Denver Health Residency in Emergency Medicine:
Resident Research Grant Program

# Grant Application Instructions

Version: August 1, 2012

## APPLICATION INSTRUCTIONS

Submission in electronic format is required. No paper copies please. Email completed applications to Emily.Caruso@dhha.org as a single PDF file.

**INCOMPLETE PROPOSALS OR PROPOSALS RECEIVED AFTER THE DEADLINE DATE WILL NOT BE CONSIDERED.**

Use English only and avoid jargon and unusual abbreviations. For terms not universally known, spell out the term the first time it is used with the appropriate abbreviation in parentheses; the abbreviation may be used thereafter. Type the application, single-spaced, and stay within the margin limitations indicated on the forms and continuation pages. The type must be clear and readily legible, and in Arial 11 point font only. Use black type; do **not** use photo-reduction.

If including figures, graphs, diagrams, charts, tables, figure legends and footnotes, a smaller type size is acceptable but must be in black ink, and in Arial typeface.

Do **not** submit an incomplete application. **An application will be considered incomplete if it is illegible, if it fails to follow instructions, or if the material presented is insufficient to permit an adequate review.** Unless specifically required by these instructions (e.g., human subjects certification, vertebrate animals verification) do **not** send supplementary material.

The application is to be submitted using the provided forms. Number the pages consecutively at the bottom throughout the application. Do not use suffixes such as 5a, 5b. Type the name of the applicant at the top of each printed page. **AN APPLICATION WILL NOT BE CONSIDERED IF PAGE LIMITATIONS ARE NOT OBSERVED**.

**The application consists of the following sections:**

### 1.0 FACE PAGES

Name the **one** person responsible for the scientific and technical direction of the project. Choose a title that is descriptive and specifically appropriate, rather than general. Do not exceed 81 characters, including the spaces between words and punctuation. The Primary Mentor should be listed on Form Page 1 where indicated.

Complete the **Project Summary** on Face Page 2. It is meant to serve as a succinct and accurate description of the proposed work when separated from the application. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving the stated goals. This section should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate reader. Avoid describing past accomplishments and the use of the first person.

The second component of Face Page 2 is **Relevance**. Using no more than two or three sentences, describe the relevance of this research to emergency medicine. In this section, be succinct and use plain language that can be understood by a general, lay audience.

Performance Site and Personnel Information should be listed on the subsequent pages of Face Page 2. Please list the name of the Primary Site for this project, as well as any other performance sites. Use the Performance Site Continuation page if necessary.

**In addition to the PD/PI, senior/key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries are requested.**

Typically, these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level should be included if their involvement meets the definition of senior/key personnel. Consultants and those with a postdoctoral role should also be included if they meet the same definition. Senior/key personnel must devote measurable effort (described in person months) to the project, whether or not salaries are requested. "Effort of zero person months" or "as needed" are not acceptable levels of involvement for those designated as senior/key personnel. Senior/key personnel should include all members of the mentorship team, if applicable.

Start with the PD/PI(s). List the PD/PI's last name first. Then list all other senior/key personnel in alphabetical order, last name first. For each individual provide name, organization name (their institutional affiliation), and role on the project. Each key personnel should provide a biographical sketch that includes a more detailed description of their role on the project.

**Other Significant Contributors**
This category identifies individuals who have committed to contributing to the scientific development or execution of the project, but are not committing any specified measurable effort (i.e., person months) to the project. These individuals are typically presented at "effort of zero person months" or "as needed." Individuals with measurable effort may not be listed as Other Significant Contributors (OSCs). Consultants should be included if they meet this definition.

## 2.0 TABLE OF CONTENTS

## 3.0 BUDGET

Use the **Budget Format Page** provided with the application packet.

