

How to Be More Competitive in the NIH Peer Review Process for Grants

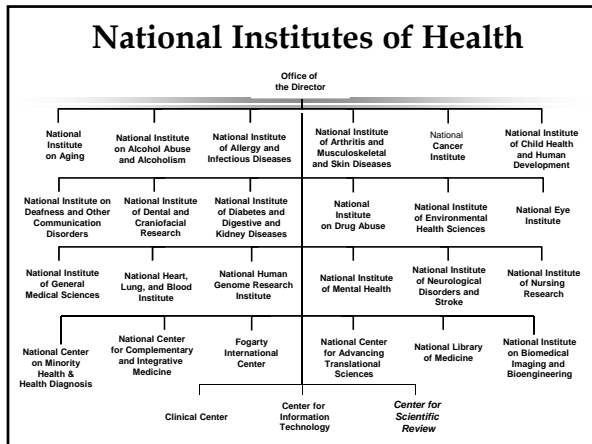
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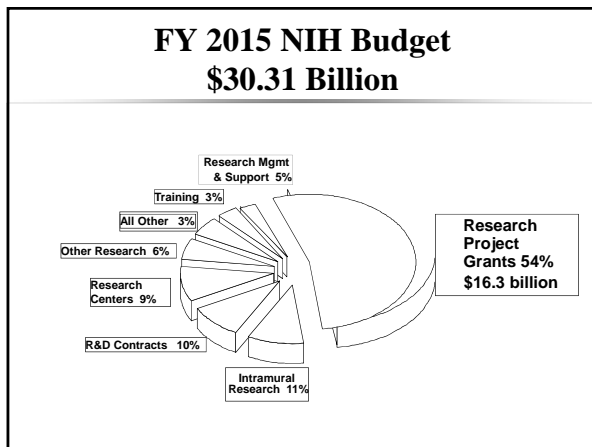
Clinical Research Projects are Hard to Design Well

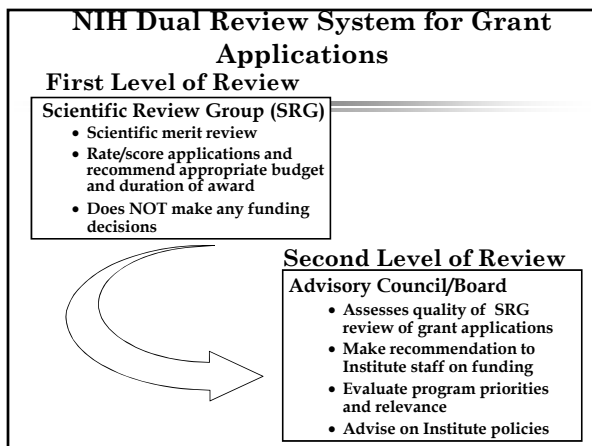
- Overall success rate of *clinical research* projects slightly lower than success rate for *basic* research projects
- Extensive NIH analysis: Difference not due to:
 - Higher budgets for clinical research
 - Review panel assignment
 - Number or % of clinical applications in review meeting
 - Number or % of clinical scientists on review panel
- Clinical projects are harder to design well
- Clinicians may “give up” rather than revise

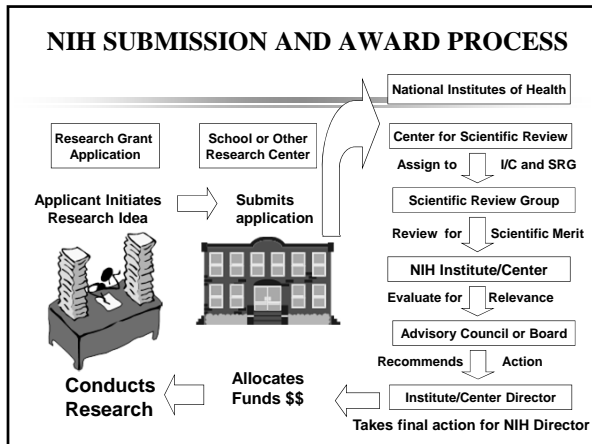
Topics for Today

- Overview of NIH Peer Review Process
- Review criteria for research project grants
- Career Development award mechanisms
- The NIH Loan Repayment Program for Clinical Researchers
- Format for Research Project applications
- Hints for preparing a stronger application









