

Research Plan Section

2. Specific Aims

Who must complete the "Specific Aims" attachment:

The "Specific Aims" attachment is required unless otherwise specified in the FOA.

Format:

Follow the page limits for the Specific Aims in the [NIH Table of Page Limits](#) unless otherwise specified in the FOA. A "Specific Aims" attachment that exceeds the page limit will be flagged as an error by the Agency upon submission.

Attach this information as a PDF file. See NIH's [Format Attachments](#) page. Hyperlinks and URLs may not be used in this section unless specified as allowed in the funding opportunity announcement.

Content:

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 have 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).

3. Research Strategy

Who must complete the "Research Strategy" attachment:

The "Research Strategy" attachment is required.

Format:

Follow the page limits for the Research Strategy in the [NIH Table of Page Limits](#), unless otherwise specified in the FOA. Although multiple sections of information are required in the Research Strategy as detailed below, the page limit applies to the entirety of the single "Research Strategy" attachment.

Attach this information as a PDF file. See NIH's [Format Attachments](#) page. Hyperlinks and URLs may not be used in this section unless specified as allowed in the funding opportunity announcement.

Content:

Organize the Research Strategy in the specified order and use the instructions provided below unless otherwise specified in the FOA. Start each section with the appropriate heading – Significance, Innovation, Approach.

Cite published experimental details in the Research Strategy attachment and provide the full reference in [R.220 - R&R Other Project Information Form, Bibliography and Reference Cited](#).

Note for Applications Proposing the Use of Human Fetal Tissue: If the use of human fetal tissue obtained from elective abortions (HFT) (as [defined in the NIH Grants Policy Statement](#)) is

included in the proposed application you must include specific information in the Approach section of the Research Strategy attachment. See specific instructions below in Section 3. Approach. This information must be provided regardless of whether Human Subjects research is proposed or not.

Applications proposing HFT that do not address these requirements will be administratively withdrawn. For further information on HFT policy refer to the NIH Grants Policy Statement, [Section 2.3.7.11 Human Fetal Tissue from Elective Abortions](#), [Section 4.1.14 Human Fetal Tissue Research](#) and [Section 4.1.14.2 Human Fetal Tissue from Elective Abortions](#).

Note for Applications Proposing the Involvement of Human Subjects and/or Clinical Trials:

- Do not duplicate information in the Research Strategy and the PHS Human Subjects and Clinical Trials Information form. Use the Research Strategy attachment to discuss the overall strategy, methodology, and analyses of your proposed research. Use the PHS Human Subjects and Clinical Trials Information form to provide detailed information for human subjects studies and clinical trials.
- The PHS Human Subjects and Clinical Trials Information form will capture detailed study information, including eligibility criteria; inclusion of women, minorities, and individuals across the lifespan; protection and monitoring plans; and statistical design and power.
- You are encouraged to refer to information in the PHS Human Subjects and Clinical Trials Information form as appropriate in your discussion of the Research Strategy (e.g., see [Question 2.4 Inclusion of Women and Minorities](#)).

Note for Applicants with Multiple Specific Aims: You may address the Significance, Innovation, and Approach either for each Specific Aim individually or for all of the Specific Aims collectively.

1. Significance

- Explain the importance of the problem or critical barrier to progress that the proposed project addresses.
- Describe the strengths and weaknesses in the [rigor](#) of the prior research (both published and unpublished) that serves as the key support for the proposed project.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.

► Additional Instructions for Research:

Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

2. 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.

3. Approach

- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project. Describe the experimental design and methods proposed and how they will achieve robust and unbiased results. Include how the data will be collected, analyzed, and interpreted, and reference any [Resource Sharing Plans](#) as appropriate. Resources and tools for rigorous experimental design can be found at the [Enhancing Reproducibility through Rigor and Transparency](#) website.
- For trials that randomize groups or deliver interventions to groups, describe how your methods for analysis and sample size are appropriate for your plans for participant assignment and intervention delivery. These methods can include a group- or cluster-randomized trial or an individually randomized group-treatment trial. Additional information is available at the [Research Methods Resources](#) webpage.
- 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.
- Explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans. For example, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex. Refer to the NIH Guide Notice on [Sex as a Biological Variable in NIH-funded Research](#) for additional information.
- Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised. A full discussion on the use of select agents should appear in the [Select Agent Research](#) attachment below.
- If research on Human Embryonic Stem Cells (hESCs) is proposed but an approved cell line from the NIH [hESC Registry](#) cannot be chosen, provide a strong justification for why an appropriate cell line cannot be chosen from the registry at this time.

