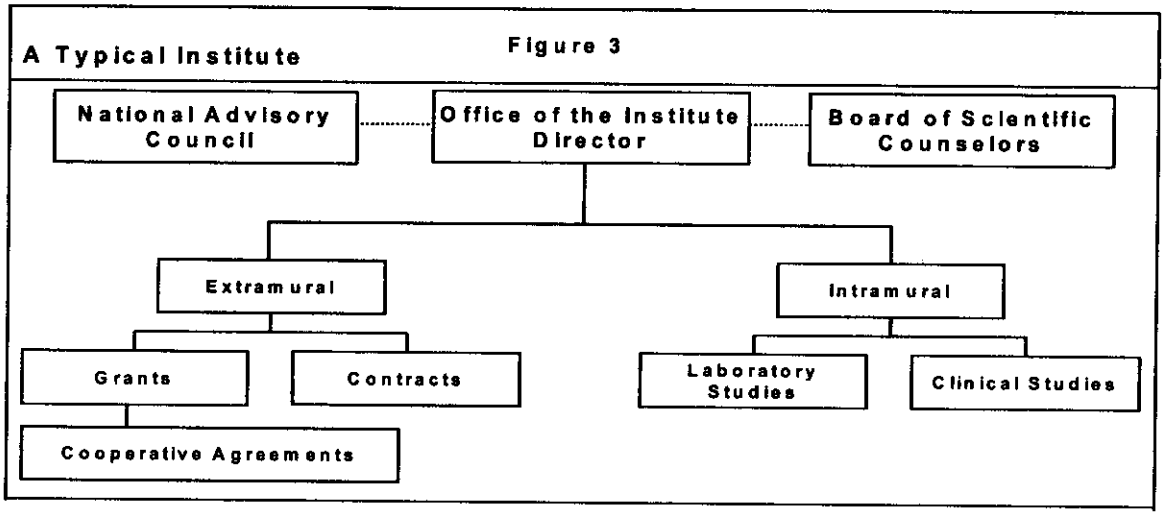
A Typical Institute

Even though there are specific internal variations among the NIH research Institutes and Centers, all of which are hereafter called "Institutes," a typical organizational pattern exists. Usually, both laboratory and clinical research are conducted directly by an Institute in its own laboratories (intramural program) and are supported in other research organizations through an extramural program of grants and contracts (Figure 3). An Institute's extramural program is organized into specific scientific areas, each of which may provide research funding through grants, contracts, and cooperative agreements.



Extramural Research Support

The diverse mechanisms for extramural research and development support are divided into three main categories: grants, contracts, and cooperative agreements. Grants for health-related research and research training projects or activities make up the largest category of funding provided by the NIH. In general, the investigator who applies for a grant, through an eligible institution, is responsible for developing the ideas, concepts, methods, and approach for a project. In contrast, the NIH awarding Institute is responsible for establishing the plans, parameters, and detailed requirements for projects that would be supported by contracts. Contract proposals are usually solicited through requests for proposals (RFPs), while most grant applications are not solicited. In certain circumstances, however, grant applications are invited to address areas of special interest to an awarding Institute, in which case requests for applications (RFAs) or program announcements (PAs) are issued. RFAs, and PAs are published in the *NIH Guide for Grants and Contracts*, which is accessed electronically. Other distinctions between contracts and grants involve variations in the review procedures and such technical issues as the reimbursement of costs, the timing of the application or proposal process, the requirements and mechanisms for award and administration, the extent of the involvement of the funding Institute, and the delivery of the end product.

Cooperative agreements are similar to grants in that they are awarded by NIH to assist and support research and related activities. They differ, however, in that while grants require minimal or no scientific involvement of the NIH awarding Institute during performance of project activities, cooperative agreements involve a substantial Institute programmatic (scientific, technical) role. This role may involve cooperation and/or coordination to assist the awardee

in carrying out the project, or review and approval of certain processes/phases in scientific management of the project. Policies and procedures for application, review, and administration of cooperative agreements are similar to those for grants. An important difference, however, is that the awarding Institute issues a specific RFA describing the program, functions, or activities that it proposes to support by a cooperative agreement, and the nature of the proposed Institute staff involvement.

Grant applications are classified according to type, such as new, competing continuation (renewal), and supplemental applications, and according to grant mechanism, such as regular research projects, program projects, centers, conferences, and fellowships. The classification of a grant application is indicated by an identification numbering system that appears in the upper right-hand corner of the first page of the application form (e.g., Form PHS 398). Each part of the identification number has a distinct meaning. For example, 1R01CA12789-01 means the application is a new(1) research project grant (R01) application assigned to the National Cancer Institute (CA) with a sequential serial number (12789) requesting a first year of support (01).

3. The Peer Review System

Because of the magnitude, diversity, and complexity of its research mission, and its pursuit of excellence, the NIH draws for assistance on the national pool of scientists actively engaged in research. These scientists assist the NIH by advising on the selection of the most meritorious and the most promising grant applications for awards.

