



DETAILED GUIDELINES FOR THE NIH PROPOSAL

(NOTE: While these guidelines are specific to the NIH proposal, the principles stated here are also applicable for proposals to other major research funders)

This document describes the basic sections of an investigator-initiated R01 NIH research grant application. Note that if you submit a proposal responding to a different grant mechanism or in response to a specific RFA, you are likely to have additional or different requirements.

Identifying a Funding Opportunity Announcement (FOA)

All applications must be submitted in response to a Funding Opportunity Announcement (FOA). To browse through current FOAs, go to <http://grants.nih.gov/grants/oer.htm>. NIH has Parent FOAs for use by applicants who wish to submit unsolicited investigator initiated R01 applications and other common grant mechanisms. In addition, NIH publishes FOAs for specific Request for Applications (RFA) and Program Announcements (PA) that identify special research opportunities. If you are submitting to a specific RFA or PA, read the announcement in detail to be sure your application is appropriate for the announcement. Deadlines for common grant mechanisms are as follows:

New R01s	February 5, June 5, October 5
Renewals and Resubmissions of R01s	March 5, July 5, November 5
New R21s (Exploratory Development Awards) and R03s (Small Research Grant Program)	February 16, June 16, October 16
Renewals and Resubmission of R21s, R33s and R03s	March 16, July 16, November 16
New K Awards (Research Career Development)	February 12, June 12, October 12
Renewal and Resubmission of K Awards	March 12, July 12, November 12
R15s (Academic Research Enhancement Award)	February 25, June 25, October 25
F Awards (Fellowships)	April 8, August 8, December 8

The deadlines for applications in response to special RFAs and Program Announcements with special receipt (PAR), may differ. Always check the FOA for the receipt date. In addition, **it is MMC’s policy to submit NIH proposals at least two days prior to the due date, to ensure there is time to correct any problems with electronic submission.**

This guide provides information for how to develop each section of the application. It is important that you also look at and adhere to the timeline for NIH applications developed by MMCRI. You should contact the MMCRI’s grant specialist, Michele Locker, roughly five-six weeks before the deadline, and you should also arrange for a mentor and/or peer reviewers to give you feedback on your proposal during the conceptualizing phase and later during the writing process. MMCRI has mentoring resources to help Investigators through this process.

Title

Title should be short and descriptive of the proposed research. Maximum space limit is 81 characters, including spaces.

Abstract

The abstract should be a self-contained description of the project. It should contain information about the significance, broad objectives, hypotheses, specific aims, and methods to be employed. There should be a statement of how the project relates to the mission of the Institute or Center. The abstract should use lay language as much as possible. Assume that all reviewers, not just those assigned to your application, will read

the abstract. Do not include proprietary or sensitive information, as the abstract will become publicly available if the grant is funded. Do not include graphs or images in the abstract. The maximum length is 30 lines of text. All abstracts for funded applications are available through the NIH Reporter. To see examples of successful abstracts, search on terms associated with your research area at <http://projectreporter.nih.gov/reporter.cfm>.

- Avoid describing past accomplishments and the use of the first person.
- Write the abstract last so that it reflects the entire application.

You may wish to consider the following questions when writing your abstract. Did you state the overall objective of the proposed research? Did you succinctly state the specific aims? Did you briefly describe the methods? Did you indicate the long-term goal of the research? Does your abstract provide a snapshot of the whole proposal?

Relevance Narrative

Using no more than two or three sentences, describe the relevance of this research to **public** health. In this section, be succinct and use plain language that can be understood by a general, lay audience.

Key Personnel/Biosketches

Mandatory review criteria include an assessment of key personnel. You should choose key personnel whose training and experience match the science proposed in the application. Senior/Key Personnel are defined as all individuals who contribute in a substantive, meaningful way to the scientific development or execution of the project, whether or not salaries are requested. Consultants should be included if they meet this definition. You should not include technicians or junior investigators unless they are providing specific expertise or skills needed to complete the proposed research. If you are awarded the grant, any changes in key personnel must be approved by the NIH program officer assigned to your grant. Your application should indicate to reviewers that the key personnel on the application are very well suited to conduct the research. This is reflected in their training and publication record. You don't need to name each person working on the project as key personnel. If collaborators from other institutions are part of key personnel, you will need to include letters of commitment in your application that clearly spell out their roles and commitment to the project. For consultants, letters should include rate/charge for consulting services.