Special Instructions for Applications Proposing the Use of Human Fetal Tissue: If the use of human fetal tissue obtained from elective abortions (HFT) (as [defined in the NIH Grants Policy Statement](#)) is included in the proposed application

- Use the specific heading: "Human Fetal Tissue Research Approach".
- Describe the proposed characteristics, procurement, and procedures for the research use of HFT. The description should be sufficiently detailed to permit meaningful evaluation by NIH.
- Justify the use of HFT in the proposed research by indicating the following:
 - Why the research goals cannot be accomplished by using an alternative to HFT.
 - What methods were used (e.g. literature review, preliminary data) to determine that alternatives could not be used.
 - Results from a literature review used to provide justifications.
 - Plans for the treatment of HFT and the disposal of HFT when research is complete.

- Description of planned written, voluntary, informed consent process for cell/tissue donation, or description and documentation of process if cells/tissue were already obtained.

Applications proposing HFT that do not address these requirements will be administratively withdrawn. For further information on HFT policy refer to the NIH Grants Policy Statement, [Section 2.3.7.11 Human Fetal Tissue from Elective Abortions](#), [Section 4.1.14 Human Fetal Tissue Research](#) and [Section 4.1.14.2 Human Fetal Tissue from Elective Abortions](#).

As applicable, also include the following information as part of the Research Strategy, keeping within the three sections (Significance, Innovation, and Approach) listed above.

Preliminary Studies for New Applications:

For new applications, include information on preliminary studies. Discuss the PD/PI's 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 can help to establish the likelihood of success of the proposed project. Early stage investigators should include preliminary data.

Progress Report for Renewal and Revision Applications:

Note that the Progress Report falls within the Research Strategy and is therefore included in the page limits for the Research Strategy.

For renewal/revision applications, provide a Progress Report. Provide the beginning and ending dates for the period covered since the last competitive review. In the Progress Report, you should:

- Summarize the specific aims of the previous project period and the importance of the findings, and emphasize the progress made toward their achievement.
- Explain any significant changes to the specific aims and any new directions, including changes resulting from significant budget reductions.
- Discuss previous participant enrollment (e.g., recruitment, retention, inclusion of women, minorities, children, etc.) for any studies meeting the NIH definition for [clinical research](#). Use the Progress Report section to discuss, but not duplicate information collected elsewhere in the application.

Do not include a list of publications, patents, or other printed materials in the Progress Report. That information will be included in the "Progress Report Publication List" attachment.

4. Progress Report Publication List

Who must complete the "Progress Report Publication List" attachment:

A "Progress Report Publication List" attachment is required only if the type of application is renewal.

Descriptions of different types of applications are listed here: NIH's [Types of Applications](#).

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page. Use of hyperlinks and URLs in this section is not allowed unless specified in these instructions or in the funding opportunity announcement.

Content:

List the titles and complete references to all appropriate publications, manuscripts accepted for publication, patents, and other printed materials that have resulted from the project since it was last reviewed competitively.

You are allowed to cite interim research products. **Note:** interim research products have specific citation requirements. See related [Frequently Asked Questions](#) on citing interim research products and claiming them as products of your NIH award.

Provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each of the following:

- Articles that fall under the [Public Access Policy](#),
- Articles that were authored or co-authored by the applicant and arose from NIH support,
- Articles that were authored or co-authored by the applicant and arose from AHRQ funding provided after February 19, 2016 (see the Guide Notice on [Policy for Public Access to AHRQ-Funded Scientific Publications](#)).

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." NIH maintains a [list of such journals](#).

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. Active hyperlinks are not allowed.