Dual Review of Grant Applications

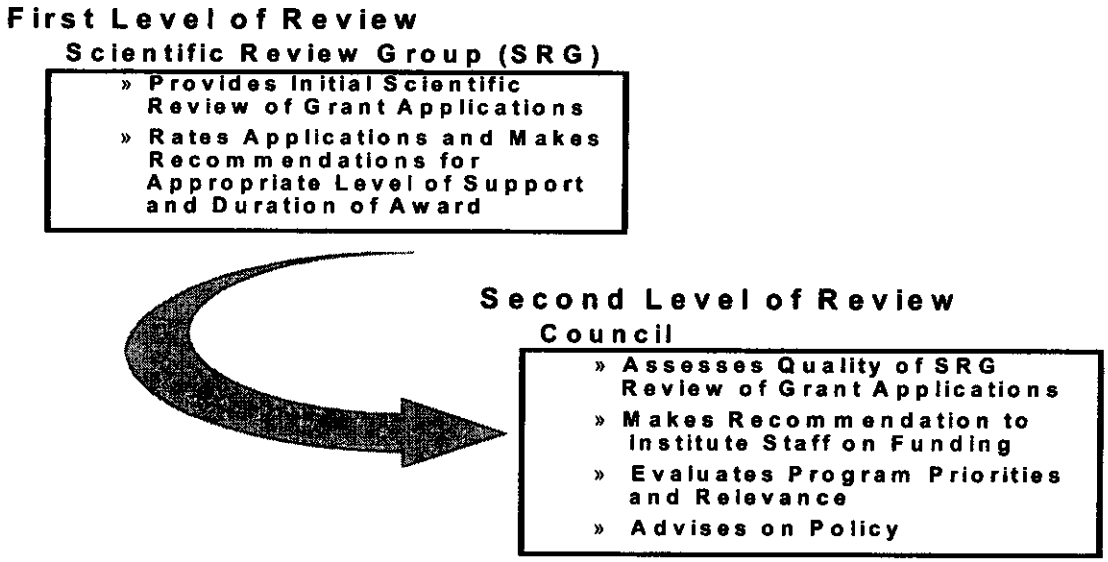
The peer review system for grant applications used by the NIH is based on two sequential levels of review, referred to as the "dual review system" (Figure 4).

The first level involves panels of experts established according to scientific disciplines or current research areas for the primary purpose of evaluating the scientific and technical merit of grant applications. These panels are referred to as scientific review groups (SRGs) within this publication. SRGs are commonly called study sections in the CSR and review committees in the funding Institutes. A cluster of SRGs chartered as a single entity and responsible for the review of grant applications in scientifically related areas is called an initial review group (IRG). IRGs share common intellectual and human resources.

The second level of review is performed by a National Advisory Board or Council, hereafter referred to as a "Council," composed of both scientific and public representatives who are noted for their expertise, interest, or activity in matters related to the mission of the specific Institute for which they serve. Council recommendations are based not only on considerations of scientific merit, as judged by the SRGs, but also on the relevance of the proposed study to an Institute's programs and priorities.

Figure 4

Dual Review System for Grant Applications



The dual review system, which separates the scientific assessment of proposed projects from policy decisions about scientific areas to be supported and the level of resources to be allocated, permits a more comprehensive evaluation than would result from a single level of review. The dual system of review provides NIH officials with the best available advice about scientific as well as societal values and needs.

How Members of Scientific Review Groups are Selected

The primary requirement for serving on an SRG is demonstrated competence and achievement as an independent investigator in a scientific or clinical discipline or a biomedical or biobehavioral research specialty. Assessment of such competence is based on the quality of research accomplished, publications in refereed professional journals, and other significant scientific or clinical activities, achievements, and honors. Usually, a doctoral degree or its equivalent is required. Service also requires mature judgement, balanced perspective, objectivity, ability to work effectively in a group context, commitment to work assignments, and personal integrity to assure the confidentiality of applications and discussions and the avoidance of real or potential conflicts of interest. NIH also considers such factors as geographic distribution, institutional representation, and adequate representation of ethnic minority and female scientists in the selection of SRG members.

The NIH invites suggestions for membership on its SRGs and Councils. The Scientific Review Administrators (SRAs), who are NIH health scientist administrators in charge of SRGs, nominate candidates based on the SRAs' knowledge of the scientific field and recommendations and suggestions of NIH staff, SRG members, and others, such as leaders of various scientific societies and journals. The Director, NIH, makes final appointments to SRGs and advisory committees. The Secretary of DHHS makes appointments to Councils, except for the National Cancer Advisory Board and the President's Cancer Panel, whose members are appointed by the President of the United States. Appointments are usually made for four years and staggered, so that about a fourth of the membership of a group is new each year.

Responsibilities of NIH Staff

As shown in Figure 5, the review, program, and grants and contracts management staff of the NIH have important but separate responsibilities in the review, award, and management processes for grants and contracts.

Figure 5

Responsibilities of NIH Staff in the Review, Award, and Management of Grants and Contracts

Review Staff

- Nominate SRG members
- Select temporary members and site visitors
- Provide orientation for SRG members
- Explain and interpret NIH review policies and procedures
- Assign review responsibilities
- Manage project site visits
- Manage SRG meetings
- Prepare summary statements
- Attend Council meetings to provide requested information in support of committee recommendations
- Communicate with program staff on review matters
- Discuss review questions with applicants prior to the SRG meeting

Program Staff

- Develop program initiatives
- Provide guidance and assistance to applicants
- Attend SRG meetings as program resource person(s)
- Interpret program policy and guidelines for reviewers upon request
- Provide scored SRG summary statements to applicants
- Present SRG recommendations to Council
- Discuss review questions with applicants after the SRG meeting
- Make the award recommendations
- Participate in identifying prospective SRG and Council nominees
- Evaluate programs
- Communicate with review staff on program matters
- Participate with grants management staff in budget negotiations
- Monitor research progress during the award period

Grants and Contracts Management Staff

- Provide business guidance to applicants and reviewers as necessary
- Participate with program staff in budget negotiations prior to and following awards
- Attend SRG meetings as resource person(s)
- Maintain official grant and contract files
- Assist in developing program policy
- Provide fiscal management of grants and contracts
- Monitor for grant-specific and institutional compliance with policies and regulations