- ### Key NIH Staff Involved in the Extramural Grants Process
- **Scientific Review Officer (SRO) (PhD or MD)**
 - In NIH Center for Scientific Review *and* each NIH Institute/Center
 - Organizes and manages scientific review groups (peer review committees/"study sections")
 - Prepares summary statements documenting the review
 - Liaison between applicants and reviewers
 - **Program Officer/Director (PhD or MD)**
 - In NIH Institutes/Centers
 - Manages a portfolio of awarded grants/contracts
 - Monitors scientific progress of grants/contracts
 - **Grants/Contracts Management Officer**
 - In NIH Institutes/Centers
 - Fiscal stewardship of portfolio of awarded grants/contracts
 - Monitors financial progress of grants/contracts

- ### Most NIH Applications are Submitted Electronically through Grants.gov
- **Grants.gov** – on-line portal to find and apply for most Federal grants
 - **eRA Commons** – the DHHS electronic system for receiving applications and transmitting review and award information to PIs and applicant institutions
 - Institutions must register in both SAM (System for Award Management) and eRA Commons
 - Institutions register in SAM
 - Institutions register institution and their Principal Investigators in eRA Commons

Electronic Submission of Applications through Grants.gov or ASSIST

- Applications **must** be in response to an **open Funding Opportunity Announcement (FOA)** in Grants.gov
 - "Parent FOAs" listed at http://grants.nih.gov/grants/guide/parent_announcements.htm
 - Science- and I/C mission-specific FOAs on various topics
- *NIH Guide for Grants and Contracts* (<http://grants.nih.gov/funding/index.htm>) provides link to correct FOA
- Download specific application package with forms and instructions from the FOA within Grants.gov.
 - **Always download application package "fresh" so you have the latest version of the Grants.gov forms!**

Parent FOAs for Common NIH Investigator-Initiated Applications

FOA Title	Announcement Number	NIH Activity Code
Research Project Grant	PA-16-160	R01
Small Research Grant	PA-16-162	R03
Exploratory/Developmental Research Grant	PA-16-161	R21
Academic Research Enhancement Award	PA-13-313	R15
Small Business Innovative Research Grant	PA-15-269	R43/R44
Small Business Technology Transfer Grant	PA-15-270	R41/R42

Note: Some NIH Institutes/Centers do not accept applications under the R21 and R03 Parent FOAs

Science-Specific NIH Funding Opportunity Announcements

- **Program Announcement (PA)**
 - New or ongoing interest of one or more NIH Institutes/Centers (I/Cs)
 - Addresses a relatively broad field/category of research
 - Usually no set-aside I/C budget
 - Usually submit on regular receipt dates for mechanism
 - Usually regular review criteria for type of applications
- **Request for Applications (RFA)**
 - New or ongoing interest of one or more NIH Institutes/Centers (I/Cs)
 - Addresses a well defined area of research
 - Set-aside budget for RFA applications
 - Submit on special, one time only receipt date
 - Often special eligibility and/or review criteria
 - Often special application format and/or submission instructions

Electronic Submission of Applications through Grants.gov

- SF424 (Research and Related [R&R]) forms
 - Most research grants are now submitted electronically
 - Grants.gov generates Adobe forms for cover page, administrative information, budget
 - PI uploads PDF attachments for biosketches, research strategy & other narrative sections, literature cited, letters of collaboration
- See <http://grants.nih.gov/grants/how-to-apply-application-guide.htm> to access a How to Apply – Application Guide

Electronic Submission of Applications through Grants.gov

- Principal Investigators prepare application
- Authorized institutional official submits application to Grants.gov
- Grants.gov and eRA Commons electronically validate forms and attachments
 - Applications with “errors” are rejected
 - Submit corrected application by the receipt date
- You may view “assembled” application in eRA Commons
 - You will see what the reviewers will see
 - Call eRA Help Desk if there are assembly problems

Multiple Principal Investigators (PIs)

- More than one PI may be designated for projects that require a “team science” approach
- Available for most types of research project grants
 - Must designate “Contact PI” for communications with NIH
 - Multiple PIs do not need to devote equal effort
 - Application must include a section describing the “Leadership Plan”
- Multiple PI option not available for career development (K) or fellowship (F) applications
- See http://grants.nih.gov/grants/multi_pi/index.htm

What Happens In A Study Section Meeting?