Each Key Personnel must submit an NIH Biosketch form which requires a personal statement describing relevant experience and qualifications that makes this person well suited for the role to be played in the project. It also includes a section on publications, which can include up to 15 manuscripts in press or published articles. The citations should include PMC numbers. (See Bibliography section below for an example of appropriate citation format.) You may wish to select recent publications and those most relevant to the application. The Grant Specialist will provide you with the proper biosketch form.

If you are a new or early stage investigator, be sure to note this when you register for eRA Commons and in the personal statement. To determine whether you qualify, go to the NIH website and read the definition (http://grants.nih.gov/grants/new_investigators/). Not only are new and early stage investigators eligible for specific funding opportunities, but reviewers must take this status into consideration as well. Reviewers will give greater consideration to the proposed approach, rather than the research track record. Early stage applicants may have less preliminary data and fewer publications than more seasoned investigators, and NIH reviewers understand this. Reviewers instead place more emphasis on how the investigator has demonstrated that he or she is truly independent of any former mentors, whether he or she has some of his or her own resources and institutional support, and whether he or she is able to independently lead the research.

In selecting key personnel, consider the following questions. Are the PI and other key personnel appropriately trained and well-suited to carry out this work? Is the work proposed appropriate to the experience level of the PI and other researchers? Do the PI and investigative team bring complementary and integrated expertise to the project, if applicable?

Facilities and Other Resources

This section provides information to indicate that the environment can support the proposed research. Reviewers will use this information to assess the capability of organizational resources to perform the

proposed research. Resources might include laboratory, animal facility, computer, office, clinical, or other facilities. Provide information on capacities, capabilities, relative proximity, and extent of availability of resources to the project. Describe only those resources that are directly applicable to the proposed research. Discuss the scientific environment of the institution, specifically, ways in which the proposed research will benefit from unique features of the environment, including special populations and investigators, opportunities for collaboration, intellectual discussion, etc. If the research will be conducted in several places, be sure to describe the resources available in each site. Mention any start-up funds, support for a technician, and other resources provided by your institution. This is a positive indicator to reviewers of institutional commitment. For New or Early Stage Investigators, describe the institutional investment that will be made to ensure the success of the investigator (e.g., resources, classes, etc.) There is no page limit for this section.

You may wish to consider the following questions. Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support? The MMC grant specialist has templates for the MMC and MMCRI resources and scientific environment which you may use and modify for your own proposal.

Equipment

List major equipment available to the project. The grant specialist has a template that includes all equipment available at MMCRI. If appropriate, use the template and modify it to include only what you will use for the project. If your work will not be done on the Scarborough campus, you will need to list the equipment available at your lab, if applicable.

Budget

The amount of money requested should reflect the scope of the science proposed. The budget includes such items as investigator time, equipment, supplies, travel expenses, and the like. Salaries generally account for 60% to 80% of direct costs. Begin to work with one of the MMC research accountants early (see timeline). Each of them are experienced with NIH budget development and financial rules. All costs must be allowable, reasonable, and necessary. If you ask for too little money given the work proposed, reviewers will see the application as naïve. If you ask for too much, reviewers will cut the budget. The budget also includes a narrative section called the Budget Justification. There are two types of budgets: 1) a modular budget, which must not be over \$250,000 per year in direct costs (for an R01) and only requires personnel justification, and 2) SF424 budget, for requests over \$250,000 or specific RFAs, which require detailed line items and detailed justifications for all items. You cannot go above \$500,000 per year in direct costs without NIH Institute approval. The FOA and your own budgetary needs will determine the budget you decide to use. Plan to spend time thinking through the budget and justification. If the budget is getting too high for the grant mechanism or your stage of career development, consider cutting back the specific aims or experiments. There are no page limits for this section.

Specific Aims

A strong proposal is driven by a strong hypothesis(es) that leads to clear research objectives. The Specific Aims section should encapsulate these concepts. It typically begins with a brief narrative paragraph or two that concisely states the issue or problem to be addressed, describes the long-term goals or objectives of the project and clearly states the hypothesis to be tested. This is followed by a numbered list of the Specific Aims. The aims test different aspects of the hypotheses, operationalize the objectives and provide a rationale for the experimental approach to be described later. For clarity, each aim should consist of only one sentence. Use a brief paragraph under each aim if detail is needed. Most successful applications have 2-4 specific aims. Make sure the aims are logical, achievable, and clearly relate back to the hypothesis.