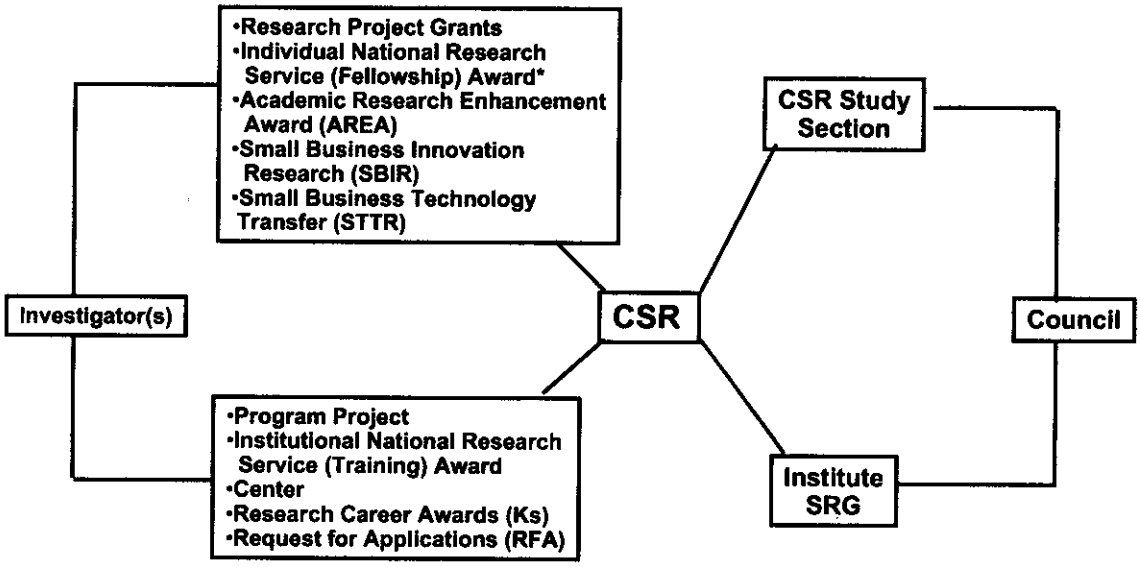
6

4. Review Process: Grant Applications

The review cycle for a grant application begins when an investigator submits an application to the NIH, generally through an organization that qualifies for NIH grants-in-aid, and concludes when the applicant organization and the principal investigator are notified about the recommendation of the Council (Figure 6). Within the NIH, the review cycle involves the interaction of the CSR and the appropriate awarding Institutes. Organizationally, the CSR is accountable to the Director, NIH and is separate from the funding Institutes. The CSR has no responsibility for either the decisions about funding or the management of grant programs.

Figure 6

Initiation and Review of a Grant Application



* Does not require council review

Assignment of Applications for Review and Possible Institute Funding

Grant applications submitted to the NIH are received centrally in the CSR. In the CSR Division of Receipt and Referral, Referral Officers, most of whom are SRAs in the CSR, determine the relevance of each application to the overall mission of the NIH. They assign acceptable applications to an appropriate review group, within CSR or an Institute, and to an appropriate Institute for possible funding. Assignment to a review group is based on the nature of the application and its conformity to the review responsibilities and scientific expertise of the membership of the review group. The principal investigator is encouraged to provide suggestions as to appropriate review groups and/or scientific expertise needed to evaluate the application. If specialized expertise is required to review an application, additional temporary members may be invited by the SRA to serve as reviewers. If the research objectives of an application or group of

applications cannot be reviewed appropriately by an existing review group, a special emphasis panel (SEP) is constituted for this review. Assignment to a funding Institute is based on the Institute's legislatively mandated program responsibilities. If the subject matter of an application is pertinent to the program responsibilities of two or more Institutes, a dual or multiple assignment may be made.

Initial Review by Peers

Depending generally upon the grant mechanism, the first level of review (scientific merit) is by a review group located either within CSR or an Institute. In the CSR, the study sections review most applications for research project and small business grants and individual postdoctoral fellowships. The review groups in the Institutes review center grant applications, most applications for program projects and other special programs, and most applications received in response to RFAs. (See Figure 6.)

Well in advance of the review group meeting, the SRA sends each member copies of the applications and supporting materials to be reviewed at the meeting. Applications with which a reviewer is considered to have a conflict of interest are omitted from individual mailings. For all applications sent, a certification of lack of conflict of interest is required of each reviewer.

Each member is expected to read and become familiar with the applications. The SRA also assigns each application to two or more review group members for detailed written reviews. (These designated reviewers present their written evaluations at the SRG meeting.) Additionally, readers or discussants are designated for each application. They are to be especially conversant about those applications, but are not routinely expected to prepare written reviews.

If additional information from the applicant is needed, reviewers should ask the SRA, well in advance of the meeting, to obtain the required materials. **Reviewers must not contact an applicant directly.** The official representative of the granting agency, in this case the SRA, must handle all communications with applicants.

For some applications, an SRA or a reviewer may feel that opinions should be obtained from specially qualified experts who are not members of the review group. The SRA will seek mail opinions from such experts. Reviewers requests to the SRA should be made as promptly as possible so that outside opinions will be received in time for the SRG meeting. Another option is to invite temporary members to the meeting to assist in the review of certain applications or to have them participate by telephone conference.

Reviewers' Preliminary Written Comments (R01)

Reviewers' preliminary written comments on assigned applications should be sent to the SRAs office as early as possible, so that the SRA can read all reviews and be aware of any major difficulties or differences of opinion. Moreover, if questions have been raised, the SRA can often obtain answers before the meeting. The reviewers written comments and the subsequent discussions during the review meeting are the basis for the final recommendation of the SRG and for the summary statement prepared by the SRA. The summary statement, which is the official document describing the deliberation of the SRG, is transmitted to the appropriate NIH Council and to the applicant principal investigator. Consequently, reviewers must provide specific substantiation of their recommendations. Also, the reviewers comments should be suitable in format, content, and phrasing so that applicants and NIH program staff clearly understand the reviewers' evaluations. Unexplained abbreviations and laboratory jargon should be avoided.