- SRO is Designated Federal Official for review meeting
 - Recruits reviewers
 - Provides orientation re: conflict of interest and confidentiality
 - Ensures reviewers follow correct policies, process, review criteria
- Study Section Composition
 - Usually 15 - 25 members, primarily from academia
 - Senior investigators in a broad range of related fields
 - Standing members + Ad hoc reviewers recruited for special expertise
- 60 - 100 applications reviewed at each meeting
 - SRO assigns at least 3 reviewers per application
 - Reviewers get applications ~1 month before meeting
 - Reviewers submit preliminary critiques and scores
 - Meetings last 1 – 2 days

What Happens In A Study Section Meeting?

- Applications discussed in preliminary impact score order
 - Persons with conflicts of interest excused
 - Assigned reviewers give preliminary scores
 - Each assigned reviewer lists strengths and weaknesses re: each review criterion
 - Questions for assigned reviewers, full panel discussion
 - Discussion of human subjects protection; gender, minority, and children inclusion; animal welfare
 - Assigned reviewers recommend final score
 - All panel members (except those in conflict) score privately; must speak up if outside recommended range
 - Budget recommendations
- Bottom half of applications not discussed

“Core” Review Criteria for Research Project Grants

- **Significance:** Does the project address an important problem or a critical barrier to progress in the field? *Is there a strong scientific premise for the project?* If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?
- **Investigator(s):** Are they well suited to the project?
 - If Early Stage or New Investigators, do they have appropriate experience and training?
 - If established, do they have record of accomplishments?
 - If Multiple PIs, is the leadership plan appropriate?

**“Core” Review Criteria for
Research Project Grants**

- **Innovation:** Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

**“Core” Review Criteria for
Research Project Grants**

- **Approach:** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? *Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?*
 - For early stage projects, will the strategy establish feasibility? How will particularly risky aspects be managed?
 - For clinical research, are the plans for protection of human subjects and inclusion of minorities, women, and children appropriate?

**“Core” Review Criteria for
Research Project Grants**

- **Environment:** Will the institutional environment, support, equipment, etc contribute to the probability of success? Will the project benefit from unique features of the environment, subject populations, or collaborations?
- Before the review meeting, each assigned reviewer gives a “subscore” for each of these 5 “core” review criteria: 1 (exceptional) – 9 (poor)**

Overall Impact or Criterion Strength	Score	Descriptor
High	1	Exceptional
	2	Outstanding
	3	Excellent
Medium	4	Very Good
	5	Good
	6	Satisfactory
Low	7	Fair
	8	Marginal
	9	Poor
Other Designations for Final Outcome		
AB	Abstention	
CI	Conflict of Interest	
DF	Deferred	
ND	Not Discussed	
NP	Not Present	
NR	Not Recommended for Further Consideration	

Other Review Criteria for Research Project Grants

- **Additional Review Criteria** – Affect the overall impact score
 - Human Subjects Protection
 - Data and Safety Monitoring Plan required for ALL clinical trials
 - Plans for Inclusion of Women, Minorities and Children in Clinical Research
 - Vertebrate Animal Protection
 - Any RFA-specific criteria, if applicable
 - Resubmission Applications – changes made in response to previous review
 - Renewal Applications – progress in current funding period
 - Biohazards

Other Review Criteria for Research Project Grants

- **Additional Review Considerations** – Do not affect the overall impact score
 - Appropriateness of the Budget
 - Resource sharing plans
 - Foreign institutions
 - Select Agent Research
 - *Authentication of Key Biological Resources*
 - *For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources*

Scientific Review Group Options

- **Impact/Priority Score Assigned**
 - 1 (exceptional) to 9 (poor)
 - Each committee member not in conflict scores in whole numbers
- **Deferred (rare)**
 - Review Committee needs more information to decide on the application
 - SRO will contact applicant to obtain needed info
- **Not Discussed**
 - Application not in top half of all applications
- **Not Recommended for Further Consideration (NRFC)**
 - Lacks significant and substantial merit and/or serious ethical problems re: Human Subjects or Animals

Overall Impact/Priority Score and Percentile Ranking

- Overall impact/priority score
 - Likelihood that project will exert a sustained, powerful influence on the research field(s) involved
 - Emphasis on each core review criterion may vary
 - NOT just average of sub-scores for 5 core criteria
 - Average impact scores from all cmte members X 10
 - Whole numbers: 10 (best) – 90 (worst)
- Percentile = rank of application score relative to all applications reviewed by the Study Section in current and past 2 review cycles
 - Range = 1st (best) – 100th (worst)
 - Rounded to nearest whole number