Depending on the goals of the application, the Specific Aims section may take on a somewhat different form if, rather than testing a specific hypothesis, the goal is to create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.

In crafting the Specific Aims section, you should consider the following questions. Do your specific aims address the research goals and objectives? Did you state your hypotheses and link them appropriately to your specific aims? Are the specific aims clearly related to each other? Do the specific aims represent an achievable amount of work? An unrealistic and overly ambitious set of specific aims is a common pitfall of many applications.

This section is limited to one page. It is by far the most important page of the application. Many applications are won or lost depending on how precisely stated and how compelling the hypothesis and specific aims are presented!

Research Strategy

The research strategy is organized into three sections: Significance, Innovation, and Approach. The assessment of this research plan will largely determine whether or not the application is favorably recommended for funding. For an application with multiple Specific Aims, the applicant may address Significance, Innovation and Approach for each Specific Aim individually, or address Significance, Innovation and Approach for all of the Specific Aims collectively. The R01 application allows for a maximum of 12 pages, which include the three strategy components: Significance, Innovation, and Approach. Other types of applications may have different length limits. Images, graphs, and charts should be included within this section, not in a separate attachment. They count against the page limit. Investigators must use image compression such as JPEG or PNG. Do not include figures or photographs as separate attachments either in the Appendix or elsewhere in the application. Applicants are discouraged from submitting proprietary information unless it is essential to the evaluation of the proposed project. .

Significance

In this section, state the research problem, current state of knowledge, and potential contributions of the research to the field. Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses. Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields. Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved. The background leading to the present application should be brief. It should include a critical evaluation of the literature and identify the gap that this project will fill. The literature review should provide only that information that directly pertains to the scientific need for your project and should reflect up-to-date knowledge of the field.

Consider the following questions. Does this study address an important problem? Will it resolve an important controversy in the field? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventive measures that drive this field?

Innovation

In this section, explain how the application challenges and seeks to shift current research or clinical practice paradigms. Describe any novel theoretical concepts, approaches or methodologies, instrumentation or interventions to be developed or used, and any advantage over existing methodologies, instrumentation, or interventions. Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation, or interventions.

Consider the following questions. Is the project original and innovative? For example, does the project challenge existing paradigms or clinical practice? Does it address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

Approach

In this section, describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Describe how you plan to carry out the research. Include details related to specific methodology, and explain why the proposed methods are the best to accomplish study goals. Describe any novel concepts, approaches, tools, or techniques. Your research methods should relate directly to the specific

aims. This section is critical for demonstrating that you have developed a clear, organized, and thoughtful study design that tests the central hypothesis. State how the data will be collected, analyzed, and interpreted. Describe statistical techniques that will be used. Include a proposed timeline for completing the work. Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims. If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work. Point out any procedures, situations, or materials that may be hazardous to personnel and precautions to be exercised.

Consider the following questions when drafting this section. Does the background provide a clear statement of the general problem being addressed? Have you compared, contrasted, and critiqued what others have done? Have you shown how existing work lays the ground work for the research you propose? Have you cited the literature appropriately? Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well-integrated, well-reasoned, and appropriate to the aims of the project? Did you provide an overview of the experimental design before giving details of the methods? Did you relate the design and methods back to each specific aim? Did you use diagrams or flow charts to explain complex protocols? Did you give enough detail to show that you know what you're talking about? Does the applicant acknowledge potential problem areas and consider alternative tactics? For applications designating multiple PIs, is the leadership approach, including the designated roles and responsibilities, governance and organizational structure consistent with and justified by the aims of the project and the expertise of each of the PIs?

Include information on Preliminary Studies as part of the Approach section. Discuss your preliminary studies, data, and or experience pertinent to this application. Except for Exploratory/Developmental Grants (R21/R33), Small Research Grants (R03), and Academic Research Enhancement Award (AREA) Grants (R15), preliminary data can be an essential part of a research grant application and help to establish the likelihood of success of the proposed project. It can also provide support for feasibility of the proposed research and for experience and competence of applicant. Discuss how the previous work leads to the current proposal. Emphasize how previous work demonstrates feasibility of proposed methods. Accuracy is critical in figures, tables, and graphs.