The following guidelines are the standard format for preliminary written reviews of R01 research project grant applications, which starting in 1998, incorporated the new review criteria described below under Critique. Detailed instructions will be provided by each SRA.

Please use the following guidelines when preparing written comments on research grant applications assigned to you for review. The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In your written review, you should comment on the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. NOTE: Your written reviews should not bear personal identifiers because unaltered comments will be sent to the investigator.

DESCRIPTION: Use the abstract on page 2 of the application unless inappropriate. Do not make evaluative statements in this section.

CRITIQUE: Include as little descriptive information in this section as possible. Please address in five individual sections each criterion listed below. In addition: for competing continuation (renewal) applications, include an evaluation of progress over the past project period; for amended applications, address progress, changes, and responses to the critiques in the summary statement from the previous review, indicating whether the application is improved, the same as, or worse than the previous submission. These comments on progress and response to the previous review should be provided in a separate paragraph and/or under the appropriate criteria.

1) Significance

Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

2) Approach

Are the conceptual framework, design (including composition of study population), methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

3) Innovation

Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
4) Investigator

Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)? PLEASE DO NOT INCLUDE descriptive biographical information unless important to the evaluation of merit.

5) Environment

Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support? PLEASE DO NOT INCLUDE description of available facilities or equipment unless important to the evaluation of merit.

OVERALL EVALUATION: In one paragraph, briefly summarize the most important points of the Critique, addressing the strengths and weaknesses of the application in terms of the five review criteria. Recommend a score reflecting the overall impact of the project on the field, weighting the review criteria, as you feel appropriate for each application. An application does not need to be strong in all categories to be judged likely to have a major scientific impact and, thus, deserve a high merit rating. For example, an investigator may propose to carry out important work that by its nature is not innovative, but is essential to move a field forward.

BUDGET: Evaluate the direct costs only. Do not focus on detail. For all years, determine whether all items of the budget are appropriate and justified. Provide a rationale for each suggested modification in amount or duration of support. For supplemental applications, comment on the requested budget in relation to the parent grant.

OTHER CONSIDERATIONS:

REVIEW OF NEW INVESTIGATOR R01S. Under a new NIH policy, new investigators are encouraged to submit traditional research project grant (R01) applications, which will be identified as being from new investigators. At the same time, First Independent Research Support and Transition (FIRST, R29) award applications are no longer accepted (effective June 1998.) The NIH is revising its application forms to allow new investigators to indicate their status on the face page of the application and thus ensure that reviewers can readily identify applications submitted by new investigators. In the interim, NIH staff will identify applications from new investigators.

When reviewing these applications, reviewers should keep in mind the experience of and the resources available to the new investigator. The five new review criteria must be evaluated in a manner appropriate to the expectations for and problems likely to be faced by a new investigator. Specifically, when considering:

approach: more emphasis should be placed on demonstrating that the techniques/ approaches are feasible than on preliminary results

investigator: more emphasis should be placed on their training and their research potential than on their track record and number of publications - emphasis should be placed on their independent status

environment: there should be some evidence of institutional commitment in terms of space and time to perform the research.

OVERLAP. Reviewers should identify any apparent scientific or budgetary overlap with active or pending support, including any non-NIH support. Potential overlap should **not** affect the merit review of an application, but it will be identified in the summary statement as an administrative note for subsequent staff action.

FOREIGN. If the applicant organization is foreign, reviewers should comment on any special talents, resources, populations, or environmental conditions that are not readily available in the United States or that augment existing United States resources, indicating whether similar research is being done domestically and whether there is a need for such additional research. These comments are important, but they should **not** influence the overall score. This consideration does not apply to applications from U.S. organizations for projects containing a significant foreign component.

RESEARCH INVOLVING HUMAN SUBJECTS. Safeguarding the rights and welfare of human subjects involved in research activities supported by DHHS is primarily the

responsibility of the institution that receives or is accountable to DHHS for the funds awarded for support of the activity. However, NIH also relies on its SRGs and Councils to evaluate all applications and proposals involving human subjects for compliance with human subject regulations (Code of Federal Regulations, title 45 part 46).

"Human subject' means a living individual about whom an investigator (whether professional or student) conducting research obtains 1) data through intervention or interaction with the individual or 2) identifiable private information. 'Intervention' includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. 'Interaction' includes communication or interpersonal contact between investigator and subject. 'Private information' includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). 'Private information' must be individually identifiable, so that the identity of the subject may readily be ascertained by the investigator or associated with the information."

"Research' means a systematic investigation designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for the purpose of this policy. 'Minimal risk' means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during performance of routine physical or psychological examinations or tests."

The DHHS will fund research covered by the regulations only if the applicant institution has filed an appropriate assurance with the NIH Office for Protection from Research Risks (OPRR), and has certified that the research has been approved by an institutional review board (IRB) and is subject to continuing review by the IRB. The IRB Approval Date must be one year or less before the receipt date for which the application is submitted. When the proposed research involves only minimal risks and meets certain other conditions, the IRB may waive the requirement for obtaining informed consent. When the research is exempt from regulations, as provided under 45 CFR 46.101(b), adherence to ethical standards and pertinent laws is still required.

SRG members are expected to evaluate the use of human subjects in their reviews. If the information is missing, the application should not be reviewed.

If Exemptions Are Claimed, express any comments or concerns about the appropriateness of the exemption(s) claimed.

If No Exemptions Are Claimed, express any comments or concerns about the appropriateness of the principal investigator's responses to the following six required points requested in the application kit, especially whether the risks to subjects are reasonable in relation to the anticipated benefits to the subjects and in relation to the importance of the knowledge that may reasonably be expected to result from the research.

