Children's Minnesota Research Institute (CMRI)

Pre-Award Handbook for Principal Investigators

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Introduction

Children's Minnesota's Research Institute (CMRI) has developed this Handbook to ensure investigators and research teams understand the steps required to start a new clinical study or submit a grant. By describing the required steps and illustrating the resources CMRI staff can provide to investigators, we hope to make the application process more approachable and efficient. Your comments and suggestions concerning how to further improve these guidelines and our assistance are always welcome. Please send updates, feedback and recommendations to rsp@childrensmn.org

The purpose of the Handbook is to provide assistance to staff seeking internal or external support for research at Children's. It is intended to:

- Help investigators with the preparation of applications to sponsors,
- Inform investigators of major institutional and sponsor policies,
- Help investigators with non-financial administration of the award

This Handbook is not intended to duplicate policies and procedures already printed in other Children's documents; links are provided to these resources where available online.

The following documents, available on Children's StarNet, should also be consulted as needed:

- Safety, Security and Emergency Management
- Laboratory Services
- Institutional Review Board Documentation
- Policies and Procedures Online

1. Children's Minnesota Research Institute Programs Overview

Children's Minnesota Research Institute (CMRI) promotes and facilitates the development and implementation of quality research at Children's. We support new and established investigators in all stages of research development, implementation, and analysis. The work we do enables our investigators to explore novel ways to deliver life-saving treatments, manage pain and symptoms, and develop new methods for preventing or treating childhood diseases.

Mission
Collaborate with investigators and facilitate their efforts to generate new knowledge that benefits children and strengthens our capacity to serve the community.

Vision
All clinical programs will engage in research to improve care and contribute to the field of knowledge.

A. CMRI Administration Services

CMRI supports research at Children's through the following services:

- Providing research staff support
- Research design and statistical consultation
- Proposal development, implementation, and analysis
- Grant writing and submission
- Grants and clinical trial budget development
- Contract preparation and negotiation
- Manuscript review
- Coordination with the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Grant Accounting, Legal, and Compliance
- Training and education

1. CMRI responsibilities include:
    - Investigator support in research study planning.
    - Preparation and submission of proposals for program funding from government sponsors.
    - Preparation and submission of proposals for research and demonstration studies.
    - Oversight of management of grant and other revenue contracts.

2. Principal Investigators (PI) responsibilities include:
    - Submitting draft proposals and budgets on appropriate timelines for review.

- Submitting final proposals on appropriate timelines for submission.
- Completing IRB applications and other mandatory compliance for research integrity.
- Complying with terms and conditions, managing the scope of work, preparing required reports and managing sponsor funds per their award agreement and Children's policies and procedures.

B. Administrative Approval

The Director of Research and Sponsored Programs must approve and sign a research grant or contract for Children's Hospital. A Grants and Contracts Specialist must approve the final budget and application before it can be submitted.

C. Grants and Contracts Specialist

Your program may have a designated Grants and Contracts Specialist. Please refer to our listing below or contact the Director of Research and Sponsored Programs to identify your representative.

Grants and Contracts Services 2.0

Official business should be done through your corresponding Grants and Contracts Specialist (GCS). **If your designated person is unavailable and it is an urgent issue, please contact the other GCS or Camerone Bey.**

Contact your GCS FIRST for the following items:

- applying for grants (as the prime OR a subcontract)
- assistance seeking funding opportunities
- have an upcoming or potential clinical trial
- any contract or agreement related items (CTAs, Master Agreements, Amendments, DUAs, CDAs, NDAs, Grant Agreements, Subcontracts, etc)

Angela Plaisance, GCS Angela.plaisance@childrensmn.org 612-813-6142	Wendi Heuermann, GCS Wendi.heuermann@childrensmn.org 612-813-6303
Emergency Medicine/Trauma CV/CC Cystic Fibrosis Diabetes and Endocrinology Research	MCRC Hematology/Oncology Neonatal Research Pain & Palliative Care Genetics
Camerone Bey- Director, RSP. Camerone.bey@childrensmn.org, 612-813-7628	

(If you department is not listed, please contact either GCS or Camerone Bey.)

2. Finding Funding

Even the most innovative, effective, and relevant research endeavors cannot be successful without sufficient financial support.
Several types of projects are eligible for external funding:

- Research projects
- Outreach/Educational projects
- Training, instruction and QA/QI projects

CMRI supports funding efforts from both intramural and extramural sources. Below you will find a description of the major categories of research funding and how to find specific opportunities that best fit your research idea. See more in the appendix to this handbook.

A. Types of Sponsors

1. Federal
2. State/local
3. Foundations
4. Nonprofits, i.e., American Medical Association
5. Industry Funding

1. Federal Programs

The number of potential sponsors for clinical research large, and there is considerable diversity in each agency's operating authority, mission, methods of procedure and funding priorities. The most significant federal agencies funding clinical research include the Department of Health and Human Services (DHHS), National Institute of Health (NIH), National Science Foundation (NSF), and Department of Defense (DOD).

2. State and Local Programs

Limited funds are available from state and local governments to fund projects promising benefit to those under the area of their responsibility. Although much of this funding does not specifically require a research component, it does require evaluation and continued funding is contingent upon positive outcomes. Most competitive State of Minnesota RFPs are released bi-annually.

3. Foundations

Foundation awards support activities which will further the specific mission of that foundation. These include foundations with research programs and corporate foundation support. Funding priorities can also change from year to year; it is important to evaluate a foundation's RFP requirement annually. Research programs fall within Research and Sponsored Programs administration while direct service initiatives and gifts from private foundations, individual donors and corporations are handled by the Children's Hospital Foundation.

4. Nonprofit Organizations

Support for Children's research programs is available from a wide-range of nonprofit, public service organizations. Some are special purpose such as the American Cancer Society and the Epilepsy Research Foundation. Others are discipline oriented: The Foundation for Physical Medicine and Rehabilitation and American Academy of Pediatrics. In addition, there are a large number of nonprofits that fund the investigator through fellowships and new researcher awards.

5. Industry

Industry-sponsored projects can be supported either by an individual company or by a consortium through research contracts or clinical trials. Each industry-sponsored project is led by a Children's Principal Investigator (PI) who guides the research, shapes the resulting technology, and is responsible for the scientific coordination with the sponsoring company.

B. Internal Funding

Children's provides grants to advance clinical research. Awards are often used to seed pilot studies and projects to increase competitiveness for external awards. These funds are made available by The Children's Hospital Foundation and are awarded through the Children's Hospital Research Committee.

Internal Research Grant Program (IRGP)

Children's Research Committee provides an annual grant opportunity to Children's Hospital researchers through the Internal Research Grant Program. The IRGP is designed to improve investigator access to intramural support for research projects. It also establishes a more uniform process so all applications meet the same high standards and receive equal consideration. The Letter of Intent is generally due in March with applications due in June. For more information, contact Mike Finch at mike.finch@childrensmn.org

C. Identifying External Funding Sources

Winning grants and contracts depends on aligning your concept with the right source of funding. Source research and selection is part art, part science. Once you have a short list of prospective funders, further screen them by gathering information on previously supported projects or talk with a funder's program officer, scientific review advisor or previously funded investigators.

CMRI assists investigators in funding source identification, screening and selection through:

1. CMRI-conducted funding search for industry-wide initiatives.
2. Development of project-specific funding calendars and strategies
3. CMRI Newsletter and research group emails
4. Workshops and presentations

5. Collaboration with Children's Foundation to conduct a private foundation search

A list of funding resources is included in the Resources and Links section.

