute, during the review process and after an award is made. They are most likely to understand your perspective and needs, since they have research experience themselves as well as knowledge and understanding of how the NIH system works.

Follow the directions provided with the grant application kit. The instructions call for a particular organization of the materials, and reviewers are accustomed to finding information in specific places. Avoid antagonizing them by forcing them to hunt through your proposal for some elementary facts. Do not exceed the specified page's limits or type sizes. Otherwise, CSR will return your application without its being reviewed.

Be brief, concise, and clear. Make your points as directly as possible. Use diagrams to help the readers understand complex models, relationships among variables, or design features.

Be organized and logical. Many applications fail because the reviewers cannot follow the thought process of the applicant or because parts of the application do not fit together. For example, an outstanding literature review may not lead logically to the hypotheses and design of the study. Similarly, provide an analysis plan that relates the research questions to specific data and appropriate analytic techniques.

Show how your work goes beyond previous research. What contribution will your study make to the field? State this as clearly as possible.

Be complete. Don't leave out vital information. In part, state what appears to be implicit or obvious, provide an adequate literature review and details of the study design, and sampling procedure and data analysis. Do not assume that all reviewers are experts in your field, especially since they need to be convinced that you are! For instance, if a t-test is "obviously" the appropriate statistic, still indicate that you will use a t-test. In many instances, you may have struggled with a crucial design question and arrived at a satisfactory solution. Don't just present your solution. The reviewers may wonder why you chose a particular route, since they won't have the benefit of your months of thought. Therefore, you should provide a rationale for your decision and discuss rejected alternatives. Similarly, if you are aware of a problem it is wisest to admit that you do not have a solution. Failure to mention this will lead the reviewers to assume that you are unaware of that problem.

Provide background on pilot instruments and data whenever possible. Such information helps to convince the reviewers that you know what you are doing and that it is feasible.

Be careful in the use of appendices. Given the slightly contradictory advice to be concise and complete, it is tempting to rely heavily upon appendices to provide the required details. However, you should be aware that only the two primary reviewers of your application receive both the main body and the appendices. The remaining members of the IRG receive only the

main text. Thus, you should not place essential information in an appendix, since most of the reviewers will not receive it and will be forced to rely solely on the comments of the primary reviewers. A possible compromise is to provide some information, for example, about an attitude scale in the main body, but then provide the full details in the appendix. This gives the secondary reviewers some sense of the scale, and provides the primary reviewer with adequate information. Be sure to follow the instructions regarding the permissible content and length of appendices.

Consider dual assignment of your application. You may request that your application be assigned to more than one Institute as potential funders (for example, NIMH and NCI). While this does not influence the review of your application by an IRG, it does provide you with a second chance for funding at no cost to you. If the primary Institute is unable to fund your approved application, then the other may be able to.

Submit your application to other potential funders such as private foundations. Be sure to inform them of such multiple submissions and of funding offers by another agency.

Be prepared to revise and resubmit. Given the competition for funds, it is usual to submit a revised application. In revising, first contact program staff for their interpretation of the summary statement, and then give careful consideration to the critique. Be sure to address each criticism in your revision, either by making appropriate changes or by indicating that you consider it invalid and why. Don't ignore any criticism or give it cursory attention. You need to show that you learned from the critique or (in a nondefensive manner) that you considered it inappropriate.

Copies of CSR Publications and PHS 398 Application Forms can be obtained from:

Grants Information Office
Center for Scientific Review
National Institutes of Health
6701 Rockledge Avenue, Suite 3032
Bethesda, Maryland 20892-7762

Other Sources of Information:

- How to write a research grant: <http://www.niaid.nih.gov/ncn/pdf/howto.pdf>
- A short guide to preparation of grants
<http://deainfo.nci.nih.gov/EXTRA/EXTDOCS/gntapp.htm>
- Tips for NIH Grant Applicants <http://www.nigms.nih.gov/funding/tips.html>
- A Straightforward Description of What Happens to Your Research Project Grant Application (R01/R21) After it is Received for Peer Review
<http://www.csr.nih.gov/REVIEW/peerrev.htm>

IX) Preparing A Successful Career Development Grant Application²

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Introduction

Clinical research offers neurologists the rewarding opportunity to advance knowledge in their field of clinical expertise. Neurologists beginning academic careers in clinical research, however, face challenges related to (1) training in the tools of clinical research and (2) funding for new investigators. Training in clinical research skills, including study design, statistics, measurement, clinical trials, bioethics, cost-effectiveness analysis, and proposal writing, is not usually taught in medical school, neurology residency, or clinical fellowships. These skills, however, are essential for carrying out rigorous and fundable clinical research. In addition, funding opportunities that provide salary support to obtain clinical research training and start-up resources for pilot data are not widely disseminated. This presentation will discuss strategies for preparing a successful career development grant application for the new clinical investigator. We will emphasize applications to the National Institutes of Health, although this model can also be applied to private foundations and other funding sources.