Principal investigators must:

1. Provide a detailed description of the proposed involvement of human subjects in the work previously outlined in the Research Design and Methods section. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, prisoners, institutionalized individuals, or others who are likely to be vulnerable.

2. Identify the sources of research material obtained from individually identifiable **living** human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

3. Describe plans for the recruitment of subjects and the consent procedures to be followed. Include the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. State if the IRB has authorized a modification or waiver of the elements of consent or the requirement for documentation of consent. The informed consent form, which must have IRB approval, should be submitted to the PHS only if requested.

4. Describe potential risks -- physical, psychological, social, legal, or other -- and assess their likelihood and seriousness. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.

5. Describe the procedures for protecting against or minimizing potential risks, including risk to confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects.

6. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

If a test article (investigational new drug, device, or biologic) is involved, name the test article and state whether the 30-day interval between submission of applicant certification to the Food and Drug Administration and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the Food and Drug Administration.

If a reviewer notes a potential problem regarding the protection of human subjects, at the meeting the SRA will determine if there is an SRG consensus on the matter. The SRG review is expected to reflect the collective standards of the professions represented within its membership. Based on the evaluations of its members, the SRG may:

- favorably recommend the activity without restrictions;

- favorably recommend the activity, but record comments or expressions of concern to be communicated to the institution and the principal investigator;

- recommend limitations on the work proposed, the imposition of restrictions, or the elimination of objectionable procedures involving human subjects;

- recommend the application receive no further consideration if the research risks are sufficiently serious and protection against the risks so inadequate as to make the entire application unacceptable; or

- recommend deferral for resolution of SRG concerns for human subjects protection.

Comments or concerns expressed by SRG members about the adequacy of the protections afforded human subjects used in the project will be included in a Special Note on the summary statement. No award may be made unless all Concerns raised have been resolved to the satisfaction of the NIH (generally at assigned awarding IC level) and the applicant institution has given the OPRR an acceptable assurance of compliance with the Regulations.

The materials listed in **Appendix A** may be useful guides in evaluating applications involving human subjects.

Inclusion of Both Genders and Minorities as Research Subjects. NIH policy requires that applicants who propose research that involves human subjects and/or human tissues include minorities and both genders in study populations, so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study. Applicants must describe and justify the gender and racial/ethnic composition of the proposed study population in terms of the scientific objectives of the study.

Reviewers are to evaluate whether the representation of minority groups and both genders is appropriate, and if not whether the justification provided by the investigator is adequate. If representation is limited or absent, **AND** the scientific justification for the selected study population is inadequate, reviewers are to consider this a scientific weakness and deficiency in the study design and reflect this in the written review statements and in the assigned priority score. The review group's findings and recommendations on this issue will be included in a special section at the end of the "Critique" under the subheading "Gender and Minority Subjects."

Participation of Children in Research. 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 scientific or ethical 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 Sections 101(b) and 401(b) of 45 CFR 46 - 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. All initial applications (type 1) for research involving human subjects submitted to NIH after the October 1, 1998, receipt date 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 include 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. SRGs 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, in addition to evaluating the plans for conducting the research in accord with these provisions.

VERTEBRATE ANIMALS. Although the recipient institution and investigator bear the major responsibility for the proper care and use of animals, NIH relies on its staff, SRGs, and Councils to review research activities for compliance with the PHS policy for the care and use of vertebrate animals. The care and use of vertebrate animals in funded projects must conform to applicable law and PHS policy. A verification of an institutional animal care and use committee (IACUC) review and an institutional assurance are required for applications involving vertebrate animals. IACUC verifications are valid for up to three years. The general intent of the law and policy can be summarized as two broad rules.

- The project should be worthwhile and justified on the basis of anticipated results for the good of society and the contribution to

knowledge, and the work should be planned and performed by qualified scientists.

 Animals should not be confined, restrained, transported, cared for, and used in experimental procedures in a manner to inflict any unnecessary discomfort, pain, or injury.

Reference materials listed in **Appendix A** are important aids to the review of projects involving the use of animals.

Reviewers should express any comments or concerns about the appropriateness of the responses to the following five required points requested in the application kit, especially whether the procedures will be limited to those that are unavoidable in the conduct of scientifically sound research.

Principal investigators must:

1. Provide a detailed description of the proposed use of the animals in the work previously outlined in the Research Design and Methods section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.

2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and their numbers.

3. Provide information on the veterinary care of the animals involved.

4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.

5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If not, present a justification for not following the recommendations.

Comments or concerns expressed by SRG members about animals used in the project will be included in a Special Note on the summary statement. When applications involve especially suitable animal models or particularly effective protocols that conserve animal resources, it should be noted in the Critique section of the summary statement. No award may be made unless all Concerns raised by the SRG have been resolved to the satisfaction of the NIH (generally at assigned awarding IC level), and the applicant institution has given the OPRR an acceptable assurance of compliance with PHS policy.

Reviewers should addressed any questions on the above human subjects and animal welfare policies to the SRA. In developing a response, the SRA may consult OPRR, which is responsible for the administration and interpretation of DHHS policy and regulations for the protection of human subjects and the care and use of animals in research.

HAZARDOUS RESEARCH MATERIALS AND METHODS. The investigator and the applicant institution are responsible for protecting the environment and research personnel from hazardous conditions. As with research involving human subjects, reviewers are expected to apply the collective standards of the professions represented within the SRG in identifying potential hazards, for example, inappropriate handling of biohazardous materials, such as oncogenic viruses, recombinant DNA, chemical carcinogens, infectious agents, and radioactive or explosive material.

If special hazards are identified, concerns about the adequacy of safety procedures will be included in a Special Note, "Biohazard," after the "Critique."

No award will be made until all concerns about hazardous conditions have been resolved to the satisfaction of the NIH.