**The Resident Research Grant Program (RRGP) does not allow Facilities and Administration Costs (F&A).**

<u>Personnel</u>

- Starting with the PD/PI(s), list the names of all applicant organization employees who are involved on the project during the initial budget period. No salary support will be provided. Include all collaborating investigators, individuals in training, and support staff.
- Identify the role of each individual listed on the project and describe their specific functions. Provide budget narrative for ALL personnel by position, role, and level of effort using person months (calendar, academic and/or summer). This includes any "to-be-appointed" positions.
- Enter the number of months devoted to the project. Three columns are provided depending on the type of appointment being reflected: academic, calendar, and/or summer months. Individuals may have consecutive appointments within a calendar year, for example for an academic period and a summer period. In this case, each appointment should be identified separately using the corresponding column.
- If effort does not change throughout the year, use only the calendar months column. If effort varies between academic and summer months, leave the calendar months column blank and use only the academic and summer months columns. In cases where no contractual appointment exists with the applicant organization and salary is requested, enter the number of months for the requested period.
- No salary support will be provided for the PI or key personnel, although funds may be used to support contractual work (e.g., data abstraction). No fringe benefits will be allowed.

<u>Consultant Costs</u>

Whether or not costs are involved, provide the names and organizational affiliations of all consultants, other than those involved in consortium/contractual arrangements. Include consultant physicians in

connection with patient care and persons who are confirmed to serve on external monitoring or advisory committees. Describe the services to be performed on Form Page 5 under “Justification.” Include the number of days of anticipated consultation, the expected rate of compensation, travel, per diem, and other related costs.

Equipment

List each item of equipment with amount requested separately and justify each purchase on Form Page 5.

Supplies

Itemize supplies in separate categories, such as glassware, chemicals, radioisotopes, etc. If animals are to be purchased, state the species and the number to be used.

Travel

Itemize travel requests and justify on Form Page 5. Funds for travel may be allowed as long as it is directly related to the scope of work or involves presentation of results from the project at a scientific meeting. Provide the purpose and destination of each trip and the number of individuals for whom funds are requested.

Patient Care Costs

If inpatient and/or outpatient costs are requested for research with human subjects, provide the names of any hospitals and/or clinics and the amounts requested in the Budget Justification.

Indicate, in detail, the basis for estimating costs in this category, including the number of patient days, estimated cost per day, and cost per test or treatment. If both inpatient and outpatient costs are requested, provide information for each separately. If multiple sites are to be used, provide detailed information by site.

Include information regarding projected patient accrual for the project/budget periods and relate this information to the budget request for patient care costs. If patient accrual is anticipated to be lower at the start or during the course of the project, plan budget(s) accordingly.

Provide specific information regarding anticipated sources of Other Support for patient care costs (e.g., third party recovery or pharmaceutical companies). Include any potential or expected utilization of General Clinical Research Centers/Clinical Translation Science Awards.

Alterations and Renovations

Itemize by category and justify in the Budget Justification the costs of essential alterations and renovations including repairs, painting, removal or installation of partitions, shielding, or air conditioning. Where applicable, provide the square footage and costs.

Other Expenses

Itemize any other expenses by category and unit cost. These might include animal maintenance (unit care costs and number of care days), patient travel, patient participation incentives, donor fees, computer charges, rentals and leases, equipment maintenance, service contracts, and tuition remission when budgeted separately from salary/fringe benefits. Justify all other expenses in the Budget Justification.

**4.0 BIOGRAPHICAL SKETCHES** (See page limits described below)

Use the **Biographical Sketch Format Page** provided with the application packet.

Information is requested for the applicant, mentor(s) and any senior/key personnel or other significant contributors who will be involved with the projects. Follow the instructions on the Biographical Sketch Format Page. The first four sections (Personal Statement, Positions and Honors, Selected Peer-reviewed Publications, and Research Support) cannot exceed 4 pages. Research Support should specifically include active and past

funding.

Other pending support ("Other Support") should also be included at the end of the Biographical Sketch section and should include only pending funding. There is no page limit for this section.

