

### American Heart Association's Strategically Focused Children's Research Network Request for Applications

Background **Program Structure** Network Intent Topics of Interest Key Requirements for Application Collaboration Eligibility Institutions Investigators Citizenship Requirements Fellowship Qualifications Team Expertise **Other Relevant Policies Application Instructions** Letter of Intent **Center Application Project Applications** Peer Review **Peer Review Process** Peer Review Criteria **Reverse Site Visit** Human Subjects & Ethical Considerations **Oversight Advisory Committee Program Evaluation** Budget **Contact Information** Glossary of Terms

#### **KEY DATES**

Activity	Date
Request for Applications Published	October 2016
Application instructions on AHA web site	October 2016
Letter of Intent Application open in Grants@Heart	October 2016
Letter of Intent deadline	December 9, 2016
Center and Center Projects Deadline	February 21, 2017
Review of proposals (two phases)	Spring 2017
Funding decisions made by AHA / Applicants Notified	June 2017
Network Kick-Off Teleconference	Summer 2017
Centers conduct research, train fellows, interact, report results	July 2017 – June 2021

#### BACKGROUND

The American Heart Association (AHA) is a non-profit, voluntary health organization funded by private contributions. The mission of the AHA is to build healthier lives, free of cardiovascular diseases and stroke. The Guiding Values of the organization include:

- Improving and Extending People's Lives
- Bringing Science to Life
- Speaking with a Trustworthy Voice
- Building Powerful Partnerships
- Inspiring Passionate Commitment
- Meeting People Where They Are
- Making an Extraordinary Impact
- Ensuring Equitable Health for All

A leading priority of the AHA is to fund research that increases an understanding of the etiology, pathophysiology, treatment and prevention of cardiovascular diseases and stroke.

The AHA has a tradition of support for research spanning more than 60 years. Research is the foundation of all other aspects of the AHA's lifesaving work, generating a tremendous impact on people's lives. After the National Institutes of Health (NIH), the AHA is the leading funder of cardiovascular disease (CVD) and stroke research in the U.S. with over \$4 billion invested in research since 1949. The AHA has adopted a goal to improve the cardiovascular health of all Americans by 20% while reducing deaths from cardiovascular diseases and stroke by 20% by the year 2020.

While AHA's primary focus is on adult cardiovascular health and disease prevention, recognition that early cardiovascular health plays a direct role of the health of the individual later in life has led to a greater interest in children's health. In the US today, many children fail to meet the AHA standard of ideal heart health for kids: no tobacco use, a healthy weight, at least 60 minutes of exercise a day, a healthy diet score and normal blood pressure, total cholesterol and blood sugar. In order to achieve its goals to reduce the prevalence of cardiovascular and stroke diseases, AHA recognizes that it must strive to maintain ideal cardiovascular health from birth through childhood to young adulthood and beyond. There are many strategies and pathways that researchers could follow to discover new knowledge and support the AHA's goal to promote healthier lives, free of cardiovascular diseases and stroke.

#### STRATEGICALLY FOCUSED RESEARCH NETWORK

A Strategically Focused Research Network (SFRN) is a mechanism that provides AHA an opportunity to address key strategic issues as determined by the AHA Board of Directors. This specific SFRN will focus on the understanding, prevention, diagnosis and treatment of children's health. Three to four (3-4) Research Centers will make up the Network (diagrammed in Figure 1 for illustrative purposes) and will be supported for a period of four (4) years. These Centers will constitute the Network and will be awarded a total of \$12-15 million over that period (including costs for Network oversight and administration). The desired characteristics of these Centers, the general requirements of the application, and the peer review criteria are described in this Request for Applications (RFA).