The Summary Statement Documents the Outcome of the Review

- Prepared by SRO after review is completed
- Contains:
 - Impact/Priority Score & Percentile Ranking (if discussed)
 - Codes for Human Subjects protection, gender, minority, children
 - Resume and Summary of Discussion (if discussed)
 - Criterion sub-scores and essentially unedited critiques from assigned reviewers
 - Budget recommendations and Administrative Notes
 - Roster of reviewers
- Used by Program staff in NIH Institute/Center and Advisory Council/Board to make funding decisions
- Retrieve score, percentile and summary statement through the NIH eRA Commons
- Discuss prospects for award or need to revise with the NIH Program Officer listed on the Summary Statement

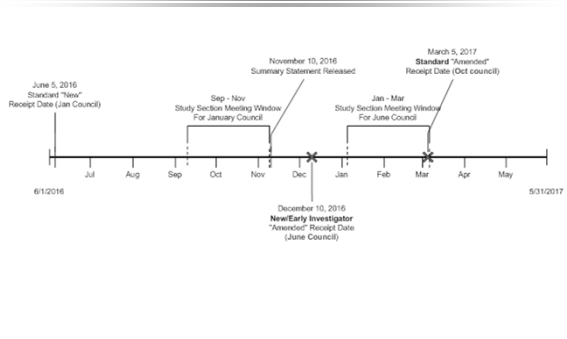
What Determines Which Applications are Awarded?

- **Impact/priority score and/or percentile ranking**
 - Each NIH Institute/Center sets its own “paylines”
 - Paylines vary for different types of grants
 - More liberal payline for New/Early Stage Investigators
- **Programmatic considerations** of the awarding NIH Institute/Center
 - Balance of models, diseases, geographic sites, approaches, etc, in portfolio
- **Availability of funds**
 - Funds for “competing” grant awards limited -- most of budget already committed to continuing grants and programs

Shortened “Next Cycle” Option for R01s from New/Early Stage Investigators

- Special receipt dates (10th of August, December, April) for resubmission R01 applications
 - Allows about a month to revise and resubmit for the very next meeting of the same study section
 - Saves about 4 months in turnaround time
 - Appropriate for projects with easily addressable problems
 - PI must decide if weaknesses cited in Summary Statement are amenable to “quick fix”
- See: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-001.html>

Shortened “Next Cycle” Option for R01s from New/Early Stage Investigators



**Format for
Research Project Application**

- Application sections align with review criteria
- Concise format focuses reviewers on strategy, impact vs details of methods
- Write critically, concisely, specifically
 - Do not repeat information different sections - Provide clear references to information in other sections
 - Emphasize rationale, strategies, analyses, criteria for moving to next aim, alternatives if exp'ts don't work
- R01 format also applies to projects within multi-project applications (P01s, P50)

**Format for
Research Project Application**

- Introduction to Resubmission – **1 page**
 - Address overarching issues/changes vs point-by-point
- Specific Aims – **1 page**
 - State overall objective
 - List aims
 - Describe potential impact on the field
- Research Strategy: R01 = **12 pgs**; R03/R21 = **6 pgs**
 - Significance
 - Innovation
 - Approach

Address "questions" under each respective review criterion

 - Preliminary Studies (for new applications)
 - Progress Report (for renewals and supplements)

**Format for
Research Project Application**

- Biosketch – Customized to each application
 - Personal statement – Experience/qualifications for role
 - Briefly describe up to five of your most significant contributions to science. While all applicants may describe up to five contributions, graduate students and postdoctorates are encouraged to consider highlighting two or three they consider most significant.