MISCONDUCT. Scientific misconduct is defined by the PHS as fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest errors, honest differences in interpretation, or judgements of data. It also does not include unintentional failure to comply with federal requirements affecting specific aspects of the conduct of research, e.g., the protection of human subjects and the welfare of laboratory animals.

Allegations of scientific misconduct are very serious, and confidentiality must be strictly observed. If reviewers identify areas of the application that might indicate the possibility of scientific misconduct before the SRG meeting, they should contact the SRA promptly. If possible misconduct is raised during the SRG meeting, the SRA will determine whether the information is compromising the scientific merit review. If the review is compromised, the application should be deferred.

OTHER RECOMMENDATIONS:

DEFERRAL: If an SRG cannot make a recommendation without additional information, deferral may be appropriate. The information may be obtained by telephone, by a project site visit, in exceptional instances, or by the submission of additional written material by the applicant. Deferred applications are not presented to Councils and are usually reviewed again at the next SRG meeting.

NOT RECOMMENDED FOR FURTHER CONSIDERATION: A small number of applications are given the designation "not recommended for further consideration." These include: (1) applications not favorably recommended for certain programs that are not streamlined, such as fellowships and AREAs; (2) some R01 applications not favorably recommended that, for various reasons, are not streamlined; (3) applications involving gravely hazardous or unethical procedures; (4) instances when no funds can be recommended, such as with supplements deemed to be unnecessary; and (5) cases in which the SRG determines that the named principal investigator will not be responsible for the scientific and technical direction of the project. Generally, no priority rating is given, and the applications are usually not presented to Councils.

Meetings of Scientific Review Groups

Within CSR, SRGs normally meet three times a year usually for two days each time, depending upon the number and types of grant applications to be reviewed. An SRG responsible for the review of research project grant applications may be assigned for review as many as 75 to 100 applications at each meeting. Each member may therefore be asked to prepare detailed written critiques for as many as 8 to 10 applications. In addition, each member will be assigned as a discussant (reader) on a group of applications. Written comments from discussants are optional, but may be requested by the SRA.

The SRA, who is the Designated Federal Official in charge of the meeting, and the chairperson, who is one of the members, conduct SRG meetings. The meeting cannot proceed in the absence of the SRA.
During the review portion of the meeting, the chairperson calls on the assigned reviewers and discussants to present their written critiques or verbal comments.

After these presentations, the Chairperson moderates any discussion. Since all members will have received and are expected to have examined all appropriate applications before the meeting, they should be prepared to contribute to the discussions and to score each application on the basis of their own assessment of its merit. Members whose assessment of an application is distinctly different from that of most members must voice and explain their views. Reviewers are encouraged not to abstain from assigning a score. However, if a reviewer is unable to assess the merit of an application without additional information, as evidenced by his or her prior discussion or recommendation for deferral, that reviewer may abstain from scoring the application.

Streamlined Review Procedures

SRGs in CSR use a streamlined review process as part of their peer review procedures for R01, SBIR, and STTR applications. Only those applications judged in the approximate upper half are discussed at the SRG meeting.

To carry out this process most effectively, the upper and lower half of the applications are tentatively identified prior to the SRG meeting. "Upper half" simply means the approximate upper half, in quality, of applications assigned to the review group. More precisely, these are the applications which reviewers believe represent qualitatively the upper half of research customarily reviewed, round to round, in their SRG. The specific steps in the streamlined review process are as follows:

1. By a predetermined date prior to the SRG meeting, assigned reviewers or discussants are asked to identify for the SRA those of their assigned applications that do **not** fall within the upper half.

2. A few days prior to the SRG meeting, all members receive a list from the SRA of those applications proposed by at least two assigned reviewers/discussants to be excluded from the upper half.

3. At the beginning of the SRG meeting, the list of applications nominated for inclusion in the lower half is read aloud for final concurrence by the entire review group. Nonconcurrence by only one member is sufficient to bring an application to full discussion at the meeting. Occasionally, it may also happen that review members will unanimously agree, either at the outset of the meeting or later during discussion of applications, to designate additional applications as not requiring full discussion and scoring.

For applications not in the upper half, reviewers' critiques, essentially unaltered, are incorporated into the summary statement and provided to the principal investigator, along with an introductory paragraph briefly describing the review process. Applications not scored during streamlined review are normally not reviewed by Council. However these applications are considered favorably recommended unless the summary statement explicitly states otherwise and in rare circumstances may be recommended for Council consideration by program staff.

4. For those applications that are considered to be in the upper half and therefore scored, reviewers are expected to modify their critiques when their assessments of merit change as a result of the discussion. Otherwise, the reviewers' critiques will be included in the summary statement, essentially unaltered by the SRA.

Additionally, for scored applications, the SRA will write a "Resume and Summary of Discussion" section. This section conveys the highlights (i.e., major strengths and weakness identified) of the discussion at the review meeting and explains how the committee arrived at the final rating.

Priority Scores

For streamlined review, the full range of priority scores from 100 to 500 is not used for the applications in the upper half. When scoring an application, members should assign a score of approximately 300 for an application of average quality, and distribute scores for applications in the upper half accordingly. However, if significantly more than 50 percent of the applications are designated in the upper half, scores beyond 300 should be assigned. In addition, reviewers are free to vote their conscience. That is, if a reviewer maintains that an application is not in the upper half, despite a discussion and general consensus of other reviewers, the reviewer should still provide whatever priority rating believed appropriate.

In rating applications, reviewers should:

- base their opinions strictly on thoughtful and objective considerations of the review criteria, not on emotional or Institute budgetary considerations;
- judge the merit of each proposal independently of other proposals and according to the "state-of-the-science" in the research area; and
- vote according to their own judgement and evaluation of the application.