New or early stage Investigators should include preliminary data if they have any. However, for R01 applications, reviewers will place less emphasis on the preliminary data in applications from new or early stage Investigators than on the preliminary data in applications from more established investigators.

In brief, the content of the Approach section should include:

- PI's preliminary studies, data, and experience relevant to the application and the experimental design;
- the overview of the experimental design;
- a description of methods and analyses to be used to accomplish the specific aims of the project;
- a discussion of potential difficulties and limitations and how these will be overcome or mitigated;
- expected results, and alternative approaches that will be used if unexpected results are found;
- a projected sequence or timetable (work plan);
- if the project is in the early stages of development, describe any strategy to establish feasibility, and address management of any high risk aspects of the proposed work;
- a detailed discussion of the way in which the results will be collected, analyzed, and interpreted;
- a description of any new methodology used and why it is an improvement over the existing ones.

NOTE: The following sections do not count against the Research Strategy page limits.

Human Subjects: Does your research involve human subjects? According to DHHS regulations, the answer is "yes" if you obtain data or biological specimens through intervention or interaction with a living individual or you obtain identifiable private information about a living individual. If you answer "yes" to human subjects' involvement, there are required sections of the application that must be written up. NIH does not require that you have IRB approval at the time of submission; however, you will need to have an IRB approval letter before the proposal is funded.

There is one scenario regarding human subjects involvement in which it is not always clear whether or not to answer “yes” to human subjects involvement. If you plan to study biological specimens or data received from living individuals, and the data were originally collected for another purpose, and you do not have access to the identities of these individuals, then the answer to the “human subjects research” question is more complicated. In this scenario, your project will fall into one of the following categories: a) NOT human research or b) “yes” to human subjects research, but exempt under exemption #4. Exemption #4 is research involving the collection or study of existing data or specimens if recorded by the investigator in a way that subjects cannot be identified.

If your study fits this description because you are using de-identified data or specimens, **then you are required to consult the MMC Institutional Review Board to make the proper determination on the category of your research.** This does not mean you need IRB approval before you submit your proposal. It means that the IRB will guide you to reporting the correct category for your project. This will be a quick (1-2 day) process and is included in the timeline. Once you know the correct category, you can proceed to do the relevant human subjects write-ups for the proposal. Below is information on the required written sections.

If you are doing Human Subjects Research (no exemptions): In this case, you must write four sections for your proposal, as follows:

1. Proposed Use of Human Subjects: Provide information on 6 issues: (1) the characteristics of the subjects; (2) the sources of research materials; (3) recruitment plans and consent procedures; (4) potential risks; (5) procedures for protecting against or minimizing potential risks; and (6) potential benefits to subjects and to mankind.
2. Inclusion of Women and Minorities: Discuss the demographics of the minority populations in the area and the criteria and rationale for selection of gender and racial/ethnic group, as well as your plan for recruiting/including women and minorities in the research.
3. Targeted Enrollment Table: This table is provided by NIH and must be filled out with estimates on participation in the study by gender and ethnicity. The table is available at mmcri.org (grants and contracts/forms and templates) or from the Grant Specialist.
4. Inclusion of Children: Discuss the participation of children and explain the rationale if children are excluded. If they are included, describe the rationale for selecting specific ages, and discuss the qualifications of investigators who will work with children.

If you are doing Human Subjects Research in a Clinical Trial: A clinical trial is a prospective study designed to answer questions about biomedical or behavioral interventions. If you are conducting a clinical trial, you must write all the four sections above PLUS you must write a **data and safety monitoring plan** which will be included in Section 1 above.. Please consult the MMC IRB website for guidance at http://www.mmcri.org/deptPages/irb/downloads/SOP_FOLDER/FO301E.pdf.

If your Human Subjects Research is Exempt under Exemption 4: In this case, you need only describe the human subjects work you will do involving specimens or data, where and how you will collect the data, and clearly justify the exemption. Make sure to refer to the definition of the exemption (above).

If your project is not considered Human Subjects but you are using human specimens or data: In this case, you must justify why the project is not considered human subjects even though you are studying data or specimens from living beings. This determination will have been made by the IRB, which can help you with the justification.

Vertebrate Animals

If vertebrate animals are involved, address each of the five points below. If all or part of the proposed research involving vertebrate animals will take place at alternate sites (such as collaborating sites), identify those sites and describe the activities at those locations. Although no page limitation applies to this section, be succinct.