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3. Creating the Research Project

Children's Minnesota Research Institute partners with researchers throughout the proposal cycle. Planning is the first step. As soon as you decide to prepare a research proposal, contact your **Grants and Contracts Specialist (GCS)**. Your GCS will assist you with proposal preparation, including budget development and compliance checks.

A. Ideation or Project Development

Sponsors typically provide funding to achieve very specific objectives, in order to:

- solve problems, such as decreasing Emergency Department visits or a shortage in the nursing workforce.
- discover new knowledge through research studies and demonstration programs.
- translate knowledge to improve practice, such as patient centered outcomes research.
- provide services to benefit a population in need, such as the Native American Disparities Project.

Project development or *ideation* is a marginalized yet critical step to winning funding as winning ideas often:

- Have not been done before.
- Propose an approach that builds on lessons learned, established in literature.
- Incorporate a strong operational plan connecting goals, objectives, timelines and staff accountabilities.
- Define outcomes, measures and methods to evaluate the impact of sponsor funds.
- Demonstrate the applicant team has capacity to execute the plan.
- Share knowledge or know-how with a broader community.
- Address how the research or program will be sustained beyond sponsor funding.
- Approach the *right funder* whose purpose, method, funding level, etc. align with the project plan.

Anyone can write a grant proposal, but winning proposals come from PIs who commit sufficient time for project design and development, literature review, project team assembly and funding source selection, in addition to the time required for proposal writing, review and improvement. It is important to note that, on average, it takes 90 to 180 hours to write a proposal, but three to six months to develop a winning project design and plan.

For this reason, CMRI staff has experience in project development and can provide consultation on the following:

- Program or research plan development
- Funding source identification
- Sponsor guidelines and past funding analysis
- Budget development, integrating sustainability
- Proposal planning and writing
- Logic model development
- Evaluator, statistician and expert engagement
- Research compliance, such as the IRB process
- Electronic grant portals
- Proposal submission

B. Study Design/Data Analysis

The Design and Analytics group is available to assist internal investigators throughout the research process. Our group provides consultation services in the following areas:

- Study design (e.g. refine research question, estimate sample size)
- Analytic methods
- Grant proposal development
- Data management
- Data analysis and statistical support
- Manuscript preparation and review
- Research education

Please contact them at: Mike.Finch@childrensmn.org

C. Research Protocol Guidelines

The research protocol is the detailed written plan of the study. Writing the protocol forces the investigator to organize, clarify, and refine all the elements of the study. Therefore, **a protocol is necessary for all research studies**, including those that are unfunded, or that are seemingly simple in design and/or methodology.

A proper research protocol describes the background and significance of the study, the design, the methodology and procedures, the analytical approach and statistical methods, a statement of statistical power, and a discussion of risks associated with the study. But before an investigator writes these parts of the protocol, he/she must develop a good research question.

1. The Research Question

The most important element of any research protocol is defining the research question. If the investigator does not have a rock solid sense of what it is he or she is trying to achieve, what question exactly he or she wants to answer, it will be impossible to conduct a good study. All subsequent decisions about how to conduct the research follow from the clear statement of the research questions, and therefore, this should be the first thing a prospective investigator works out when contemplating a potential study.

All good research questions come from a thorough understanding of the current state of the relevant literature and the ability to articulate clearly what the key gaps in knowledge are that the investigator wants to fill.

A good description of the research question has several elements:

a. A general statement of the problem, the gap in knowledge, and/or the unresolved question that the study is seeking to address. There can be some description of the context that gives meaning to the research question, but the investigator should reserve a detailed description of the background for the "Background and Significance" section.

b. A numbered set of specific aims for the research. After defining the general question, the investigator then needs to identify the 2-4 specific pieces of information this study will provide as a means of helping to fill in the knowledge gap identified in step 1.

c. Hypotheses. Each specific aim should come with one or two hypotheses. A hypothesis is a statement about what the investigator expects his or her data will show if the theory of disease or medicine that he or she is using to explain and justify the hypothesis is true. A good hypothesis will be specific and will have directionality (*i.e.*, "treatment X will result in longer disease-free survival compared to current standard of care" rather than simply "treatment X will be different from standard of care").

The following is a simplified, hypothetical example of how one might describe the research question using this approach:

> Poor nutrition is known to be a major contributor to impaired growth and cognitive achievement in children. The specific aspect of nutrition (lack of protein or lack of total kcals) responsible for these developmental deficits is unknown. To address this question we will conduct a feeding study using a multi-factorial design with the following specific aims:
>
> 1. Identify the unique role of protein in childhood growth.
> **Hypothesis**: Children given protein supplements will grow better than those given placebo
>
> 2. Identify the unique role of supplemental kcals in childhood growth

Hypothesis: Children given kcal supplements will grow better than those given placebo

3. Determine the differential roles of protein and kcals in childhood growth. **Hypothesis**: Children given protein and kcal supplements will show improved growth beyond the multiplicative effects of each type of supplement given individually.

Many investigators who run into difficulties when trying to write effective protocols (or trying to make sense of their data after the study is complete) can trace their troubles to a poorly constructed or incompletely thought out research question.

This is also the most important part of the protocol for any reviewers who may have to approve the study or rate it for potential funding. If they cannot tell from the start what the investigator is trying to achieve, or if they think the investigator has not defined his or her aims clearly and in a way that leads to testable hypotheses that a study might reasonably answer, it will be hard for them to review the protocol favorably.

It is critical that this step be done well.

2. The Research Protocol

Having defined the research question, the investigator can move on to completing a protocol that will describe how he or she will attempt to answer the question, achieve the aims, and generate evidence to support (or refute) the hypotheses. The important sections of a research protocol are as follows:

a. Project Title

A concise, descriptive title will allow the reader to understand instantly what the research project is about even if the reader is not an expert in the specific field of study.

b. Study Team

The protocol should indicate who is the PI or Co-PI's. In addition, the protocol should list all other key personnel. This would include any co-investigators (personnel who will be providing creative, intellectual effort or who will be providing expertise or unique resources to the study), the research coordinator, research associate, research assistant, pharmacist, lab scientist, and statistician. Not all studies will require each of these roles, and some may require additional roles. The description of the study team should also list any consultants who may contribute to the study. Descriptions of personnel should also indicate their institutional affiliation(s) – especially important if collaborating with investigators outside of Children's.

c. Research Question and Specific Aims

As described above, the statement of the research question should come immediately after the listing of the study personnel and before the background and significance. It will be the point from which all subsequent sections of the protocol follow.

d. Background and Significance

This section sets the study in context and gives its rationale. What is currently known about the topic (cites all relevant studies and developed a synthesis of these as a means of explaining what we know)? What are the important gaps in our knowledge and understanding of the field? From this description it should be easy to construct a logical argument as to why the proposed research question makes sense and is important to answer. The amount of background information depends on the nature of the study and the risks involved.
A key component of this section is a compelling description of the significance of the study if it were to achieve its aims. The significance should take into consideration the study question's relevance to the goals of the institution, to the significant advancement of knowledge in the field, and to the practice of medicine. In other words, how will this study make a difference? And how important is that difference? Studies do not need to produce Nobel Prize-worthy results to be good studies, but all good studies should have the potential to produce impact. Explaining the importance and significance of a study is paramount to the success of a research study.

e. Study Design and Methodology

Study Design: The study design is the approach that is taken to answer the research question. Examples of study designs include the following: ecological, case study, case series, cross-sectional, case/control, cohort, and clinical trial. The investigator should do more than name the design, however. This section should include a detailed description of how the investigator will implement the design, one that specifies all the relevant design elements (e.g., a general description of the subjects, where they come from, what the relevant exposure is and how it will be assessed, what is the comparison, how will that comparison be set up through the study design, what type of follow-up will there be if there is any, and what are the outcomes?).