List all pending intramural and extramural research funding for the applicant, mentor(s) and co-investigators. For each item indicate the grant identification number, grant type, PI, funding source, annual direct costs, funding period, percent effort, grant title, and brief description of project. For all items indicate whether there is any scientific or budgetary overlap with the current proposal.

## 5.0 RESOURCES AND ENVIRONMENT

Use the **Resources Format Page** provided with the application packet.

Describe the research facilities using the following headings: laboratory; clinical, animal; computer; office; and other. If appropriate, indicate their capacities, pertinent capabilities, relative proximity and extent of availability to the project. Describe only those resources that are directly applicable to the proposed work. Provide any information describing the Other Resources available to the project (e.g., machine shop, electronic shop) and the extent to which they would be available to the project.

Describe how the scientific environment in which the research will be done contributes to the probability of success (e.g., institutional support, physical resources, and intellectual rapport). In describing the scientific environment in which the work will be done, discuss ways in which the proposed studies will benefit from unique features of the scientific environment or subject populations or will employ useful collaborative arrangements.

## 6.0 RESEARCH PLAN

The Research Plan consists of items 1-10 in Section 6.1 below, as applicable. It should be self-contained and include sufficient information to evaluate the project, independent of any other document (e.g., previous application). Be specific and informative, and avoid redundancies. Carefully follow all instructions. There is no specific format page – please use the **Continuation Format Page**.

For grant writing tips, see http://grants.nih.gov/grants/grant_tips.htm.

## 6.1 CONTENT OF RESEARCH PLAN

The Research Plan consists of the following items (6.1.1 – 6.1.10), as applicable. Begin each section of the Research Plan with a section header (e.g., Introduction, Specific Aims, Research Strategy, etc.).

The Research Strategy, Section 6.1.3, is composed of three distinct sections – Significance, Innovation, and Approach. Note the Approach section also includes Preliminary Research for new applications.

### 6.1.1 Introduction to Application (Resubmission or Revision Applications Only) (limit 2 pages)

RRGP will consider revised proposals, and two additional pages are provided to introduce reviewers to the revised proposal. Key things to keep in mind when submitting a revised grant:

- The introduction to the revision should provide a concise summary of reviewers' comments from the previous application and should, point-by-point, discuss how the revised application has addressed these concerns.
- Revised applications are not reviewed outside of the normal review process. Such applications may be more competitive than first-time submissions, but not necessarily so.
- Revised applications are reviewed as new science. Revised applications will not automatically be considered better applications within the review process.
- In the event of a resubmission, the committee will attempt to return applications to their original

reviewers when possible. However, RRGP cannot guarantee that a grant will be reviewed by the same individuals reviewing the original application.

**6.1.2 Specific Aims** (limit 1 page)

- State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will exert on the research field(s) involved.
- List succinctly the specific objectives of the research proposed (e.g., to test a stated hypothesis, 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), using testable hypotheses.

**6.1.3 Research Strategy** (limit 6 pages)

*Significance*

- 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.

*Innovation*

- 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.

*Approach*

- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project.
- 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.
- Include information on Preliminary Studies. Discuss the PD/PI's preliminary studies, data, and or experience pertinent to this application. Preliminary data can be an essential part of a research grant application and help to establish the likelihood of success of the proposed project.

**6.1.4 Bibliography and References Cited**

Provide a bibliography of all references cited. Each reference must include 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. Include only bibliographic citations. Follow scholarly practices in providing citations for source materials relied upon in preparing any section of the application.

The references should be limited to relevant and current literature. While there is not a page limitation, it is important to be concise and to select only those literature references pertinent to the proposed research.

When citing articles that fall under the Public Access Policy, were authored or co-authored by the

applicant and 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." A list of these Journals is posted at: http://publicaccess.nih.gov/submit_process_journals.htm.

Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PubMed ID (PMID) numbers along with the full reference (note that copies of these publications are not accepted as appendix material).