After the meeting, the individual reviewers' ratings for each scored application are averaged and multiplied by 100 to provide a three-digit rating called the priority score. Priority scores are included in summary statements, which are forwarded to the NIH Institutes for Council review and to the applicant principal investigators.

In addition to the priority score, percentile ranks are displayed on the summary statements of R01 applications reviewed by CSR. Percentiles are calculated against a reference base of research grant applications reviewed by a chartered or qualified review group at three consecutive meetings. The percentile represents the relative position or rank of each priority score (along a 100.0 percentile band) among the scores assigned by a particular SRG. Applications not recommended for further consideration and unscored applications are included with the scored applications in the calculation of percentile ranks. Thus with streamlined review, there is no mathematical advantage to the SRG that scores more applications in the "upper half."

The percentile ranks and priority scores guide and usually influence the Councils and Institutes in deciding which applications to fund. Although Councils may not change these scores, they may recommend -- usually on the basis of high or

low "program relevance" -- whether an application should be funded and in what order.

Summary Statements

Immediately after the SRG meeting, the SRA prepares a summary statement for each application, which becomes the official document describing the deliberations of the review group. The summary statements for all applications, except unscored streamlined reviewed applications, are a combination of the reviewers written comments and the SRAs summary of the members discussion during the SRG meeting. The summary statements for unscored streamlined applications, which contain only the reviewers written comments, and applications Not Recommended for Further Consideration are mailed directly to the principal investigator by CSR and are generally not presented to Council.

Summary statements for scored applications include the recommendations of the SRG, generally a recommended budget, and notations of any special points. Aspects of an application other than scientific or technical merit, which the SRA or SRG considers important enough to be brought to the attention of the Institute or Council, are prepared as notes in the summary statement and are referred to as Administrative Notes.

Summary statements have numerous and important uses.

- Council members use summary statements as the main source of information about applications and as the primary basis for their recommendations.

- Institute staff use summary statements as a basis for discussions with Councils and applicants, and as guides in the future management of any resulting grants.

- After SRG meetings, Institute staff send each principal investigator a copy of the summary statement with the priority score and the percentile rank, if any, displayed. The summary statement is therefore important to investigators in reassessing, adjusting, or revising their research projects.

- Summary statements, whenever appropriate, can provide background information to the reviewers which can be useful when reviewing a revised, supplemental, or competing continuation application submitted in the future.

Initial Review of Applications for Major Types of Grants Other Than R01s

The previous section covered the initial review of individual R01s research project grant applications. Specific considerations for some of the other major grant mechanisms reviewed in CSR are described in this section.

Interactive Research Project Grant (IRPG) Applications

Objective

The Interactive Research Project Grant (IRPG) program encourages the coordinated submission of related research project grants (R01) from investigators who wish to collaborate on research, but do not require extensive shared physical resources. These applications must be scientifically interrelated in some manner, and must describe the objectives and scientific importance of the interchange of, e.g., ideas, data, or materials, among the collaborating investigators.

Initial Review

Each application in an IRPG group is referred (assigned) independently usually to a CSR study section.

Review Criteria

Each application is reviewed independently. The interactions/collaborations within the IRPG Group are evaluated separately from the scientific merit of each application. The reviewers comment on whether the proposed collaborations and interactions with the other components of the IRPG and the proposed shared resources described in the application are effective, adding significantly to the scope, importance, or originality of the research, and the methodology being employed. Such comments are especially useful to the NIH program staff.

Program Project Grant (PO1) Applications

Objective

The objective of the program project grant is to support a broadly based, multi-disciplinary research program that has a well-defined major goal or basic theme. The individual component projects must have scientific merit on their own as well as being complementary or contributing to the central theme of the PO1.

Initial Review

While applications for program project grants are usually reviewed by Institute SRGs, some are reviewed in CSR.

Review Criteria

The initial review for scientific and technical merit emphasizes two major aspects of the program project grant application: each component project and core unit, and the program as an integrated research effort focused on a central theme.

Review of Research Projects. Each research component is individually reviewed and scored. Each research component must meet the same standards required in the review of regular (individual R01) research grants. The guidelines for the review of the individual research components reflect the new NIH review criteria and basis for assigning a priority score. In addition, each non-research core component is evaluated (but not scored) for its quality, utility to the program, and the extent to which it benefits two or more of the research components. Following review of the individual research and core components, the program project grant is reviewed and scored as a whole.

Review of the Program as an Integrated Effort. The review criteria are:

- the overall scientific strengths and weaknesses of the application, including the significance of the overall scientific question(s) being addressed, and the scientific gain (or loss) accrued by this combination of individual research components into a program project;

- the scientific and administrative coherence among the research components, including any administrative mechanisms proposed to promote coordinated scientific planning and interaction among the participants;

- the interactions and collaborations among the participating investigators;

- the program director's scientific and administrative experience and ability with respect to the leadership and administration of the proposed program;

- the mechanisms proposed to evaluate the progress of the individual components and of the entire program and to allocate and manage resources, including the use of internal and external advisory groups;

- the scientific and intellectual environment and adequacy of the physical resources (noting any special resources, animal models, and clinical facilities that would affect the conduct of this application).

Site Visits. The review of an application for a program project grant may include a site visit because of the complexity and multidisciplinary characteristics of this type of grant.

Academic Research Enhancement Award (R15) Applications

Objective

The objective of the Academic Research Enhancement Award (AREA) is to stimulate research in educational institutions which provide the baccalaureate training for a significant number of our Nation's research scientists but which historically have not been major participants in NIH programs. The goals of the AREA program are to strengthen the research environment at less research-intensive schools, to expose students at such schools to research, and to support meritorious research. The AREA program enables qualified scientists at AREA-eligible schools to receive support for small-scale, new or ongoing health-related research projects (including pilot research projects and feasibility studies; development, testing, and refinements of research techniques; secondary analysis of available data sets; and similar discrete research projects that demonstrate research capability.)