NIH training and career development programs

A variety of NIH programs exist for new investigators, including the K23 and K02 awards. These NIH programs will be discussed later in the seminar. A fundamental element of these programs is to provide the investigator with protected research time and funding (including tuition) to obtain the training necessary to carry out successful clinical research. The applicant's institution makes a commitment to the scientific development of the candidate and to an appropriate balance of research and clinical responsibilities. Given the purpose of these grants (i.e., training), outlining a detailed plan for research training is an essential piece of a successful application. Such a plan may include:

1. Participating in a comprehensive program in clinical research training. An increasing number of Medical Schools and Schools of Public Health now offer comprehensive programs in the skills needed for clinical research including study design, statistics, measurement, clinical trials, bioethics, cost-effectiveness analysis, and proposal writing (including mock NIH study sections). Several of these grant degrees. Some are open to participants outside the institution. For example, the University of Michigan On Job/On Campus Master Program in Clinical Research Design and Statistical Analysis meets four days a month (Thursday through Sunday) for 20 months and is open to outside participants. A compendium of other such comprehensive programs has been developed by the AAN Clinical Research Subcommittee and is available on the AAN Website (see other resources below)

² AAN 53rd Meeting Education Program Syllabus, May 7, 2001

2. Learning a specific technique that will be used extensively in the proposed research and future research (e.g. PET scanning, quantitative MRI, or hormonal assay). Include the resources available at your institution or elsewhere for learning this technique.
3. Enlisting the mentorship of an established clinical researcher. The NIH Mentored Clinical Scientist Development Award (KO8), the Mentored Patient-oriented Research Career Development Award (K23), and the Mentored Research Scientist Development Award (KO1) specifically requires a mentor with extensive research experience (see other resources below). A mentor provides a valuable resource of feedback in learning specific techniques, project design, preparation of manuscripts, and development of a research program. Do not feel that you need to limit the guidance you receive to one individual, however. Additional consultants may be indicated in the application. Including a statistician as a consultant and having this person review your application before submission is helpful. Getting letters from these consultants outlining their role in the career development award and their commitment to participate will strengthen your application.

The other portion of the NIH training program is the research plan. This plan consists of four sections which are standard across all NIH grants:

1. *Specific Aims*, which outlines the hypotheses and a brief introduction preceding the hypotheses.
2. *Background and Significance*, which discusses why the problem is important.
3. *Preliminary Studies*, which includes work the investigator has already done as support for the proposal
4. *Experimental Design and Methods*, which includes a detailed description of how the work will be carried out and the rationale for the design.

Successful grants, regardless of type or the level of expertise of the investigator, contain research plans that are carefully prepared, have testable hypotheses, and include detailed methodology. In the seminar, we will critique specific parts of the grant, using examples from a variety of neurological topics. Specific pointers applicable to new grant writers include:

1. *Don't attempt too much in the first grant.* Doing an observational or descriptive study is reasonable; save the multicenter randomized clinical trial for the future.
2. *Hypotheses:* Be sure that your hypotheses can be tested to determine if they are correct or incorrect.

Weak hypothesis: Drug B will decrease headache severity.

Better hypothesis: The average severity of headaches per month, as measured by the Kalamazoo pain scale, a validated measure of headache severity, will be higher in patients receiving drug A compared to those receiving drug B.