Subjects: Having laid out the design, the investigator then needs to describe in detail that the subjects are and how the recruitment will happen.

Inclusion Criteria: In this section the investigator should describe the characteristics of the subjects who will be enrolled in the study. These criteria should be well thought out and as specific as possible. The inclusion criteria should identify the precise subjects who will be best suited to provide the data that will answer the research question. Important considerations include (but are not limited to) age, sex, disease status, demographics, language requirements, co-morbidities, and social/family factors. If the protocol includes the enrollment of special groups whose ability to give valid consent/assent may be questioned (*e.g.*, mentally disabled people) the protocol must provide justification for their inclusion.

Exclusion Criteria: In this section the investigator should describe any characteristics that will lead to a subject being excluded from participating in the study. To avoid redundancy, the exclusion criteria should not simply be logical opposites of the inclusion criteria (*e.g.*, if one inclusion criterion is "children with disease X" there is no need to list as an exclusion criterion

"children without disease X"). It is also not essential to have both inclusion and exclusion criteria, just so long as the eligibility requirements are clearly defined.

Recruitment: Describe how you will identify and recruit potential patients. All recruitment materials must be included in the Appendix.

Enrollment: This section should include a description of the consent process, specifying at what point this process will occur. In a randomized trial, consent must occur before the randomization.

Study Procedures: This section should provide a complete, detailed explanation of the study procedures. In cases where information given to the subjects as to the procedures and purposes of the study would invalidate the objectives (e.g., a blinded study), the investigator should report to the IRB reasons for not informing subjects of the procedures and purposes and if applicable, for debriefing subjects after the procedures are completed.

This section should contain an outline of what each subject will be asked to do as a participant in the study once enrolled.

- What measurements will be done at baseline?
- What intervention, if any will be done? What will the subject have to do to complete the intervention?
- How will the investigator assess compliance?
- What are the follow-up procedures? What will the subject have to do during the follow-up period? How will the investigator track the subjects? What will subjects have to do at the conclusion of follow up? What is the exit protocol for the study subjects, if relevant (typically useful in clinical trials)?
- How will the investigator assess endpoints? What are the end points? How are they measured?
- Will any questionnaires be used to collect data from subjects? How valid are these? Will these be self reports or interviews? Who will manage questionnaire responses and how?
- What laboratory procedures, if any, will be used? How valid are these? Who will do them?
- What data management procedures are planned?

Visit Schedule: If the study involves multiple clinical assessments, a visit schedule is highly useful. The visit schedule provides a quick reference of all protocol requirements. It is a map or plan of what the investigator is expected to do at each critical time point.

Drug/Device, Handing, Storage (If Applicable): Any special procedures involving radioisotopes, investigational new drugs (IND's), or investigational devices (IDE's) must be described and appropriate approval for their use must be documented.

Patient Withdrawal, Completion, and Death: In this section you must describe what procedures will be completed and what you will do with the data when a patient withdraws from the study, completes the study, or dies during the study. It is important to clarify whether the data will be included in the data set if you are not able to collect all required data points.

Time Frame/Duration: What is the duration of the study? The investigator should provide a timeline detailing the when each phase of the study will be conducted.

f. Analysis

Power or Effect Size: A good research study must be sufficiently powered (*i.e.*, must enroll a sufficient number of subjects) to allow for the identification of differences in effects between exposed and unexposed subjects that are clinically meaningful and statistically different from chance. The smaller the anticipated difference between groups, or the greater the normal variability in the outcome, the larger the required sample size to rule out chance as an explanation for that difference. In studies with a fixed sample size (where the patient population is of a known and relatively unchanging number – for example, current cystic fibrosis patients at Children's), a sample size calculation is not relevant. Instead, the investigator should provide an effect size calculation. This will specify the minimum difference in effect that the study will be able to detect between groups. In studies without a practical limit on potential patient enrollment, the investigator should specify the clinically meaningful difference he or she expects to see in the study and then do a sample size calculation to identify the number of subjects required to see such an effect. When reporting these values, investigators should specify the (usually 0.05) and β (usually 0.80, but sometimes higher) used in the calculations.

Analytic Approach: The analytic approach starts with a description of how the investigator will organize the relevant comparisons for determining the effect of the exposure on the outcome. This should include a description of the exposure and a description of the outcome for each analysis the investigator is planning. These descriptions should follow directly from the specific aims and their corresponding hypotheses. Having defined the comparisons, the investigator should then specify the statistical test(s) he or she will use to determine whether the differences between groups are likely due to chance or not. Which test to use is a function of the type of data available and the nature of the comparison being made. For observational studies, the investigator should specify his or her plan to address the issue of confounding. If the investigator is considering effect modification or interaction as a potentially-important element for assessing the data, he or she should specify the proposed effect modifiers *a priori* and provide a strategy for addressing this issue.

A note on p values: It is not necessary to identify what p value the investigator will consider "significant." The conventional value is 0.05, and this number is so well established it is not informative to specify that choice. More importantly, this number is arbitrary and its use is often poorly understood. A p value is not a result. A p value merely indicates the probability that the result was different from chance. It is never acceptable to report p values (or values of

test statistics such as a chi square or t statistic) as primary findings from a study. In most studies, it is not desirable simply to report a result as "significant" because the p value for the statistical test in less than 0.05. What the investigator should report is the magnitude of the difference between exposed and unexposed groups, and then he or she should indicate the likelihood that that result is different from the null value by referring to a p value.

g. Risks/Benefits

Potential Risks: The investigator must describe any potential physical, psychological, emotional, social, economic, legal, or confidentiality risks. IRBs are required to assess all risks to subjects, not just physical risks. For example, collecting medical record data for research purposes presents the risk of a breach of confidentiality for the research subjects. Use of existing, de-identified data in an observational study does not involve risk and will be ruled exempt from IRB review, but the formal request for exempt status must be submitted to the IRB who will have final say in this determination. There are no studies enrolling new patients without at least some risk. At a minimum there will always be the risk of breach of patient confidentiality. These all require formal IRB review, though in some cases it may be possible to obtain expedited review. It is strongly advised that investigators consult the IRB administrator before completing a research protocol.

Methods to Minimize Risks: The investigator must describe how any risks will be minimized.

Potential Benefits: There are two types of benefits: 1) those to subjects, and 2) those to science/society, such as contributions to generalizable knowledge. If the subject will not receive direct medical benefit then this fact should be explicitly stated both here and in the consent form. It is unethical to mislead subjects into thinking they will directly benefit when they will not.

Adverse Events: Adverse events must be defined in this section. What will be considered an adverse event? What steps will the investigator take if an adverse event occurs?

Stopping Rules and Data Safety Monitoring Plan**:** For clinical trials, the investigator must detail the sequence of events that will determine if the project is to be terminated. This could include a) evaluation of individual stopping rules; b) evaluations of several individuals as aggregate data; c) determination of the likelihood that the adverse events are drug related; d) determination if the severity of study related adverse experience(s) is judged extreme, etc.

h. References

The investigator should list the references used to develop the background and significance section and potentially in the methods section if referring to established procedures validated by others.

i. Appendix

The investigator should include all additional, relevant materials in the Appendix. This might include the following: Data Collection Forms (DCFs), including abstract sheets, questionnaires, interview questions, phone screenings, solicitation letters, surveys, etc. If the investigator is

using an existing instrument, he or she needs to document the validity of that instrument in the methods section.

4. Proposal Development

A. Responding to an RFP

As soon as you know you will be applying for external funding, contact your Grants and Contracts Specialist and provide them with a copy of the proposal announcement.