**6.1.5 Protection of Human Subjects**

**If the proposed project does involve human subjects, sections 6.1.5 – 6.1.8 should not be included.**

For all research involving human subjects, a part of the review process will include careful consideration of protections from research risks, as well as the appropriate inclusion of women, minorities, and children. The RRGP will assess the adequacy of safeguards of the rights and welfare of research participants, and the appropriate inclusion of women, minorities, and children, based on the information in the application. This evaluation will be factored into the overall score. The information on the protection of human subjects that you are required to provide in this section is identical to information that you will be required to provide for IRB at your own institution and are required by most Federal agencies.

The applicant should include specific measures on how protected health information (as defined by the Human Health Services) will be handled in accordance with the Privacy Rule of the Health Insurance Portability Accountability Act (HIPAA).

Although no specific page limitation applies to this section of the application, be succinct. Complete this section using the **Continuation Format Page**. Use the subheadings to address the issues listed below:

Risks to Human Subjects

*Human Subjects Involvement, Characteristics, and Design*

- Describe and justify the proposed involvement of human subjects in the work outlined in the Research Strategy section.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status if relevant.
- Describe and justify the sampling plan, as well as the recruitment and retention strategies and the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special vulnerable populations, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. Note that 'prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins.
- If relevant to the proposed research, describe procedures for assignment to a study group. As related to human subjects protection, describe and justify the selection of an intervention's dose, frequency and administration.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites and collaborating investigators in performing the proposed research. Explain how data from the site(s) will be obtained, managed, and protected.

*Sources of Materials*

- Describe the research material obtained from living individuals in the form of specimens,

records, or data.
- Describe any data that will be collected from human subjects for the project(s) described in the application.
- Indicate who will have access to individually identifiable private information about human subjects.
- Provide information about how the specimens, records, and/or data are collected, managed, and protected as well as whether material or data that include individually identifiable private information will be collected specifically for the proposed research project.

*Potential Risks*

- Describe the potential risks to subjects (physical, psychological, financial, legal, or other), and assess their likelihood and seriousness to the human subjects.
- Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

Adequacy of Projection Against Risks

*Recruitment and Informed Consent*

- Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.
- Include a description of 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. If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Informed consent document(s) need not be submitted to the RRGP unless requested.

*Protections Against Risk*

- Describe planned procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data, and assess their likely effectiveness.
- Research involving vulnerable populations, as described in the DHHS regulations, Subparts B-D must include additional protections. Refer to DHHS regulations, and OHRP guidance:
    - Additional Protections for Pregnant Women, Human Fetuses and Neonates: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb
    - Additional Protections for Prisoners: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc
    - OHRP Subpart C Guidance: http://www.hhs.gov/ohrp/policy/index.html#prisoners
    - Additional Protections for Children: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd
    - OHRP Subpart D Guidance: http://www.hhs.gov/ohrp/policy/index.html#children
- Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (biomedical and behavioral intervention studies) must include a general description of the plan for data and safety monitoring of the clinical trials and adverse event reporting to the IRB, the RRGP and others, as appropriate, to ensure the safety of subjects.
- If the proposed project includes a clinical trial, please include a heading in this section entitled “Data and Safety Monitoring Plan” as described below.

Potential Benefits of the Proposed Research to Human Subjects and Others

- Discuss the potential benefits of the research to research participants and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to

research participants and others.

Importance of the Knowledge to be Gained

- Discuss the importance of the knowledge gained or to be gained as a result of the proposed research.
- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonable may be expected to result.

NOTE: Test articles (investigational new drugs, devices, or biologics) including test articles that will be used for purposes or administered by routes that have not been approved for general use by the Food and Drug Administration (FDA) must be named. State whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the FDA, and/or the status of requests for an Investigational New Drug (IND) or Investigational Device Exemption (IDE) covering the proposed use of the test article in the Research Plan.