3. *Methods.* Your methods section will then go on to show how the measurements needed to test these hypotheses will be obtained. For example, how will patients be recruited to ensure a representative sample, how will headache severity be measured in a valid and reliable way, what is the plan for data analysis. The level of attention that the applicant pays to detail is a signal to the reviewers of how meticulous the applicant will be in carrying out the research. Do not assume that the reviewers will guess how you are planning to recruit patients, analyze

the data, etc. State what you are going to do up front. Don't forget to include the difficulties you anticipate encountering (e.g., patient recruitment) and how you intend to (a) pick up on these difficulties early (e.g., monitoring number of patients recruited on a monthly basis) and (b) remedy them (e.g., expand pool for recruitment if necessary)

4. *Link to basic mechanisms.* The grant will be much more appealing to reviewers if the hypotheses can be linked to basic mechanisms (e.g., basic research has demonstrated that drug B increases the pain threshold of rats) because: (1) it demonstrates that the hypothesis has a rational basis; (2) it demonstrates an extension of basic research to the bedside; and (3) it fosters a connection between your research and that of the animal research for your basic science reviewers.

5. *The "sparkle" factor or*

"Imagination is more important than knowledge." -Albert Einstein

"The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them." Sir William Bragg

There is increasing emphasis placed by reviewers on research that is not only well conceptualized, but imaginative, unique, and somewhat high-risk. The challenge to the new investigator is to balance the "sparkle" factor with a solid, feasible research plan.

6. *Preliminary data.* In a training grant, showing that you have carried out a portion of the methodology previously or that you are going to learn this methodology by working with individual X are valid statements to include in the preliminary data section. It is not necessary to have performed half of the experiments proposed. One suggestion is to carry out several portions of the experiment in one patient and demonstrate competence with these portions.
7. *Timetable.* A timetable, possibly in the form of a GANTT chart in which timelines are represented by horizontal bars, is an effective way to impress reviewers with your organizational skills.
8. *Overall look of the grant.* Remember that your reviewer will be probably be reading your grant at 2AM and will be favorably influenced by the readability of your proposal. Be sure to leave plenty white space and employ headers effectively to lead the reviewer through the proposal in the most painless way possible. Have someone with writing experience review the grant for grammar and readability.
9. *Adherence to guidelines.* Read the guidelines carefully, several times.
10. *Presubmission critiques.* Have two senior people in your department or at another institution critique the grant and leave plenty of time to incorporate their suggestions into the final product.

What If You Don't Get a Fundable Score? Answering Critiques.

"I have not failed. I've just found 10,000 ways that won't work." -Thomas Edison.

Many good grants do not get funded the first time around. The key phrase to remember is "the first time around". In fact, some grants that are ultimately funded get "triated" (judged to be in the bottom 50% of applications) the first time and are not even discussed by the study section. If you believe that you have a good idea and that the work you propose is important and will make a significant contribution, you should swallow your pride, read the critique, take nothing personally and re-submit. Fortunately, even "triated" applications have reviewers' comments and therefore you have some idea why your application was not met with more enthusiasm. Many times problems arise because you have not stated things clearly enough or you have made assumptions not obvious to the reviewers. Keep this in mind when you think about how to respond to the reviewers' comments. Also remember that you **must** respond to the criticism with significant changes in your revised proposal or provide a rationale for why the changes should not be made or you will be doomed to failure. It **seriously** annoys reviewers when they review a revised application and criticism was ignored. Also remember that the exercise of responding to criticism of your proposal will serve to improve it (usually substantially) by forcing you to make your hypotheses, aims and experimental design absolutely crystal clear.

Begin by reading the critique, and then reading your proposal with the criticism (and positive comments) in mind. Be sure to ask all of your Co-investigators to do the same. Then make a list of each point the reviewers have made and group similar criticisms together so that they can be addressed together in your reply. Re-read each reviewer's comment and go to the corresponding section of the proposal, re-read the section, try to better understand why the comment was made and what you would have to change or re-state in order to satisfy the criticism. After you have gone through this exercise yourself, go through it with your Co-investigators, and then finally, go through it with one or more senior investigators not involved in your project. It can also be quite helpful to discuss the critique and your proposed responses to it with NIH Staff, e.g. the Executive Secretary of the Study Section that reviewed your proposal or the Project Officer who your grant would be assigned to when funded. The NIH staff will be able to help you most if you contact them after you have already spent the hours it takes to accomplish what is described above and you have very specific questions for them about how to approach addressing several difficult key criticisms. Don't forget to acknowledge the positive comments in your reply, as it will remind the reviewers that your proposal had good features to start with that you have now made even better.