Plan on meeting with your GCS to develop a budget. Areas to think about are personnel and their time, supplies, travel, etc. A Budget Template is available to help you develop your budget. Your GCS must approve the budget before the proposal can be submitted.

Most sponsors have specific application forms that must be followed in detail. Your GCS will help to complete these forms and check for errors.

Let your GCS know if there will be subcontracting institutions or consultants. They will work with the other institution to ensure all paperwork and approvals are in place.

If the PI has a third-party offering matching funds, a commitment letter from the third-party must be sent to CMRI administration. This commitment letter must specifically outline the matching funds for the project.

Only CMRI Administration can submit a research grant on behalf of Children's Hospital.

Your GCS will ensure the proper forms have been completed and signed, and will review the budget to ensure accuracy and that Children's interests are represented. In addition, your GCS will review the application to certify that it follows sponsor guidelines and includes all required paperwork. If requested, CMRI staff will read over the application for grammar and formatting.

To ensure adequate time for review and approval, all application materials must be submitted to CMRI no later than **five (5)** working days before the due date to the sponsor. Your GCS will review the application, suggest changes if required per guidelines and work with the PI to make these changes. If the sponsor requires paper copies, your GCS will print and copy as well as mail out the submission.

If awarded, CMRI Administration will work with the sponsoring agency to negotiate award.

B. Steps of Proposal Development

Step 1 – Literature search
Step 2 – Assemble team
Step 3 – Meet with CMRI's Design and Analytics Team
Step 4 – Write first draft
Step 5 – Draft budget with GCS
Step 6 – Finalize proposal and submit

Step 1 – Literature search
Initiate a preliminary literature search to identify what has already been published in your area of pursuit. Be confidant that your subject matter is one that has not been addressed or that your methods improve on pre-existing study designs, and/or your population may yield unique results.

Literature Searches
For assistance with literature searches, to obtain full text journal articles, or to conduct you own literature search using either PubMed/MEDLINE or OvidSP/MEDLINE, go to Allina Health Library Services or email Library Services. For OvidSP. For OvidSP, use any of the generic logins IDs: ahs4390, ahs4391, ahs4392, ahs4393, or ahs4394. The password for each is chclib.

Step 2- Assemble team
Identify and assemble team members who can lend their support and expertise of the project. Schedule meetings to work through program ideas, budget items, letters of support, etc.

Step 3- Meet with CMRI
If you have not done so already, contact Mike Finch to schedule an initial meeting with CMRI's Design and Analytics team. Topics covered during this meeting will be: project feasibility, the literature review process, study design, technical writing support, and timelines.

The Design and Analytics team will also discuss with you:

- The study question and its significance
- The study design: population, sample size, measurement tools, etc.
- Methods for evaluation (survey, analytic)
- Database specification to support the research project
- Post study data collection services
    - Analysis
    - Support in reporting for presentation and publication

Once you have identified the funding organization, contact your Grants and Contracts Specialist so that they can go to their website and carefully review ALL details of the proposal guidelines. Your GCS will prepare a proposal checklist; maintain copies of all completed forms and required attachments.

TIP: Quick facts is a compilation of information frequently requested by sponsors including who signs proposals, what our DUNS and EIN #'s are, what congressional district Children's is in and much more!

Step 4 – Write first draft
Begin crafting your first draft. Follow the funding agencies' project description in detail to make sure that you include all of the requested information. Flesh out ideas and determine timeline for drafts.

TIP: Insert references as you go.
TIP: Give specific writing assignments to appropriate team members based on their expertise. Set up timelines for delivery of each segment.

Step 5 – Draft budget
Work with your Grants and Contracts Specialist to create the internal and external budget. Provide your GCS with copies of your grant narrative to make sure that all budget items have been identified. The final budget must be approved by your GCS prior to submission.

Step 6 – Finalize proposal
Complete proposal. Ask peers to review for content, relevance and study design. Finalize proposal items and proposal checklist with your GCS. Submit all proposal materials to your GCS institutional signatures and for submission.

C. Components of a Research Grant Application

Though each funder is unique, most proposals request for the following items:

1. **Title/Cover Page**: Often provided in grant application package. Provides factual information on the project such as project director's name and contact information, organization contact information, etc.
2. **Abstract**: The Abstract contains the Project Summary which briefly describes the proposed work, long-term objectives, specific aims and research design and methods. Also, describe the relevance of this research to clinical and health policy, public health, or future research directions.
3. **Statement of Need and Significance**: Cite all relevant studies and develop a synthesis of these as a means of explaining what we know. A key component of this section is a compelling description of the significance of the study if it were to achieve its aims. The significance should take into consideration the study question's relevance to the goals of the institution, to the significant advancement of knowledge in the field, and to the practice of medicine.
4. **Program Plan or Research Plan:** The goals, objectives and action steps of the program should be clearly delineated. May use or reference a program plan (logic) model. For research plans, this is where you outline your aims, sub-aims, target population, critical variables, data sources, and data collection and analysis.
5. **Study Design and Method (Management Plan)**: The study design is the approach that is taken to answer the research question. Examples of study designs include the

following: ecological, case study, case series, cross-sectional, case-control, cohort, and clinical trial. This section should include a detailed description of how the investigator will implement the design, one that specifies all the relevant design elements (*e.g.*, a general description of the subjects, where they come from, what the relevant exposure is and how it will be assessed, what is the comparison, how will that comparison be set up through the study design, what type of follow-up will there be if there is any, and what are the outcomes?).

6. **Evaluation Plan:** Indicates internal and external evaluation strategies. Describe how, when and by whom the outcomes of the project will be measured and analyzed.
7. **Dissemination Plan:** Describe how project outcomes, data, and products (if applicable) will be shared with larger audiences.
8. **Sustainability Plan:** Describe plans to continue the program or to advance the research beyond the grant.
9. **Institutional Capacity and Resources**: Describe the internal skills, staffing, support, facilities, equipment and other support available to conduct the research.
10. **Budget and Budget Justification:** Indicates, within the parameters provided, amounts requested from the grantor and others sources (matching funds). The justification provides calculations and descriptions for each budget item.
11. **Letters of Support or Commitment:** Letters that indicate a valuable commitment to the work you are proposing. Commitment letters outline specific intentions and roles of project collaborators. Support letters are a more general reinforcement of the proposal, organization or person proposing to do the work and should emphasize the need the proposal addresses.
12. **Resumes/Bio-Sketch:** Information on the experience and roles of key staff in relation to this project. A specific staffing plan would be further detailed the overall management plan of the proposal.
13. **References:** Include literature cited and/or bibliography
14. **Assurances and Certifications:** Grantees sign assurances committing to basic contractual obligations. This is further detailed in the award management and compliance sections of this manual.

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5. Clinical Trials

In this section, we hope to facilitate quality clinical trial research, providing effective and efficient evaluation of new pharmaceuticals and medical devices. Your Grants and Contracts Specialist can assist principal investigators (PI) with trials that are funded by federal, state and foundation grants and industry contracts, including investigator-initiated trials. Grants and Contract Specialist services include comprehensive budget development and contract negotiation and regulatory guidance.

A. Human Clinical Trial Phases

Phase I studies assess the safety of a drug or device. This initial phase of testing, which can take several months to complete, usually includes a small number of healthy volunteers (20 to 100), who are generally paid for participating in the study. The study is designed to determine the effects of the drug or device on humans including how it is absorbed, metabolized, and excreted. This phase also investigates the side effects that occur as dosage levels are increased. About 70% of experimental drugs pass this phase of testing.