Other Research Plan Section

5. Vertebrate Animals

Who must complete the "Vertebrate Animals" attachment:

Include a "Vertebrate Animals" attachment if you answered "Yes" to the question "Are Vertebrate Animals Used?" on the [R.220 - R&R Other Project Information Form](#).

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page.

Do not use this attachment to circumvent the page limits of the Research Strategy.

Content:

If live vertebrate animals are involved in the project, address each of the following criteria:

1. **Description of Procedures:** Provide a concise description of the proposed procedures to be used that involve live vertebrate animals in the work outlined in the "Research Strategy" attachment. The description must include sufficient detail to allow evaluation of the procedures. Identify the species, strains, ages, sex, and total numbers of animals by species, to be used in the proposed work. If dogs or cats are proposed, provide the source of the animals.

2. **Justifications:** Provide justification that the species are appropriate for the proposed research. Explain why the research goals cannot be accomplished using an alternative model (e.g. computational, human, invertebrate, *in vitro*).
3. **Minimization of Pain and Distress:** Describe the interventions including analgesia, anesthesia, sedation, palliative care and humane endpoints that will be used to minimize discomfort, distress, pain, and injury.

Each of the criteria must be addressed. Failure to adequately address the criteria may negatively affect the application's impact score. In addition to the 3 criteria above, you should also:

- Identify all project performance (or collaborating) sites and describe the proposed research activities with vertebrate animals that will be conducted at those sites.
- Explain when and how animals are expected to be used if plans for the use of animals have not been finalized.

See the following pages for more information:

- NIH's [Office of Laboratory Animal Welfare](#) website
- NIH's [Vertebrate Animals Section Worksheet](#)
- See the [NIH Grants Policy Statement, Section 4.1.1: Animal Welfare Requirements](#) (an applicable Animal Welfare Assurance will be required if the grantee institution does not have one)

6. Select Agent Research

Who must complete the “Select Agent Research” attachment:

Include a “Select Agent Research” attachment if your proposed activities involve the use of select agents at any time during the proposed project period, either at the applicant organization or at any performance site.

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page.

For more information:

Select agents are hazardous biological agents and toxins that have been identified by HHS or the U.S. Department of Agriculture (USDA) as having the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal and plant products. The Centers for Disease Control and Prevention (CDC) and the Animal and Plant Health Inspection Service (APHIS) Select Agent Programs jointly maintain a list of these agents. See the [Federal Select Agent Program](#) website.

See also the [NIH Grants Policy Statement, Section 4.1.24.1.1: Select Agents](#).

Content:

Excluded select agents: If the activities proposed in the application involve only the use of a strain(s) of select agents which has been excluded from the list of select agents and toxins as per [42 CFR 73.3](#), the select agent requirements do not apply. Use this “Select Agent Research” attachment to identify the strain(s) of the select agent that will be used and note that it has been excluded from this list. The CDC maintains a list of exclusions, which is available on the [Select Agents and Toxins Exclusions](#) website.

Applying for a select agent to be excluded: If the strain(s) is not currently excluded from the list of select agents and toxins but you have applied or intend to apply to HHS for an exclusion from the list, use this section to indicate the status of your request or your intent to apply for an exclusion and provide a brief justification for the exclusion.

All applicants proposing to use select agents: Address the following three points for each site at which select agent research will take place. Although no specific page limitation applies to this section, be succinct.

1. Identify the select agent(s) to be used in the proposed research.
2. Provide the registration status of all entities* where select agent(s) will be used.
 - If the performance site(s) is a foreign institution, provide the name(s) of the country or countries where select agent research will be performed.
 - *An "entity" is defined in [42 CFR 73.1](#) as "any government agency (Federal, State, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity."
3. Provide a description of all facilities where the select agent(s) will be used.
 - Describe the procedures that will be used to monitor possession, use, and transfer of select agent(s).
 - Describe plans for appropriate biosafety, biocontainment, and security of the select agent(s).
 - Describe the biocontainment resources available at all performance sites.