Other sources of funding for new investigators

A variety of sources exist for those starting careers in clinical research. These sources are extremely helpful in providing the investigator with the resources to obtain pilot data for NIH grants. They include

1. Resources within the investigator's institution (internal support). Check with your university's division of research grants and development.
2. Clinical Research Centers will often provide the clinical research resources (e.g., polysomnography rooms and technical support) that is not provided through NIH training grants
3. Foundations associated with specific diseases (e.g., Epilepsy Foundation, Headache Foundation). See the Clinical Research Funding Database (see other resources below) for a

comprehensive list of foundations and other sources of funding⁴. Pharmaceutical companies. They are often approachable for funding for small pilot grants.

Other resources

1. NINDS Websites: <http://www.ninds.nih.gov/>;
<http://www.ninds.nih.gov/scientists/default.htm>; and <http://grants.nih.gov/>
2. AAN compendium of clinical research training programs:
<http://www.aan.com/resources.html>
3. AAN clinical research funding database: <http://www.aan.com/resources.html>
4. Your university's division of research grants and development: information on internal support and databases of external support. One example is SPIN (Sponsored programs Information Network). A database containing over 6,500 separate funding opportunities.
5. Books and articles on writing successful clinical research grants and on choosing an area of investigation for those starting out:
 - a. *Ogden, Thomas E. Research Proposals, A Guide to Success, 2nd ed. Lippincott-Raven, 1995.*
 - b. *Cuca JM, McLoughlin WJ. Why clinical research grant applications fare poorly in review and how to recover. Cancer Invest 1987;5(1):55-58*
 - c. *Kahn, CR. Picking a research question. NEJM 1994; 1530-1533.*

X) Types of NIH Grants

Activity Code	Grant Type	Description
R01	Research Project Grant	A Research Project Grant supports a focused research program conducted by a principal investigator with or without collaborators, postdoctoral trainees, graduate students and/or technicians
R21	Exploratory Developmental Grant	Supports pilot or feasibility studies; novel high risk/high payoff research. Up to two years of support. Non-renewable
P01	Research Program Project Grant	Grant to support a multi-investigator research program with a well-defined research focus or objective. All subprojects must be united in a common theme and be interdependent.
P50	Specialized Center Grant	To support any part of the full range of research and development activities comprising a multidisciplinary attack on a specific disease entity or biomedical problem area.
R13	Conference Grant	Conference grants support recipient sponsored scientific meetings and conferences that may facilitate advancement of NINDS mission objectives.
R03	Small Grants	

Career & Training Awards

	Program	Description	Duration	Stipend*	Research Costs*	% Effort
K01	Mentored Research Scientist Development Award	Assist basic and clinical neuroscientists who have experienced an interruption in their research careers to re-enter active careers in science 5/9/01	4 years	Maximum \$85,000	Maximum \$35,000	50% to research and training
K02	Independent Scientist Award	For support an independent scientist committed to research in need of additional experience 5/23/01	5 years (Years 4 & 5 require R01)	Maximum \$85,000	Maximum \$50,000	75% to research and training
K08	Mentored Clinical Scientist Development Award	Prepare clinically trained persons for careers in basic or clinical neuroscience. Applicants must apply within 3 years of completing clinical training 5/23/01	5 years	Maximum \$85,000	Maximum \$50,000	75% to research and training
K23	Mentored Patient-Oriented Research Career Development Award	Career development of individuals committed to patient-oriented research 5/23/01	5 years	Maximum \$85,000	Maximum \$50,000	75% to research and training
K24	Mid-Career Investigator Award in Patient Oriented Research	Supports clinicians to devote time to patient-oriented research and to act as mentors for beginning clinical investigators 5/23/01	5 years	Maximum \$80,600	Maximum \$25,000	25% -50%
T32	Training Grant	Institutional training grants for those with PhD or MD degree 1/8/01	5 year award 3 year/ trainee	\$28,260-\$44,412	\$3,500 per trainee per year	100%
F32	Postdoctoral Fellowships	Individual fellowships for individuals seeking postdoctoral research training in the basic and clinical neurological sciences 1/8/01	3 years	\$28,260-\$44,412	\$5,000 per trainee per year	100%