Format for Research Project Application

- **Resources**
 - Describe how scientific environment contributes to probability of success
 - If Early Stage Investigator, describe institutional investment in PI's success
 - Resources for classes, training, travel for professional development
 - Collegial support/guidance, institutional career enrichment programs
 - Logistic, administrative and/or salary support

Other Application Components

- Face page/administrative sections
- Budget components/forms
- Human Subjects sections – no page limit
 - Address all required points
 - Address power calculations/statistical issues
 - Provide details about subject populations, eligibility criteria, enrollment/retention strategies
- Animal Welfare – no page limit
 - Address all required points
 - Address power calculations/statistical issues
 - Derivation of specific models, breeding strategies, etc
- Appendix - rules and limitations

Individual Career Development Awards

(See NIH "K" Kiosk at <http://grants.nih.gov/training/careerdevelopmentawards.htm>)

- **K01 - Mentored Research Scientist Development Award (PA-14-044)**
 - Usually for Ph.D.'s, for basic research; not accepted by all NIH Institutes/Centers
- **K02 - Independent Scientist Award (PA-14-045)**
 - Additional time/effort support for new researcher with R01
- **K08 - Mentored Clinical Scientist Development Award (PA-14-046)**
 - For clinicians to get basic/laboratory research training
- **K22 - Career Transition Awards**
 - For postdoctoral fellows transitioning to their first faculty position
 - See specific FOAs from NCI, NIAID, NIDCR, NIEHS, NIMH, NINDS, NHLBI
- **K23 - Mentored Patient-Oriented Research Career Development Award (PA-14-049)**
- **K24 - Mid-Career Award in Patient-Oriented Research (PA-14-047)**
- **K25 - Mentored Quantitative Research Development Award (PA-14-048)**
- **K99/R00 - Pathway to Independence (PI) Award (PA-16-077)**
 - For postdoctoral fellows with no more than 4 yr of training
 - 1 - 2 yr mentored phase followed by 2 yr independent phase

**Format for
Career Development Award Applications**

- Biosketches and Resources as already described for R01 applications
- Introduction to resubmission – 1 page
- Specific Aims – 1 page
- Candidate Information + Research Strategy sections – total of 12 pages
 - Candidate's Background
 - Career Goals and Objectives
 - Career Development/Training Activities
 - Training in Responsible Conduct of Research
 - Research Strategy, including preliminary studies

**Review Criteria for
Individual Career Development Awards**

- Individually scored review criteria
 - Candidate
 - Career development plan
 - Research plan
 - Mentor(s), Consultant(s), Collaborator(s)
 - Environment
- Additional review criteria (Human Subjects, Animals, resubmission, biohazards), as applicable
- Overall Impact Score: Likelihood for the candidate to maintain a strong research program
- Additional review considerations: Training in responsible conduct of research, select agents, resource sharing plans, budget

**The NIH Loan Repayment Program:
Special Opportunity for Clinical Researchers**

- Designed to attract health professionals into research
 - Clinical
 - Pediatric
 - Health disparities
 - Contraception and fertility
- Also a program for researchers from disadvantaged backgrounds
- Repays up to \$35,000 per year (for 2 yrs) of qualified educational debt (student loans) in exchange for 2 – 3 yr commitment to research
- Must be US citizen
- One receipt date per year, special application form
- See <http://www.lrp.nih.gov/>

Tips for Better Grantsmanship

Understand the “Psychology” of the Review Process

- **Reviewers are:**
 - Over committed, over worked and tired
 - Inherently skeptical and critical
 - “Informed strangers”
- **A happy reviewer is likely to be more positive, so make their job easier:**
 - Flow diagrams, charts, figures
 - Well organized, clearly written application
- **Avoid things that reflect poorly on PD/PI:**
 - Not following instructions
 - Putting information in the wrong section, omitting or mislabeling references/figures
 - Dense text, tiny fonts, no “white space” on pages
 - Spelling, grammar, and math errors, etc.

Preparing to Write a Grant Application

- **Critically assess yourself**
 - Do you have the necessary expertise, resources, personnel, and preliminary data to be competitive?
- **Assess the competition**
 - Who are the important contributors to the field? (remember, they might end up being your reviewers)
 - What have they accomplished?
 - Search the literature and the RePORTER NIH database of funded grants in the field (<http://projectreporter.nih.gov/reporter.cfm>)
- **Assess the potential impact of your project**
 - What has already been done/reported/funded in your area? What are the “gaps”?
 - How can you take what’s been done a step farther?