7. Multiple PD/PI Leadership Plan

Who must complete the “Multiple PD/PI Leadership Plan” attachment:

Any applicant who designates multiple PD/PIs (on the [R.240 - R&R Senior/Key Person Profile \(Expanded\) Form](#)) must include a Multiple PD/PI Leadership Plan. For applications designating multiple PD/PIs, all such individuals must be assigned the PD/PI role on the [R.240 - R&R Senior/Key Profile \(Expanded\) Form](#), even those at organizations other than the applicant organization.

Do not submit a Multiple PD/PI Leadership Plan if you are not submitting a multiple PD/PI application.

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page.

Content:

A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, including communication plans, processes for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PD/PIs and other collaborators.

If budget allocation is planned, the distribution of resources to specific components of the project or the individual PD/PIs should be delineated in the Multiple PD/PI Leadership Plan. In the event of an award, the requested allocations may be reflected in a footnote on the Notice of Grant Award.

For more information:

For background information on the multiple PD/PI initiative, see NIH's [Multiple Principal Investigators](#) page.

8. Consortium/Contractual Arrangements

Who must complete the “Consortium/Contractual Arrangements” attachment:

Include a “Consortium/Contractual Arrangements” attachment if you have consortiums/contracts in your budget.

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page.

Content:

Explain the programmatic, fiscal, and administrative arrangements to be made between the applicant organization and the consortium organization(s). If consortium/contractual activities represent a significant portion of the overall project, explain why the applicant organization, rather than the ultimate performer of the activities, should be the grantee.

Note: The signature of the authorized organization representative in [R.200 - SF 424 \(R&R\), Authorized Representative](#) signifies that the applicant and all proposed consortium participants understand and agree to the following statement:

The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the agency's consortium agreement policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy.

For more information:

Refer to the [NIH Grants Policy Statement, Section 15: Consortium Agreements](#) for more information.

9. Letters of Support

Format:

Combine all letters of support into a single PDF file and attach this information here. Do not place these letters in the Appendix.

Follow the attachment guidelines on NIH's [Format Attachments](#) page. Use of hyperlinks and URLs in Letters of Support is not allowed unless specified in the funding opportunity announcement.

Content:

Attach a file with all letters of support, including any letters necessary to demonstrate the support of consortium participants and collaborators such as Senior/Key Personnel and Other Significant Contributors included in the grant application.

Letters should stipulate expectations for co-authorship, and whether cell lines, samples, or other resources promised in the letter are freely available to other investigators in the scientific community or will be provided to the particular investigators only.

For consultants, letters should include rate/charge for consulting services and level of effort / number of hours per budget period anticipated. In addition, letters ensuring access to core

facilities and resources should stipulate whether access will be provided as a fee-for-service.

 Material Transfer Agreements may be included in this section.

Letters must focus on the topics listed above and not contain data / figures / tables / graphs, preliminary data, methods, background and significance details that are expected to be found in Research Strategy section of the application. Letters of Support serve to describe terms of a collaboration or consultation and also are not de facto letters of reference from persons not actively participating in the project. Applications with letters containing such excess information may be withdrawn from the review process.

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.

Do not include consultant biographical sketches in the "Letters of Support" attachment, as consultant biosketches should be in the "Biographical Sketch" section.

10. Resource Sharing Plan(s)

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page.

Content:

Data Sharing Plan: Investigators seeking \$500,000 or more in direct costs (exclusive of consortium F&A) in any budget period are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible (for example human subject concerns, the Small Business Innovation Development Act provisions, etc.). Specific FOAs may require that all applications include this information regardless of the dollar level. Applicants are encouraged to read the FOA carefully and discuss their data-sharing plan with their program contact at the time they negotiate an agreement with the Institute/Center (IC) staff to accept assignment of their application. **For more information**, see the NIH [Data Sharing Policy](#) or the [NIH Grants Policy Statement, Section 2.3.7.10: NIH Genomic Data Sharing](#) and [Section 8.2.3.3: Genomic Data Sharing \(GDS\) Policy/ Policy for Genome-Wide Association Studies \(GWAS\)](#).