Phase II studies test the efficacy of a drug or device. This second phase of testing can last from several months to two years, and involves up to several hundred patients. Most phase II studies are randomized trials where one group of patients receives the experimental drug, while a second "control" group receives a standard treatment or placebo. Often these studies are "blinded" which means that neither the patients nor the researchers know who has received the experimental drug. This allows investigators to provide the pharmaceutical company and the FDA with comparative information about the relative safety and effectiveness of the new drug. About one-third of experimental drugs successfully complete both Phase I and Phase II studies.

Phase III studies involve randomized and blind testing in several hundred to several thousand patients. This large-scale testing, which can last several years, provides the pharmaceutical company and the FDA with a more thorough understanding of the effectiveness of the drug or device, the benefits and the range of possible adverse reactions. 70% to 90% of drugs that enter Phase III studies successfully complete this phase of testing. Once Phase III is complete, a pharmaceutical company can request FDA approval for marketing the drug.

Phase IV studies, often called Post Marketing Surveillance Trials, are conducted after a drug or device has been approved for consumer sale. Pharmaceutical companies have several objectives at this stage: (1) to compare a drug with other drugs already in the market; (2) to monitor a drug's long-term effectiveness and impact on a patient's quality of life; and (3) to determine the cost-effectiveness of a drug therapy relative to other traditional and new therapies. Phase IV studies can result in a drug or device being taken off the market or restrictions of use could be placed on the product depending on the findings in the study.

B. Evaluating the Proposed Trial

Many Children's Minnesota investigators are approached to evaluate and participate in industry-sponsored clinical trials. The questions below can help the investigator determine if they would like to proceed with the project:

1. Questions to Review:
    - Does the protocol provide scientific value?
    - Will I be able to subjects?
    - Does the budget support the work to be performed?

If you cannot answer yes to each of these questions – then you may decide to decline the trial.

2. Evaluation Steps
   - Analyze the protocol
   - Study the Case Report Form (CRF)
   - Know your costs and overhead
   - Reconcile the schedule of events with the budget
   - Communicate with the study team to ensure they agree with the assessment

3. Site Obligations

In determining the budget, you will need to examine the site obligation. The budget services to map out the assumed costs associated with conducting a clinical trial, both directly and indirectly. Typically the budget will include the estimated per subject cost as well as the total cost for completing the study.

Other site obligations will include:

- Regulatory compliance
- Data collection
- Record retention
- Adverse event reporting
- Financial disclosure of key personnel (PI, Co-Inv, CRC)
- IRB and informed consent
- HIPAA
- Inspections

6. Budget Development

Sometimes budgets developed as part of program planning must be adapted for specific proposal submissions. While all budgets follow a common format, funder guidelines introduce unique rules. However, all budgets must ensure revenues are sufficient to cover project costs and expenses are allowable, allocable, reasonable and consistent with how the same costs are treated across Children's departments.

Generally, 2 budgets are created for each project. The Internal Budget is created to satisfy the business requirements of Children's. The External Budget is created to satisfy the requirements of the funder/sponsor.

A. Internal Budget

Develop the Internal Budget with your Grant and Contracts Specialist (GCS). This budget will be used to create the external budget for your proposal.

Use Children's Budget Planning Spreadsheet and:

1. Identify personnel costs; estimate effort
    - Budget adequate effort to get the work done.
    - Define who will work on the project:
    - Number of people, variety of expertise, and level of effort involved
    - Be cognizant of staffing needs that may change over the life of the grant
      (Individuals on Children's payroll are personnel
      Non-Children's personnel participate as consultants or subcontractors)

2. Calculate non-personnel services (equipment, supplies, travel, other)
3. Equipment - Items costing >$5,000 with a useful life of more than one year
   If your equipment requires special installation or renovation, contact YOUR GCS.
4. Supplies/consumables
    - Instrumentation (costing <$5,000, unless otherwise specified by sponsor), e.g., tape recorders, digital cameras, etc.
    - Office supplies – must be essential for your project and well justified as they are typically paid for in facilities and administrative costs.
    - Animals (must have IACUC approval prior to acquisition & use)
5. Travel
    - Domestic or international travel (be specific)
    - Conference registration fees
6. Subcontracts/Collaborators/Consultants
7. Other Expenses
    - Transcription/translation
    - Poster expenses
    - Equipment service agreements
    - Specialty software and licensing
    - Publication/copying
    - Phone, Fax, etc., if appropriate
    - Advertising for recruitment(subjects or personnel)
    - Mailings
    - If hosting a conference, participant costs
    - Patient reimbursement/incentives
      Subject Reimbursements and Incentives
      All subject reimbursements and incentives need to be a part of the project's financial planning spreadsheet and have approval by the IRB before any payments can be processed. Your HIPAA Authorization form should indicate that Finance will view the following Protected Health Information (PHI) for each subject:

- Name
- Home address
- Social Security number

8. Use study schema to identify patient care costs; itemize all patient care expenses. What is standard of care? What is research-only?
9. Request ancillary services (radiology, pharmacy, etc)
10. Complete project budget spreadsheet; send electronically to your GCS

B. Ancillary Services Contacts:

Contact these departments for pricing and details of ancillary services	Contact	Description of services
Pharmacy	Charlet Allen	Investigational drug services
Radiology & Imaging Services	Chart Master	X-ray, CTs, MRI, MUGA
Clinical Laboratory Services	Jennifer Jacobson	Ventipuncture, blood processing, clinical lab tests
All other services pricing	Chart Master	Tissue collection, pathology reads, etc.

C. Clinical Trials Budgets and Patient Service Grid

The Grants and Contract Specialist will work directly with you and your study team to ensure an appropriate budget is developed. You will need to identify all the procedures in the protocol as either standard of care or research related. A key point in making this decision is to recognize if the patient would have the service regardless if he or she is enrolled in the protocol. If the answer is no, then the sponsor must cover the expense of the service.

In addition to billable patient services, the budget must include salary support for coordinator or other support staff, overhead, CMRI/Departmental set-up fees and invoiced items. Salary support is determined by estimating the number of hours each task will require, taking into account time for data entry, query resolution, regulatory document maintenance, etc. All industry clinical trials must include a 38.4% indirect rate per the Children's Hospital F & A policy. Set up costs are non-refundable fees due once the CTA has been executed. These costs might include:

- Start up costs (salary support for regulatory document & IRB submission, trainings, etc)
- Contract & budget negotiations
- Pharmacy & lab startup fees

If your sponsoring organization does not provide you with a patient service grid, please contact your Grants and Contracts Specialist for help in setting one up.

D. Institutional Endorsements

Children's Minnesota Research Institute (CMRI) assists Children's staff with the proposal preparation process. Timing is essential; please contact our office as early as possible. Please refer to the following guidelines to assist you with your proposal's internal review and approval.

Obtaining Required Signatures

Each proposal will require institutional signatures; Camerone Bey, Director of Research and Sponsored Programs must sign these documents prior to submission. Your Grants and Contracts Specialist will assist you in obtaining these final signatures. These items may include:
-Cover letter
-Grant Cover Sheet
-Budget pages

When to Route

All proposals involving NEW money (*i.e.*, money not already awarded) should be routed through CMRI Administration prior to being submitted to the sponsor.

Please forward these directly to the Grants and Contracts Specialist:

- Award notices for proposals that have already been routed
- Requests or authorizations for additional time
- Draft contracts
- Requests to carry-forward money
- Requests or authorizations for re-budgeting

Why to Route

Routing information will be used to:

- Establish the eligibility of an individual to be a PI
- Define the appropriate department to receive recognition for the proposal and award
- Identify the location of the project
- Identify the correct human and/or animal protocols associated with the project
- Identify any proposed cost sharing, and whether it is mandatory or obligatory

Routing Responsibilities - All parties should read and understand the certification before signing.