Initial Review:

The initial merit review of AREA applications is performed in CSR.

Review Criteria

The Guide for Assigned Reviewers' Preliminary Comments on R15 applications is available on the CSR Home Page at http://www.csr.nih.gov/guidelines/area.htm.

Small Business Innovation Research (SBIR) Program (R43) (R44) Applications

Objective

The objective of the SBIR program is to promote technological innovation within the American small business community and thereby create jobs, augment industrial productivity, increase competition, and spur economic growth.

Phase I (R43): The objective of this phase is to establish the technical merit and feasibility of proposed R&D efforts that may ultimately lead to commercial products or services, and to determine the quality of performance of the small business awardee organization prior to providing further Federal support in Phase II.

Phase II (R44): The objective of this phase is to continue the R&D efforts initiated in Phase I which are likely to result in commercial products or services. Funding is based on the results of Phase I and the scientific and technical merit of the Phase II application. Only Phase I awardees are eligible to apply for Phase II funding. Phase II applications may be submitted before or after the Phase I budget period has expired.

Award Period and Dollar Levels: Normally the award period for Phase I is for six months and the statutory guideline is $100,000 and, normally, Phase II is for two years and the statutory guideline is $750,000. However, these award levels are guidelines and not ceilings. Applicants may propose longer periods of time and greater amounts of funds necessary for completion of the research project.

Initial Review

The initial review of SBIR applications is generally done in CSR.

Review Criteria Phase I

Since Phase I is to be a technical feasibility study, reviewers should not expect the application to provide data establishing feasibility of the project. In considering the scientific and technical merit of each application, the following

criteria are used:

1. soundness and technical merit of the proposed approach;

2. qualifications of the proposed principal investigator, supporting staff, and consultants;

3. scientific, technical, or technological innovation of the proposed research;

4. potential of the proposed research for commercial application or societal importance;

5. appropriateness of the budget request;

6. adequacy and suitability of the facilities and research environment; and

7. where applicable, adequacy of assurances detailing the proposed means for a) safeguarding human or animal subjects and/or b) protecting against or minimizing any adverse effect on the environment. If human subjects are involved, the plans to include minorities and both genders and children (for calendar year 1999 and later receipt dates) in study populations should be assessed.

The authenticity and structure of the small business and the relationship of the key personnel to the small business and to other institutions, etc., are administrative matters. Comments are appropriate for Administrative Notes, but these factors should not affect the scientific and technical merit evaluation.

Review Criteria Phase II

A Phase II grant application will be reviewed based on the following criteria:

1. degree to which progress toward the Phase I objectives were met and feasibility demonstrated;

2. scientific and technical merit of the proposed approach for achieving the Phase II objectives;

3. qualifications of the proposed principal investigator, supporting staff, and consultants;

4. technological innovation or originality of the proposed research;

5. potential of the proposed research for commercial application or societal importance;

6. reasonableness of the budget requested for the work proposed;

7. adequacy and suitability of the facilities and research environment; and

8. where applicable, adequacy of assurances detailing the proposed means for a) safeguarding human or animal subjects and/or b) protecting against or minimizing any adverse effect on the environment. If human subjects are involved, the plans to include minorities and both genders and children (for calendar year 1999 and later receipt dates) in study populations should be assessed.

The recommended action and the priority score will be based on an assessment of the results of the Phase I effort (as reflected in the final report) and the technical merit of the proposed Phase II research. Expectations of Phase I results should take into consideration the brevity of the Phase I grant period (six months).

The authenticity and structure of the small business and the relationship of the

key personnel to the small business and to other institutions are administrative matters. Comments are appropriate for Administrative Notes, but these factors should not affect the scientific and technical merit evaluation.

Small Business Technology Transfer (STTR) Program (R41) (R42) Applications

Objective

The objective of the STTR program is to facilitate cooperative R&D -- with potential for commercialization -- between small business concerns and U.S. research institutions.

Phase I (R41): The objective of this phase is to determine the scientific, technical, and commercial merit and feasibility of the proposed cooperative effort and the quality of performance of the small business concern, prior to providing further Federal support in Phase II.

Phase II (R42): The objective of this phase is to continue the research or R&D efforts initiated in Phase I. Funding shall be based on the results of Phase I and the scientific and technical merit and commercial potential of the Phase II application. Only Phase I awardees are eligible to apply for Phase II funding. Phase II applications may be submitted before or after the Phase I budget period has expired.

Award Period and Dollar Levels: Normally the award period for Phase I is for one year and the statutory guideline is $100,000 and, normally, Phase II is for two years and the statutory guideline is $500,000. However, these award levels are guidelines and not ceilings. Applicants may propose longer periods of time and greater amounts of funds necessary for completion of the research project.

Initial Review

The initial review of STTR applications is generally performed in CSR.

Review Criteria

The review criteria for STTR applications are the same as for SBIR applications.

SBIR/STTR Fast-Track Applications

Fast-Track, the concurrent submission and review of both a Phase I and Phase II application, applies to both SBIRs and STTRs. The initiative is designed to expedite the funding of Phase II grants for scientifically meritorious applications for projects that have a high potential for commercialization. The Phase I application must specify clear, measurable goals (milestones) that should be achieved prior to initiating Phase II. Failure to provide clear, measurable goals may be sufficient reason for the SRG to exclude the Phase II application from Fast-Track review. The SRG will evaluate the goals and may suggest other milestones that should be achieved prior to Phase II funding. The Phase II application must be accompanied by a commitment(s) for funds and/or resources for commercialization of the product(s) or service(s) resulting from the SBIR or STTR grant, and a concise Product Development Plan. The Phase I and Phase II applications will receive a single rating.