Sharing Model Organisms: Regardless of the amount requested, all applications where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms or state why such sharing is restricted or not possible. **For more information**, see the [NIH Grants Policy Statement, Section 8.2.3.2: Sharing Model Organisms](#).

Genomic Data Sharing (GDS): Applicants seeking funding for research that generates large-scale human or non-human genomic data are expected to provide a plan for sharing of these data. Examples of large-scale genomic data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Supplemental Information to the NIH GDS Policy provides examples of genomic research projects that are subject to the Policy. For guidance on developing a Genomic Data Sharing Plan, please see [NIH Guidance for Developing Genomic Data Sharing Plans for NIH-Funded Studies](#). **For more information** see the [NIH GDS Policy](#), the [NIH Grants Policy Statement, Section 8.2.3.3: Genomic Data Sharing \(GDS\) Policy/ Policy for Genome-Wide Association Studies \(GWAS\)](#), and the [GDS](#) website.

Note on GDS: For proposed studies generating human genomic data under the scope of the [GDS Policy](#), an institutional certification may be submitted at the time of application submission, but it is not required at that time. The institutional certification, however, will be requested as Just-in-

Time (JIT) information prior to award. The institutional certification, or in some cases, a provisional institutional certification, must be submitted and accepted before the award can be issued.

For more information:

NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds, and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. See the [NIH Grants Policy Statement, Section 8.2.3: Sharing Research Resources](#).

11. Authentication of Key Biological and/or Chemical Resources

Format:

Attach this information as a PDF file. See NIH's [Format Attachments](#) page.

Content:

If applicable to the proposed science, briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies. A maximum of one page is suggested.

For more Information:

Key biological and/or chemical resources are characterized as follows.

- Key biological and/or chemical resources may or may not have been generated with NIH funds and: 1) may differ from laboratory to laboratory or over time; 2) may have qualities and/or qualifications that could influence the research data; and 3) are integral to the proposed research. These include, but are not limited to, cell lines, specialty chemicals, antibodies, and other biologics.
- Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.
- See NIH's page on [Rigor and Reproducibility](#) for more information.

Appendix

12. Appendix

Refer to the FOA to determine whether there are any special appendix instructions for your application. See the updated NIH Guide Notice on the [Appendix Policy](#).

Format:

A maximum of 10 PDF attachments is allowed in the Appendix. If more than 10 allowable appendix attachments are needed, combine the remaining information into attachment #10.

Use filenames for attachments that are descriptive of the content.

A summary sheet listing all of the items included in the Appendix is encouraged but not required. When including a summary sheet, it should be included in the first appendix attachment.

Content:

The only allowable appendix materials are:

- Blank data collection forms, blank survey forms, and blank questionnaire forms - or screenshots thereof
- Simple lists of interview questions

Note: In your blank forms and lists, do not include items such as: data, data compilations, lists of variables or acronyms, data analyses, publications, manuals, instructions, descriptions or drawings/figures/diagrams of data collection methods or machines/devices.

- Blank informed consent/assent forms
- Other items *only if* they are specified in the FOA as allowable appendix materials

No other items are allowed in the Appendix. Simply relocating disallowed materials to other parts of the application will result in a noncompliant application.

Some FOAs may have different instructions for the Appendix. Always follow the instructions in your FOA if they conflict with these instructions.

Note: Applications will be withdrawn and not reviewed if they do not follow the appendix requirements in these instructions or in your FOA.

Information that expands upon or complements information provided in any section of the application – even if it is not required for the review – is not allowed in the Appendix unless it is listed in the allowed appendix materials above or in your FOA. For example, do not include material transfer agreements (MTA) in the appendix unless otherwise specified in the FOA.

For more information:

- The NIH Guide Notice on [Reminder: NIH Applications Must Be Complete and Compliant With NIH Policy and Application Instructions At Time of Submission](#).
- Failure of reviewers to address non-required appendix materials in their reviews is not an acceptable basis for an appeal of initial peer review. For more information, see the [NIH Grants Policy Statement, Section 2.4.2: Appeals of Initial Scientific Review](#).
- [Appendix Policy Frequently Asked Questions](#)