1. **Principal Investigator/Project Leader** for the proposed project is responsible for 1) the technical content and quality; 2) assuring that the project and other professional activities are compatible; 3) ensuring that no individuals will have commitments in excess of 100 percent effort; 4) accepting responsibility for the proper technical and financial conduct of the project as indicated in the certification statement on the routing form; and 5) obtaining approval signatures from the Medical Director/Chief for the proposed project, before being sent to CMRI.

2. **Institutional Endorsement** is provided by CMRI. The CMRI Administration Director's signature indicates that 1) Children's and sponsor policies have been met; 2) all approvals are obtained; 3) the budget is in order; 4) unusual requirements or commitments are brought to the attention of the Children's administration; and 5) the application is complete; and 6) verification of regulatory compliance, (e.g., human subjects and/or animal care protocols) are approved. CMRI requests a minimum of 2 weeks to process each grant application. If it is a contract proposal, negotiation and approval may take longer.

7. Award Agreements & Contract Management

CMRI Administration is responsible for working with investigators on all aspects of contract negotiations. Upon notification of a federal grant, CMRI will receive the Notice of Grant Award and review. Such notices are in a standard federal format and thus do not need to be negotiated nor signed. Many foundation grants are similar, and may only require an agreement signature from the CMRI Administration Director.

Federal and state contracts and commercial sponsor contracts are more specialized and require careful reading and, many times, negotiation between Children's and the sponsor. These contracts are legal documents that define publication, indemnification, confidentiality data ownership and intellectual property rights. If any of the language in the sponsor's contract is unacceptable, your Grants and Contracts Specialist will work directly with the sponsor to negotiate mutually acceptable language. Children's Legal Department must provide final approval before language can be returned to the sponsor.

CMRI Administration is responsible for:

- preparing, interpreting, negotiating and accepting grants on behalf of Children's Hospital for sponsored projects.
- preparing, submitting, negotiating and accepting all federal, state, city/county, contracts and subcontracts for research and clinical services.
- preparing, interpreting, negotiating and accepting all research agreements with for-profit companies and non-profit organizations.

A. Award Review/Negotiation

1. CMRI receives the award documentation.
2. CMRI reviews award details to confirm that the agreement matches the proposal and confirms the details with the PI. The budget reflects the amount awarded and the correct indirect costs calculation. The dates of the research match what was proposed and that there are no gaps in funding. The researcher is aware of any changes to the terms and conditions of the award, or is aware of terms and conditions that could impact the intellectual property or performance of work. Any change in scope of work.

3. CMRI submits agreement to Legal Department for review. CMRI submits revisions to the sponsor for review.
4. CMRI reviews and negotiates the terms and conditions of the sponsored research agreement.

Every award is reviewed to ensure the terms are consistent with federal laws and regulations, comply with Children's Hospital policies, and meet the needs of our researchers.

B. Contracts Management

Sub-award, consulting and other agreements paid with sponsor funds must be processed through CMRI to ensure forms align with Children's policies and sponsor's unique terms, certifications and regulatory requirements.

Sub award Agreements

The general process for creating outgoing sub award agreements is:

- CMRI integrates Sponsor requirements and the investigators' approved work plan and budget to create the sub-award package.
- PI drafts & routes sub-awardees action steps, scope of work, deliverables, and budget to CMRI.
- CMRI submits documents to legal for review and changes
- CMRI finalizes package changes and sends to sub-awardees for signature.
- Additional changes and negotiation between sub-awardees, CMRI and Legal Dept. may be necessary.
- Signed contracts/agreements are routed to all investigators and departments involved. CMRI maintains copies for recordkeeping.

Clinical Trial Agreement Process

In order to reduce the start-up time for industry-sponsored clinical trials, the language of the contract and financial terms can be negotiated concurrently with the submission of regulatory documents and IRB application. CMRI can start working to negotiate the terms of the agreement. You or your study team will need to send the following items to your GCS electronically:

- Study protocol
- Sponsor's template clinical trial agreement
- Sponsor's budget proposal

Your GCS works with Children's Legal Department who must provide their final approval before language can be returned to the sponsor.

C. *Types of Agreements*

Clinical Trial Agreement
For every clinical trial performed at Children's, there is a research agreement called the Clinical Trial Agreement (CTA) that is negotiated between Children's Health Care (the legal contracting name for Children's Minnesota) and the sponsor, or the Contract Research Organization, representing the sponsor. The CTA is a legal document and defines the important issues such as conduct of the study, publication, indemnification, confidentiality and data ownership.

Collaborative Research Agreement
A collaborative research agreement is a contract between organizations that wish to work together but generally do not want to exchange funding. Collaboration agreements are not considered sponsored research, per se, but govern the exchange of equipment, data and inventions. A funded collaboration agreement is sponsored research as the sponsor provides funding and other resources for the collaboration.

Confidentiality Agreement (CDA) or Non-Disclosure Agreement (NDA)
Before the sponsor will share the protocol with the PI, a CDA or NDA must be signed between the two parties. This is a legally binding document. A CDA or NDA requires an institutional signature and therefore must be routed through CMRI for review and approval prior to signature.

Data Use Agreement
A data use agreement (DUA) is an agreement required by the Privacy Rule between a covered entity and a person or entity that receives a limited data set. The DUA must state that the recipient will use or disclose the information in the limited data set only for specific limited purposes.

Gift
Gifts provide general, unrestricted support for broadly defined activities in one or more program areas. Reporting procedures are usually minimal to none. Rights to patents/copyrights are not retained by the donor and no provisions are imposed by the donor concerning publication of data and information derived from the activity.

Grant
A grant is support for a specific project that is designed by the funds recipient. The sponsoring agency has expectations about how the funds are spent and the project usually has stated goals, objectives, deliverables and financial reports.

Master Agreement with Addendum

On occasion, some non-federal sponsors that fund multiple research programs at Children's with frequent awards will ask to negotiate a single Master Research Agreement (MRA) that will govern all research activities supported by that sponsor at Children's. As with Sponsored Research Agreements, the MRA is a contract between Children's and the sponsor; it specifies the obligations of Children's and the sponsor in funding and conducting any scope of work that the sponsor may propose. With MRAs, however, all the project-specific information is combined into an addendum. New addendums are submitted to Children's in order to fast track new projects or programs.

Material Transfer Agreement
A material transfer agreement (MTA) is a contract between two parties that defines all of the terms, conditions, expectations, and deliverables associated with the receipt and use of materials by one or more Children's researchers from a party (company, non-profit, university, institute, government, individual, etc.) external to Children's.

Memorandum of Understanding
A Memorandum of Understanding is a non-binding memorandum between Children's and one or more organizations planning to create a new cooperative research and/or education program. MOUs attempt to outline the type of relationship that will be created, the objectives for the relationship, and the actions that each party plans to take to bring the program into existence. The planned activity may or may not come to fruition as described in the MOU, but there is no penalty for failure

Sub awards
A sub award (subcontract) is an agreement that uses sponsored research funding to engage an institution or agency outside of Children's to perform a specified scope of work. The scope of work may or may not include deliverables. CMRI is responsible for processing and set up of all sub awards. Terms and conditions for sub award agreements flow down from the prime award, especially when federal funding is involved.

8. Managing Projects

After an award has been issued and the terms and conditions of the award have been agreed to by both parties, it is the responsibility of the PI to ensure that these requisites are followed. Because a variety of different issues may arise during this phase of a sponsored project, it is important to review the notice of award to see what specifications are listed. Please contact your GCS if you are unsure of any of the guidelines or terms and conditions of the award.

A. Research Staff Hiring

All Research staff hires are initiated through CMRI. Dependent upon the hours required, work to be completed and skill level needed, CMRI will first call upon existing Research staff to determine if there is a compatible staff person available. Should the need arise to hire a new staff person, CMRI will coordinate the hiring process with you to ensure the appropriate research staff is hired.