1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Strategy 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 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 American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. If not, include a scientific justification for not following the recommendations.

NOTE: Michele Locker, the MMC grant specialist, has a template to describe Points 3 and 4 at MMC.

Depending on how the project is designed, there may be additional sections required, such as Select Agent Research, Multiple PI Leadership Plan, Consortium/Contractual Agreements, Letters of Support, and others. See SF424 Instructions if any of these sections apply and consult the grant specialist with questions.

Bibliography and References Cited

Provide a bibliography of any references cited in the project narrative and any other parts of your application. This section shows your breadth of knowledge in your field. There is no page limit for this section. Each reference must include the names of all authors (in the same sequence in which they appear in the publication), the article and journal title, book title, volume number, page numbers, and year of publication. When citing articles that fall under the Public Access Policy (i.e., arose from NIH support), provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the Pubmed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal – In Process." Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PMCID numbers along with the full reference. The following is an example of an appropriate citation in the bibliography: Pillai SK, Good B, Pond SK, Wong JK, Strain MC, Richman DD, Smith DM. Semen-specific genetic characteristics of human immunodeficiency virus type 1 env. *J Virol.* 2005 79(3):1734-1742. PMCID: PMC544119. Copies of publicly available publications are not accepted as appendix material. The references should be limited to relevant and current literature.

Appendix

A maximum of 10 PDF attachments is allowed in the Appendix. Publications are not longer allowed as appendix materials except if the manuscript is accepted for publication but not yet published or if the journal link is not available. Not all grant mechanisms allow publications to be included in the appendix. When allowed there is a limit of 3 publications that are not publicly available. If a patent is directly relevant to the project, the entire document should be submitted as a PDF attachment. Surveys, questionnaires, and other data collection instruments; clinical protocols and informed consent documents may be submitted in the Appendix as necessary. Photographs and images of gels, micrographs, etc. are no longer accepted as appendix material. They must be included in the Research Strategy section.

Resource Sharing

Describe your plan to share research findings with the wider scientific community, including, if applicable, the development of model organism, genome wide associate data studies, and overall data sharing. The MMCRI grant specialist has a template for this section which you may modify as needed.

Cover Letter

Cover letters are not required but can be helpful for several reasons. Generally the cover letter is used to request assignment of the application to a specific NIH Institute or Center or a specific initial review group. It

can also be used to exclude individuals from reviewing your application. It is only used for administrative purposes; it does not get shared with peer reviewers. The letter should include: (1) the application title; (2) the FOA title; (3) request for assignment to a particular Institute or Center and a Scientific Review Group; (4) if appropriate, a list of people (e.g., competitors) who should not review your application and why; (5) a list of scientific expertise represented in the proposed research so appropriate reviewers can be identified; and (6) if requesting direct costs greater than \$500K per year, documentation of Institutional approval to submit.

OVERALL CONSIDERATIONS

1. Observe application guidelines strictly.
2. Use basic English and avoid jargon.
3. Make sure all acronyms are spelled out when used initially.
4. Observe the type size and page limitations; Arial 11 point font and margins .5" all the way around.
5. Include only those graphs, tables, etc., that are unpublished and essential to the narrative.
6. Make sure all citations are complete: title, authors, book or journal, volume number, inclusive pages, year of publication. When citing articles that fall under the Public Access Policy, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each article. Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PMCID numbers along with full ref.
7. Make sure you work with a mentor and/or peer reviewers; have an outside reader review the application for clarity and consistency.

The Review Process

Your application has three audiences: the majority of reviewers who will probably not be familiar with your techniques or field, a smaller number of reviewers who will be familiar with the field, and NIH program staff. All reviewers are important to you because each reviewer gets to score your application. Program staff is important because they will serve as your internal champion if you get a good score. To succeed in peer review, you must win over the assigned reviewers. The assigned reviewers can act as advocates in guiding the review panel's discussion of your application. Make sure your application is polished, interesting, and easy to read. Make sure that all sections of the application are consistent. You want the assigned reviewers, especially the primary reviewer, to readily grasp and explain your research to other reviewers.

The review and selection process for applications takes 8 to 10 months. Submit your very best application because reviewers expect you to have taken the time needed to think it through before submitting. For new investigators, there is an opportunity for resubmission of your application in the next review round when there are only minor concerns.