Data and Safety Monitoring Plan (if applicable)

If the proposed project includes a clinical trial, create a heading entitled "Data and Safety Monitoring Plan." Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the IRB, the FDA (in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations), and the RRGP. The frequency of monitoring will depend on the potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:

- PD/PI (required)
- Institutional Review Board (IRB) (required)
- Independent individual/safety officer
- Designated medical monitor
- Internal Committee or Board with explicit guidelines

### 6.1.6 Inclusion of Women and Minorities

Create a section heading entitled “Inclusion of Women and Minorities” and place it immediately following the “Protection of Human Subjects” section. Although no specific page limitation applies to this section, please be succinct. Complete this section using the **Continuation Format Page**. In this section of the Research Plan, address, at minimum, the following four points:

- The targeted/planned distribution of subjects by sex/gender and racial/ethnic groups for each proposed study or protocol using the format in the Targeted/Planned Enrollment Table. (Instructions for completing this table are provided below in 6.1.8) If using existing specimens and/or data without access to information on the distribution of women and minorities so state and explain the impact on the goals of the research as part of the rationale that inclusion cannot be described (item 3 below). Alternatively, describe the gender and minority composition of the population base from whom the specimens and/or data will be obtained. Include the Targeted/Planned Enrollment Tables in this section.
- A description of the subject selection criteria and rationale for selection of sex/gender and racial/ethnic group members in terms of the scientific objectives and proposed study design. The description may include, but is not limited to, information on the population characteristics of the disease or condition under study.
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group (see examples below).

- A description of proposed outreach programs for recruiting sex/gender and racial/ethnic group members as subjects.

### 6.1.7 Inclusion of Children

Create a section heading entitled “Inclusion of Children” and place it immediately following “Inclusion of Women and Minorities” section. Although no specific page limitation applies to this section, please be succinct. Complete this section using the **Continuation Format Page**.

- For the purpose of implementing these guidelines, a child is defined as an individual under the age of 21 years.
- Provide either a description of the plans to include children, or, if children will be excluded from the proposed research, application, or proposal, present an acceptable justification for the exclusion (see **Additional Guidance Section**).
- If children are included, the description of the plan should include a rationale for selecting a specific age range of children. The plan also must include a description of the expertise of the investigative team for working with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.
- Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the age-appropriate inclusion or exclusion of children in the proposed research project.
- When children are involved in research, the Additional Protections for Children Involved as Subjects in Research (45 CFR Part 46 Subpart D) apply and must be addressed under the Protections Against Risk subheading (4.1.2.b).

### 6.1.8 Targeted/Planned Enrollment Table

All projects involving human subjects should collect and report information on participants with respect to two categories of ethnicity and five categories of race.

When reporting these data in the aggregate, investigators should report: (a) the number of research participants in each ethnic category; (b) the number of research participants who selected only one category for each of the five racial categories; (c) the total number of research participants who selected multiple racial categories reported as the “number selecting more than one race,” and (d) the number of research participants in each racial category who are Hispanic or Latino. Investigators may provide the detailed distributions, including all possible combinations, of multiple responses to the racial designations as additional information. However, more detailed data should be compiled in a way that they can be reported using the required categories.

### 6.1.9 Vertebrate Animals

For all applications involving vertebrate animals, the applicant must address the following five items.

- Provide a detailed description of the proposed use of the animals in the work 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.
- 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.
- Provide information on the veterinary care of the animals involved including the name of the supervising veterinarian. Include information from the Association for Assessment and Accreditation of Laboratory Animal Care International: the name of the accredited parent organization (e.g., University of X) and the certificate number and date of last inspection.
- 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.
- 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.

### 6.1.10 Letters of Support

Provide all appropriate letters of support, including any letters necessary to demonstrate the support of the primary mentor, all other mentors, and collaborators such as senior/key personnel and other significant contributors included in the grant application. Letters are not required for personnel (such as research assistants) not contributing in a substantive, measurable way to the scientific development or execution of the project. For consultants, letters should include rate/charge for consulting services. Consultant biographical sketches should be in the Biographical Sketch section.