B. Changes to Programs during the Life of an Award

When a grant or contract is awarded in response to a proposal, the sponsor expects the project to be carried out in accordance with the proposed scope of work and budget and sponsors may evaluate the project against the budget at any time. Since the course of research is often uncertain and circumstances can change, sponsors must make provisions for adjusting the scope of work and budget throughout the life of an award. All requests for changes must be in writing and endorsed by your GCS.

C. Monitoring Project Budgets

Depending on the terms of the award, you may be required to submit a revised budget to the sponsor, explaining the need for re-budgeting project costs. You should first check the sponsor's award document to see if the sponsor has specific guidelines for when a revised budget is required.

If a budget is required, it should be submitted to the GCS for review. The GCS will then work with you on the revision and submission of the new budget to the sponsor. In some cases, a budget will not be required for submission to the sponsor; however, it is a good idea to build a projection based on the new budget so that you can maintain an accurate profile for the project. It is not uncommon for a PI to determine that he/she must re-budget funds in order to complete his or her research.

D. No-Cost Extensions

A no-cost extension extends the project period beyond the original project end date. As the phrase "no cost" suggests, there is no additional funding. A no-cost extension may be requested by the PI when all three of the following conditions are met:

- The end of the project period is approaching, AND
- There is a programmatic need to continue the research, AND
- There are sufficient funds remaining to cover the extended effort

Written requests for no-cost extensions should be prepared by the PI and then endorsed and submitted by your GCS. Some sponsors have developed electronic systems to handle no-cost extension requests and approvals. Call your GCS if you have questions.

9. Research Compliance & Regulatory Support

A. Regulatory/Compliance Issues

Children's investigators are required to conduct research and manage the financial aspects of research in compliance with Hospital policy, federal and state laws, and sponsor requirements. Principal Investigators must ensure that they, their fellow investigators, and staff meet compliance requirements, including any necessary training.

Below are the frequent areas of compliance to consider when preparing a proposal.

Conflict of Interest (COI)
According to Children's Policy #1048, a conflict of interest exists when an individual's decision-making may be influenced by outside employment, business arrangements, or personal or family contacts. A conflict can result when you have a financial, business, or family relationship with a competitor, vendor, or contractor of Children's, or a patient or co-worker. It can also include outside employment or serving on a board of directors for an organization that does business or competes with Children's.

Researchers may have financial interests in research sponsors and/or entities with business interests closely related to their research. These interests must be disclosed.

Human Subjects
According to Children's Policy #110, any research involving human subjects which takes place at, is sponsored by, recruits subjects at, or uses any facility, resources, or personnel of Children's Minnesota (Children's) is required to apply for and receive approval from the Institutional Review Board (IRB). Children's may apply additional requirements to those of the IRB, including the need for all IRB proposals to be reviewed by CMRI prior to going to the IRB. The Children's Hospital's Institutional Review Board is responsible for ensuring the ethical and equitable treatment of human research subjects. The IRB reviews and makes decisions on all research involving human subjects performed by Children's investigators and staff, regardless of funding source or the location of the research.

Animal Subjects
According to Children's Policy #1805, all research conducted at Children's Minnesota (Children's) is subject to review to determine institutional approval. Research involving live, vertebrate animal subjects is additionally subject to review by Children's Institutional Animal Care and Use Committee (IACUC). Such animal subject research cannot be conducted at Children's without prior approval of the IACUC. This policy does not apply to research conducted on non-living or non-vertebrate animals. The Institutional Animal Care and Use Committee (IACUC) oversees all Children's research that involves vertebrate animals. The IACUC ensures that the highest ethical and animal welfare standards are met.

B. Regulatory/Compliance Contacts

Most research involves compliance with some federal laws and regulations governing the conduct of the work. The following resources can help you determine what protections you need to put in place in your research study.

Grant Accounting

The Grant Accounting Office provides financial oversight for research grant accounts, following standard accounting practices, Children's policies and federal regulations. This includes establishing grant accounts, drawing down revenues or invoicing sponsors per grant and contract agreements, submitting financial reports to sponsors, and closing out awards and responding to audits.

Contact Lou Urban at lou.urban@childrensmn.org or visit their web page on StarNet at http://khan.childrensmn.org/departments-and-committees/finance/grant-accounting/

Institutional Review Board (IRB)

The Institutional Review Board monitors any research involving human subjects which takes place at, is sponsored by, recruits subjects at, or uses any facility, resources, or personnel of Children's. The IRB also monitors the access and use of protected health information under HIPPA. Investigators are required to apply for and receive approval from the Institutional Review Board (IRB).

Contact Debra McKeehen at debra.mckeehen@childrensmn.org or visit the IRB Intranet page on StarNet at http://khan.childrensmn.org/manuals/IRB/Chapters.asp.

Research Compliance & Integrity

Children's is committed to providing an environment that promotes ethical research as well as the free exchange of scientific ideas. Scientific integrity is a key tenet in upholding this philosophy. Children's will work diligently to prevent research misconduct and will support to the utmost those individuals who come forth with allegations in good faith.

Contact Christa Steene-Lyons, Privacy Officer at christa.steene-lyons@childrensmn.org or contact the Privacy Hotline at (612) 813-6911 or privacy.officer@childrensmn.org

10. Resources and Links

A. Training and Education Modules

CMRI offers a variety of educational products that may help you prepare your research project. All of these can be accessed on the StarNet website.

- Protection of Human Subjects and Financial Conflict of Interest Course
- How to Write a Successful IRGP Application (PDF)
- Clear Writing for Researchers (PDF)
- Research and Sponsored Programs 101 (PDF)
- Clinical Trials Budgeting (PDF)
- Writing a Successful Grant (PDF)
- Protocols for the Beginner (PDF)
- Clinical Research Methods and Study Design Part 1 (PDF)
- Clinical Research Methods and Study Design Part 2 (PDF)

B. Handbook Links

Build Collaborations - Resources

Have an idea, solution or new technology that you think could benefit Children's? Contact us to talk further.

Experts@Minnesota
Find collaborators at the University of Minnesota by searching this database of faculty and staff subject experts
iBridge Network
This online community enables researchers to share ideas, research, and knowledge regarding early-stage technologies and inventions.

Find Funding - Resources

General Funding Websites

Duke University Funding Opportunities Database
A website that allows users to use advanced search to find information on funding sources for research and other scholarly projects
Minnesota Council on Foundations

Grants.gov Grants.gov is the source to find and apply for Federal government grants. There are over 1,000 grant programs offered by all Federal grant making agencies, including NIH. Grants.gov also offers various emails and RSS feeds for subscription.

- NIH forms can be accessed online http://grants.nih.gov/grants/forms.htm. Note that as most NIH mechanisms require online submission, the SF424 R&R forms must be used (http://grants.nih.gov/grants/funding/424/index.htm). The PHS 398 forms are used for mechanisms such as career development grants (K series) and training grants (T series) as well as some program grants (P series). PHS 398 forms are found at: http://grants.nih.gov/grants/funding/phs398/phs398.html.
- NIH offers several different grant mechanisms, or programs. The most popular of the "R series" includes the small grant program, R03, the conference grant support, R13, the developmental research program, R21, and the research project grant program, the R01. Not all of the NIH Institutes and Centers participate in all mechanisms, so be sure to read the program announcement carefully. A list of the most frequently used NIH mechanisms is available here: http://grants.nih.gov/grants/funding/funding_program.htm.
- As the majority of NIH grant submissions are investigator-initiated, NIH has created a "parent" mechanism webpage listing these investigator-initiated program announcements http://grants.nih.gov/grants/guide/parent_announcements.htm.