* Varies with institute

XI) Non-governmental Funding Sources

Agency	Type	Area	Link
Alzheimer's Association	Junior Faculty Research	Aging	http://www.alz.org/aboutus/overview/research2000.htm
American Federation for Aging Research	Fellowship Junior Investigator Career Development	Aging	http://www.afar.org
American Health Assistance Foundation	Research	Aging	http://www.ahaf.org/alzdis/about/adabout.htm
McKnight Endowment Fund for Neuroscience	Research Junior Investigator	Aging	http://www.mcknight.org/neuroscience/
American Heart Association NY Affiliate	Fellowship Career Development Research	Cardiovascular Disease	http://www.americanheart.org/research/app/nys_grid.html
American Heart Association	Career Development Research	Cardiovascular Disease	http://www.americanheart.org/research/about/nrp_about.html
Doris Duke Charitable Foundation	Junior Faculty	Cardiovascular Disease	http://ddcf.aibs.org/medical/index.asp
American Epilepsy Society	Fellowship	Epilepsy	http://www.aesnet.org
Epilepsy Foundation	Junior Investigator	Epilepsy	http://www.efa.org/research/index.html
Esther A. & Joseph Klingenstein Fund	Fellowship	Epilepsy	http://www.bcm.tmc.edu/pda/announcements/Funding/Klingenstein.html
Rockefeller Brothers Fund	Fellowship Career Development	Epilepsy	http://www.culpeper.org
Tuberous Sclerosis Alliance	Fellowship Junior Faculty Research	Epilepsy	http://www.tsalliance.org/ForMedical/RFP.asp
American Parkinson Disease Association	Fellowship Junior Investigator	Movement Disorders	http://apdaparkinson.com

Agency	Type	Area	Link
Dystonia Medical Research Program	Fellowship Research	Movement Disorders	http://www.dystonia-foundation.org
Hereditary Disease Foundation	Fellowship Research	Movement Disorders	http://www.hdfoundation.org/funding/lieberma.htm
Myoclonus Foundation	Research	Movement Disorders	http://www.myoclonus.com/research.htm
American Academy of Neurology	Fellowship	Neurology	http://www.aan.com/public/csrch2001/
American Philosophical Society	Fellowship	Neurology	http://www.amphilsoc.org/grants
Burroughs Welcome Fund	Fellowship Career Development Research	Neurology	http://www.bwfund.org
Rockefeller Brothers Fund	Fellowship Career Development	Neurology	http://www.culpeper.org
ALS Association	Research	Neuromuscular	http://www.alsa.org
Muscular Dystrophy Association	Fellowship Research	Neuromuscular	http://www.mdausa.org/research/guidelines.html
United Mitochondrial Disease Foundation	Fellowship Junior Faculty Research	Neuromuscular	http://www.umdf.org/
American Brain Tumor Association	Fellowship Junior Investigator	Neurooncology	http://www.abta.org
National Brain Tumor Foundation	Research	Neurooncology	http://www.braintumor.org/
Grass Foundation	Fellowship	Neuroscience	http://www.mbl.edu/labs/grassfdn/
Howard Hughes Medical Institute	Fellowship Junior Investigator	Neuroscience	http://www.hhmi.org/grants/research_resources/
Human Frontier Science Program Organization	Fellowship Junior Investigator	Neuroscience	http://www.hfsp.org

Agency	Type	Area	Link
Life Sciences Research Foundation	Fellowship	Neuroscience	http://lsrf.org/lrfginfo.html
March of Dimes Birth Defect Foundation	Career Development Research	Neuroscience	http://www.modimes.org/Research2/RFPs/
McKnight Endowment Fund for Neuroscience	Research Junior Investigator	Neuroscience	http://www.mcknight.org/neuroscience/
NARSAD	Junior Investigator Research	Neuroscience	http://www.mhsource.com/narsad/research/reindex.html
Pfizer Pharmaceuticals	Fellowship	Neuroscience	http://www.physicianscientist.com

XII) Budgets

In preparing the budget for an application, two factors should be carefully considered: the needs of the project, and the funding limitations imposed by the agency (either explicit or customary). The requested amount should not be so small as to preclude successful completion of the stated goals nor so large that the agency will not seriously consider funding the proposal.

Also keep in mind fringe benefits and indirect costs

NIH forms and budget pages can be found at the following website:

<http://grants1.nih.gov/grants/funding/phs398/phs398.html>

Personnel

Name – start with Principal Investigator and then list all individuals of applicant organization that are involved in the project.

Role on project – identify role, does not have to be official university title and justify and describe specific functions in budget justification section.