Choosing Your Research Project

- **What makes a research project likely to have a high impact?**
 - Addresses an important problem clearly
 - Potential to lead to seminal new observations or new ways of thinking
 - Lays the foundation for further research in the field
 - Addresses a difficult problem in a way that seems simple in retrospect, making reviewers wonder why they didn't think of the idea themselves
 - All aspects of the project are clearly linked

Preparing the Research Plan

- Limit research plan to 2 - 4 closely related specific aims
- Explicitly state the rationale for the proposed studies and the proposed methods
- Use flow diagrams for overview, and for complex experiments and protocols
- Include easy to follow tables and figures
- Address priorities if patients, reagents or resources will be limited
- Include plans and methods for data analysis and interpretation
- Involve the statistician EARLY in project design
- Excite reviewers about where results will lead

Key Features of Successful Applications

- **Hypothesis**
 - A meaningful hypothesis AND a means of testing it
 - A sound rationale for the hypothesis
- **Preliminary Data**
 - Documents feasibility of the proposed project
 - Shows training for research proposed & ability to interpret results
 - Include alternative interpretations and address limitations of methods
- **Well Organized Research Plan**
 - Aims focused - related to each other and the hypothesis
 - Rationale for methods proposed, with alternatives addressed
 - Research flow and priorities clearly indicated
 - Sufficient experimental detail to show you understand methods
 - Emphasize MECHANISM - avoid "descriptive data gathering"

Key Features of Successful Applications, con't

- **Biosketches**
 - Address your qualifications to carry out the work proposed
 - Don't "pad" with lots of "in preparation" manuscripts
 - Add a senior collaborator, if needed, to provide expertise you lack
- **Literature Cited/Bibliography**
 - Be thorough, but critical, in citing previous work in the field
- **Description (Project Summary in SF 424 applications)**
 - Most read part of the application
 - Basis for referral to study section and funding Institute/Center
 - Write it last, after the Research Plan is finished
 - State problem, specific aims, types of methods to be used
- **Letters of Collaboration**
 - Should be strong and definitively state what will be provided

Most Common Reasons for "Not Discussed" or Not Recommended for Further Consideration

- Preliminary data do not support the hypothesis
- Aims don't address hypothesis
- Diffuse/unfocused research plan
- Descriptive or superficial research plan
- Rationale for choosing proposed methods not clear
- Experimental design/flow not clear
- Flaws in experimental approaches – especially inadequate controls
- Models not relevant to human situation
- Inadequate statistical power
- Unrealistically large amount of work proposed
- Project is confirmatory/doesn't address data in literature
- Lack of experience in essential methods
- Serious risks to human subjects or animals

Make Sure Your Application is Complete and Correct as Submitted

- **START EARLY** – Registering in SAM and eRA Commons AND planning the science
- Read instructions thoroughly and follow them carefully
 - Especially important for electronic applications
 - Avoid validation errors in Grants.gov and eRA Commons
- Allow time for frank feedback on aims, research strategy from senior colleagues with review experience
- Correction/supplemental materials allowed **only** for unforeseen administrative issues
 - Loss of investigator, news of article accepted for publication
 - New data, correction of omissions or errors in text, figures, new letters of collaboration not permitted
 - See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-13-030.html>

NIH Program and Review Staff Can Help

- **Know the NIH program officer(s) in your field**
 - Check programs in several NIH Institutes and Centers
 - Information about upcoming initiatives, opportunities, "gap" areas
 - Information about potential collaborators, NIH resources
 - Explain NIH policies, procedures, award mechanisms, eligibility requirements
 - Advice in revising unfundable applications
- **Know the Peer Review System and your SRO**
 - Review criteria and receipt/review schedules
 - Explain NIH policies, procedures, award mechanisms, eligibility requirements
 - Problems with referral or review
- Use the NIH website to get latest forms and information about peer review policies and procedures

Selected Web Sites of Interest

- **National Institutes of Health** (<http://www.nih.gov>)
 - NIH Office of Extramural Research homepage, with links to the NIH Guide, grants policy information, and resources for new investigators: <http://grants1.nih.gov/grants/oer.htm>
 - NIH Electronic receipt <http://grants.nih.gov/grants/how-to-apply-application-guide.htm>
 - Enhancing peer review <http://enhancing-peer-review.nih.gov/index.html>
 - Links to homepages for each NIH Institute and Center <http://www.nih.gov/institutes-nih/list-nih-institutes-centers-offices>

Selected Web Sites of Interest

- **NIH Center for Scientific Review** (<http://www.csr.nih.gov>)
 - Links to Resources for Applicants, standing Study Section rosters, policy information, review procedures and review criteria, video of mock study section, and advice for investigators submitting clinical research applications
- **Grants.gov** (<http://www.grants.gov>)