Catalog of Federal Domestic Assistance: Compiled by the Office of Management and Budget, the Catalog provides the user with access to all assistance and benefit programs of federal departments and agencies, including loans, subsidies and technical assistance programs.

Other Agencies besides NIH:

Health Resources and Services Administration: HRSA helps provide health resources for medically underserved populations.
Substance Abuse and Mental Health Services Administration: SAMHSA works to improve the quality and availability of substance abuse prevention, addiction treatment, and mental health services
Agency for Healthcare Research and Quality: The AHRQ supports research designed to improve the outcomes and quality of health care, reduce its costs, address patient safety and medical errors and broaden access to services ().
National Science Foundation: NSF offers a compilation of funding opportunities offered by the National Science Foundation for research and education in science, mathematics, and engineering

Non-Federal Sites- These are just a sample

American Diabetes Association: The American Diabetes Association funds projects aimed at preventing, treating, and curing all types of diabetes. Projects cover such areas as genetics, islet cell biology, immunology, diabetes education and behavioral research

American Cancer Society: The ACS focuses its funding on investigator-initiated, peer-reviewed proposals.
American Heart Association: The AHA has many different types of funding.
National Kidney Foundation: The NKF has a new initiative to increase the support of clinical research through its Postdoctoral Fellowship, Young Investigator Grants, and Clinical Scientist programs
Robert Wood Johnson Foundation: For RWJ competitive national programs, RWJ issues a call for proposals or other invitational announcement. RWJ also funds unsolicited projects

Professional Societies
Association of Clinical Research Professionals (ACRP)
Oncology Nursing Society (ONS)
Society of Clinical Research Associates, Inc

Creating the Research Project

Study Design/Data Analysis

The Design and Analytics group. Please contact them at: mike.finch@childrensmn.org

Statistical Notes in the British Medical Journal
10 Basic Statistics Concepts
Clinical Epidemiology & Critical Appraisal of the Medical Literature
Selection of appropriate statistical tests

Data management plan - This online application can help you create a data management plans that meets institutional and funder requirements.
Dataverse Network - Data management plan best practices, templates, and background information.
Patient-Centered Outcomes Research Institute (PCORI) Methodology Report
Provides methodology standards for patient-centered outcomes research.
CHOP Protocol Templates - Includes instructional templates with instructions and suggested text, and working shells for drafting your own protocol.
Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Protocol design recommendations, and a 33-item checklist of scientific, ethical, and administrative elements to include in a clinical trial protocol.

Regulatory/Compliance Resources

Federal Register
Code of Federal Regulations (CFR)
The Food and Drug Administration
National Institutes of Health

National Center for Research Resources
Handling Misconduct – Department of Health and Human Services Office of Research Integrity
Public Health Service Policy on Humane Care and Use of Laboratory Animals

NIH Bioethics Resources on the Web - This NIH website aims to help individuals and groups explore the vast array of issues in bioethics; the content spans a wide range of topics, including human subjects and animal research, institutional review boards, clinical ethics, international research ethics issues, genetics, among others.
The Belmont Report - The Belmont Report summarizes ethical principles and guidelines for research involving human subjects; this content is hosted by the U.S. Department of Health & Human Services.
Administrators and the Responsible Conduct of Research - This Department of Health and Human Services tutorial provides research administrative staff with a review of the regulatory and policy environment with a discussion of the ethical issues that administrative staff may experience.
Investigational New Drug (IND) or Device Exemption (IDE) resources -Resources on the Food and Drug Administration (FDA) website about administering an investigational drug or biological product to humans.
Medical device resources - Information and databases on the FDA website about regulatory policies, and how to comply with the federal laws and regulations governing medical devices.
Human specimens resources - Information on the Clinical Laboratory Improvement Amendments (CLIA) website about federal standards applicable to all U.S. facilities or sites that test human specimens for health assessment or to diagnose, prevent, or treat disease.

Background Research

Allina Library services - Allina Library Health Services can assist with conducting literature searches or obtaining full text articles. For assistance with literature searches, to obtain full text journal articles, or to conduct your own literature search using either PubMed/MEDLINE or OvidSP/MEDLINE, go to Allina Health Library Services or email Library Services. For OvidSP, use any of the generic logins IDs: ahs4390, ahs4391, ahs4392, ahs4393, or ahs4394. The password for each is chclib.
Mendeley - A free reference manager and academic social network that can help you organize your research, collaborate with others online, and discover the latest research.
http://www.mendeley.com/
Zotero - A free Mozilla Firefox plug-in that provides full citation manager functionality.
PubMed - Comprises over 24 million citations for biomedical literature from MEDLINE, life science journals, and online books. PubMed citations and abstracts include the fields of biomedicine and health, covering portions of the life sciences, behavioral sciences, chemical sciences, and bioengineering.

Ovid Medline - A biomedical bibliographic database that was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM). MEDLINE contains citations to over 23 million articles and covers basic biomedical research and the clinical sciences. Subscription and pay per view.
NIH Research Portfolio Online Reporting Tools (RePORTER) database - A repository of NIH-funded research projects -- and the publications and patents resulting from NIH funding -- that allows you to verify that your research idea is novel and not currently being funded by the NIH. http://projectreporter.nih.gov/reporter.cfm
National Library of Medicine - Provides a vast print collection, produces electronic information resources on a wide range of health sciences topics, and conducts research, development, and training in biomedical informatics and health information technology.
Dataverse Network - This open source application enables you to publish, share, reference, extract, and analyze research data.

Writing Resources

Demographics

- Healthy People 2010
- National Center for Health Statistics (NCHS)
- Minnesota Department of Health Data & Statistics
- Minnesota Census Data
- Minnesota County Health Tables (1996 - 2015)
- Healthy Minnesotans – Public Health Improvement Goals for 2020
- Community Engagement Website
- The Office of Minority and Multicultural Health website
- Statewide Health Assessment 2012
- State Demographic Center

Grant Writing Tools

- Foundation Center Proposal Writing Short Course
- All about NIH Grant Applications: Samples and Tutorials, How to Write an NIH Research Project Grant Application (From NINDS):
- Writing a Grant 101- Great links from the National Organization of Research Development Professionals.
- NIH's guide to application writing - The National Institutes of Health (NIH) provides this guide to writing an NIH grant application. Select topics of interest include:
  - Plain Language: Getting Started or Brushing Up: An online NIH training module about how to use plain language to communicate research aims and findings.
  - NIH Grant Writing Tips Sheets: A selection of grant writing guides created by NIH Institutes.

Publishing

NIH Public Access Policy

- **Revised Policy on Enhancing Public Access to Archived Publications Resulting from NIH Research** - mandate effective April 7, 2008 requires all investigators funded by the NIH submit or have submitted for them to **PubMed Central** an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication.
- **NIH Manuscript Submission System (NIHMS)** - login to the NIHMS system when you are ready to submit your manuscript.
- **NIH Manuscript Submission System (NIHMS) Frequently Asked Questions** - answers to questions regarding the submission process.
- **NIH Public Access Frequently Asked Questions** - answers to questions regarding scope of policy and how to comply
- **NIH Public Access Website** - background and guidance on compliance with the requirements of this U.S. policy to enhance the public access to publications resulting from NIH-funded research
- **NIH Manuscript System Slide Show Help** - detailed instructions on how to submit a manuscript to NIH

NOTE: A separate submission is not necessary if a manuscript has been accepted by a journal that submits articles directly to PubMed Central on behalf of their authors. Publication in one of these journals requires no further action on part of authors to comply with the submission requirement of the NIH Public Access Policy.