Type of appointment – No. of months of appointment; if not full-time, asterisk and provide explanation

Percent of effort on project – percent of time spent on this project

Institutional base salary – includes base salary + A1 salary; prorate for budget period; take into consideration 7/1/ and 10/1 increases for professional and support staff respectively; current NIH cap is \$161,200

Salary requested – usually institutional base salary X percent effort; may request less – explain in budget justification

Fringe benefits – check current rate

Consultants

Whether or not costs are involved, provide the names and organizational affiliations of all consultants, other than those involved in consortium/contractual agreements. Describe the services to be performed under justification. Include the number of days of anticipated consultation, the expected rate of compensation, travel, per diem, and other related costs.

Equipment

Items costing \$2,000 or more with a lifespan of at least two years; list each item separately; justify; may include price quotes.

Supplies

Itemize supplies in separate categories, such as glassware, chemicals, radioisotopes, etc. Categories in amounts less than \$1,000 do not have to be itemized. If animals are to be purchased, state the species and the number to be used.

Travel

Itemize; justify purpose, destination of each trip, and number of individuals traveling

Patient Care Costs

Separate outpatient and inpatient costs; provide names of hospitals and clinics; state whether each has a DHHS research patient care rate agreement; include number of patient days, cost per day, and cost per test or treatment

Discuss patient accrual and relate to budget; discuss other sources of support for patient care; discuss utilization of Irving Center (GCRC)

Patient care refers to items and services (routine and ancillary) ordinarily furnished in the treatment of patients by providers of patient care under the supervision of the physician or other responsible health professional. Such items or services may be diagnostic, therapeutic, rehabilitative, medical, psychiatric, or any other related professional health services. These expenses are for care that would have been incurred even if the research study did not exist.

Other Expenses

Itemize by category – animal maintenance, patient travel, donor fees, publication costs, computer charges, rental and leases, service contracts, publication costs, phone/fax and mail costs specific to project, computer charges, core facilities, GRA tuition and health fees

Consortium/Subcontracts

Separate detailed budget from each organization; include other organization's total cost (direct + indirect) as a direct cost on budget

Indirect Costs (F & A costs)

Federally negotiated rate on modified total direct costs (equipment, patient care costs, subcontracts >\$25K) not included in direct cost base

Training grants and career awards have a lower rate

Voluntary and foundations usually have a lower rate

Budget – future years

Most categories are usually increased 3%-4% per year

Modular Grants

Applies to all competing R01, R03, R15, R21, R41 & R43 and RFA proposals up to \$250,000 requested direct costs in any year

Direct costs requested in module amounts of \$25,000

Applicant will provide personnel and other budget information in narrative format only

Budget justification – Under personnel, list all personnel including their

Names

Percent of effort

Roles on project

Do not provide salary information

Provide a justification for any variation in the number of modules requested

Consortium/Contractual costs – names of participating institutions and whether foreign or domestic; estimate of total costs for each year rounded to nearest \$1,000; percent of effort for all personnel; roles of all personnel on the project.

XIII) Common Mistakes in NIH Applications

(from http://www.ninds.nih.gov/funding/grantwriting_mistakes.htm)

Innovation is not necessary, but the results should have compelling significance.
The five review criteria for most NIH grant applications are:

Significance, approach, innovation, investigator, and environment.

1) Problems with significance:

- a. Not significant nor exciting nor new research
- b. Lack of compelling rationale
- c. Incremental and low impact research

2) Problems with specific aims:

- a. Too ambitious, too much work proposed
- b. Unfocused aims, unclear goals
- c. Limited aims and uncertain future directions

3) Problems with experimental approach:

- a. Too much unnecessary experimental detail
- b. Not enough detail on approaches, especially untested ones
- c. Not enough preliminary data to establish feasibility
- d. Feasibility of each aim not shown
- e. Little or no expertise with approach
- f. Lack of appropriate controls
- g. Not directly testing hypothesis
- h. Correlative or descriptive data
- i. Experiments not directed towards mechanisms
- j. No discussion of alternative models or hypotheses
- k. No discussion of potential pitfalls
- l. No discussion of interpretation of data

4) Problems with investigator:

- a. No demonstration of expertise or publications in approaches
- b. Low productivity, few recent papers
- c. No collaborators recruited or no letters from collaborators

5) Problems with environment:

- a. Little demonstration of institutional support
- b. Little or no start up package or necessary equipment