## 7.0 APPENDIX

Do not use appendix to circumvent page limitations for research plans. Do not include experimental methods, protocols or figures that should be incorporated within the research project description. No page numbering is necessary for Appendix. The appendix can include:

- Up to 5 publications, manuscripts (***accepted*** for publication), abstracts, patents, or other printed materials directly relevant to this project. *Do not include manuscripts* ***submitted*** *for publication.*
- Publications in press**:** Include only a publication list with a link to the publicly available on-line journal article or the NIH PubMed Central (PMC) submission identification number. Do not include the entire article.
- Manuscripts accepted for publication but not yet published: The entire article should be submitted and may be stapled.
- Manuscripts published but an online journal link is not available**:** The entire article should be submitted and may be stapled.
- Surveys, questionnaires, data collection instruments, clinical protocols, and informed consent documents.
- Original glossy photographs or color images of gels, micrographs, etc., provided that a photocopy (may be reduced in size) is also included within the 25-page limit of *Items a-d* of the research plan. *No photographs or color images may be included in the Appendix that are not also represented within the Research Plan.*

## ADDITIONAL GUIDANCE

Inclusion of Women and Minorities

Below are examples of acceptable justifications for the exclusion of one gender, minority groups or subgroups.

*One Gender*

One gender is excluded from the study because:

- Inclusion of these individuals would be inappropriate with respect to their health;
- The research question addressed is relevant to only one gender;
- Evidence from prior research strongly demonstrates no difference between genders; or
- Sufficient data already exist with regard to the outcome of comparable studies in the excluded gender, and duplication is not needed in this study.

One gender is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens).

Gender representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete gender documentation are used), and this does not compromise the scientific objectives of the research.

*Minority Groups or Subgroups*

Some or all minority groups or subgroups are excluded from the study because:

- Inclusion of these individuals would be inappropriate with respect to their health;
- The research question addressed is relevant to only one racial or ethnic group;
- Evidence from prior research strongly demonstrates no differences between racial or ethnic groups on the outcome variables;
- A single minority group study is proposed to fill a research gap; or
- Sufficient data already exists with regard to the outcome of comparable studies in the excluded racial or ethnic groups and duplication is not needed in this study.

Some minority groups or subgroups are excluded or poorly represented because the geographical location of the study has only limited numbers of these minority groups who would be eligible for the study, and the investigator has satisfactorily addressed this issue in terms of:

- The size of the study;
- The relevant characteristics of the disease, disorder or condition; or
- The feasibility of making a collaboration or consortium or other arrangements to include representation.

Some minority groups or subgroups are excluded or poorly represented because the purpose of the research constrains the applicant's selection of study subjects by race or ethnicity (e.g., uniquely valuable cohorts, stored specimens or existing datasets are of limited minority representation, very small numbers of subjects are involved, or overriding factors dictate selection of subjects, such as matching of transplant recipients or availability of rare surgical specimens).

Racial or ethnic origin of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens or data sets with incomplete racial or ethnic documentation are used) and this does not compromise the scientific objectives of the research.

Justifications for the Exclusion of Children

For the purposes of this policy, all individuals under 21 are considered children; however, exclusion of any specific age group, such as individuals under 18, should be justified in this section. It is expected that

children will be included in all clinical research unless one or more of the following exclusionary circumstances apply:

- The research topic to be studied is not relevant to children.
- Laws or regulations bar the inclusion of children in the research.
- The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be needlessly redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
- A separate, age-specific study in children is warranted and preferable. Examples include:
    - The condition is relatively rare in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition); or
    - The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
    - Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested, or the interventions planned, to allow inclusion of children rather than excluding them.
- Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). Although children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
- Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).
- Other special cases can be justified by the investigator and found acceptable to the review group.