Specifically, this RFA seeks to have basic, clinical and/or population/behavioral health teams join together and submit proposals which address the topic of children's health via their individual areas of expertise. A Center

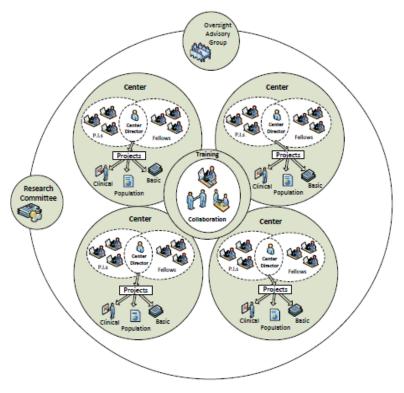


Figure 1: AHA Strategically Focused Research Network Structure

may be sited at one or at multiple U.S. institutions under the leadership of one. Each Center applies for funding individually and is peer reviewed by the AHA. The most meritorious Center applications and their research projects will be combined by the AHA to form the AHA Strategically Focused Children's Research Network. Broad collaborations for expertise are highly encouraged. A Center's application can consist of three (3) proposals from their one (1) institution; or they can reach out and bring in other projects from other institutions. For example: a basic project could come from laboratory X in Delaware; a clinical project from hospital Y in Texas and a population/ translational project from University Z in California, with the primary applicant being any of these institutions.

It should be noted that the increased availability of consumer-oriented health tools and social media, among others, has created new opportunities for natural experiments and novel interventions that could inform the development of effective health behavior change strategies that might improve disparities in risk factor control or enhance patient recovery. Multidisciplinary research that takes advantage of such innovative tools could also fall within the scope of this RFA. Furthermore, collaboration is encouraged with social and behavioral scientists, health policy experts, community-facing organizations and other experts to identify programs that effectively aid individuals in beneficial lifestyle modifications or engage clinical interventions in a fashion that unequivocally reduces the risk of heart disease and stroke or improves outcomes after an event.

#### PROGRAM STRUCTURE

The Network will include:

- Three-four (3–4) Centers working together to advance the field of children's research.
- One (1) Oversight Advisory Committee (see pg. 16)
- Nine-twelve (9–12) post-doctoral fellows over the course of four years, three at each Center.
- Nine-twelve (9–12) research projects: Each Center must have three (3) research projects in at least two (2) of these disciplines: basic, clinical, population. All will focus on children's health related to cardiovascular disease (CVD) and stroke and the topics of interest listed below.

Each Center will:

- Conduct three (3) cohesive research projects of scope equivalent to an R01
- Provide a training program for fellows, training three (3) Center-funded postdoctoral fellows during the period of the award
- Be linked to the other Centers by AHA-organized interactions and meetings with the intent to accelerate exchange of ideas, encourage sharing of commonly-useful knowledge and methods, and provide networking opportunities for trainees
- Report annually on its efforts towards integration with the other centers, as well as observations on successes/challenges of such integration
- Interact as part of the AHA Strategically Focused Children's Research Network according to the <u>Collaboration Expectations</u> outlined in this RFA and further defined by the <u>Oversight</u> <u>Advisory Committee</u>

#### NETWORK INTENT

The AHA is committed to an investment of \$12-15 million to establish this Children's Network which will provide almost \$4 million per Center.

The AHA intends to fund three–four (3–4) Centers that will encompass the following goals:

- Accelerate generation of important, novel ideas
- Answer significant questions addressing gaps in knowledge
- Yield important gains in knowledge and research capacity (developing new investigators is one such gain)
- Link research and training components through the program
- Prioritize multidisciplinary approaches with frequent collaborative interactions within the Centers and across the Network
- Demonstrate productive and effective data collection and evaluation
- Demonstrate the effectiveness or the applicability of clinical findings in clinical, public health or community-based settings such as workplaces, schools, churches or other "real-life" settings.

It is anticipated that the results of the funding and formation of the AHA Strategically Focused Children's Research Network will:

- Produce a cadre of new investigators who will energize the field of children's research and generate an expansion of the numbers of such investigators in later years
- Produce new research results based on the initial ideas of the funded Centers and on ideas generated by the collaboration of the Centers and their investigators
- Provide insights into and report on both successful mechanisms for and the challenges to active collaboration
- Identify programs that focus on children's health to reduce gender, racial and ethnic disparities in cardiovascular disease, stroke and risk through a variety of approaches

that could include seeking better understanding of disease etiology, pathophysiology, treatment, prevention and health care delivery across the lifespan.

Although successful applicants are asked to demonstrate the effectiveness of the research by articulating a plan proposing how the results could be implemented in clinical or public health settings, this does not guarantee that funds will be available for the proposed implementation. It is strongly preferred that successful applicants articulate such a plan, as it will assist the AHA in furthering its mission by exploring opportunities to advance the research findings.

#### **TOPICS OF INTEREST**

The intent of this initiative is to support a collaboration of basic, clinical and population researchers from different disciplines whose collective efforts will lead to new approaches to study children's health. Population studies are inclusive of projects ranging from cohort studies to translational work involving community interventions.

**Note:** Centers are highly encouraged, where applicable, to align with AHA initiatives which are addressing children (e.g. Voices for Healthy Kids, NFL Play 60 Challenge, Healthy Way to Grow, etc.) and/or other AHA Networks and Centers currently in progress (i.e. AHA's Strategically Focused Networks on: Prevention, Hypertension, Disparities in Cardiovascular and Stroke Health, Women, Heart Failure, Obesity, and the Bugher Stroke Network). Please see the <u>AHA's SFRN website</u> for a complete listing of AHA initiatives.

Researchers are encouraged to use AHA metrics as their research outcomes measures, health metric scores, or improving health metric scores. Researchers are encouraged to address interventions where efficacy can be measured via AHA mission metrics.

The following is an illustrative list of overarching themes that could be addressed by a Center. Successful applications will provide strong evidence of synergy among the proposed projects and will address at least one of the issues below <u>or an alternate issue of equal importance</u>.

## What are the patterns and regulation of expression of GENETICS & GENOMICS associated with children's health?

- What are reliable markers of disease progression in congenital or inherited forms of cardiac disease in children?
- What are novel ways of quantifying early atherosclerosis in children?
- What genetic and epigenetic factors influence emergence of a clinical phenotype in inherited forms of cardiac disease of childhood?
- What genetic and epigenetic factors influence the drive to be physically active?

## What effective measures including interventions of *LIFESTYLE / BEHAVIOR / PRIMARY OR SECONDARY PREVENTION* can improve children's health?

- What is the role of preventive therapy to attenuate the emergence of a clinical phenotype?
- What is the ideal physical activity regimen to be incorporated into educational settings for children in order to achieve improved cardiovascular health and sustained desire to remain physically active?
- What clusters of CV risk factors are associated with the greatest acceleration of age-related increases in arterial stiffening in youth?
- Atherosclerosis is recognized as a lifelong disease, but most current interventions target

secondary prevention. What factors lead to progression, and what factors lead to regression of early atherosclerotic lesions?

# How do *SOCIAL DETERMINANTS* and healthcare system actions impact a child's lifelong experience with CVD and stroke?

- What is the etiology or basis for social, economic, and geographical disparities?
- How does the maternal-fetal interaction and the intra-uterine environment influence congenital heart disease?
- What is the role of ideal CV health on cognition in later years? Does hypertension during adolescence impair cognitive function?

#### KEY REQUIREMENTS FOR APPLICATION

This RFA embraces a Network "Center" concept. Thus, it is expected that three (3) studies will be submitted from each Center applying to be in the Network, and to have an integration of these studies within each Center. Each Center will include several components: a designated Center Director, three (3) synergistic projects related to the topic of children's, and a research postdoctoral fellowship training component. Centers should also demonstrate a high degree of collaboration by working on one comprehensive research focus across all sites.

The development of each Center will be the responsibility of the Center Director, who will coordinate the projects and the training program, to ensure that they are not only complementary, but also effective in producing a greater outcome than if they were executed individually. The Director will provide administrative and scientific leadership and will be responsible for the organization and operation of the Center, and for communication with the AHA Strategically Focused Children's Research Network Oversight Advisory Committee. Each Center application must name one Center Director. If strong rationale is provided, an opportunity exists to train a future Center Director within the terms of the grant period. If this option is selected, compelling justification must be provided within the narrative of the Center application.

A major component of the Centers will be their ability to implement a successful program for the interdisciplinary training of a new generation of scientists who, from their earliest experiences in research, will collaborate with other scientists through monthly meetings with established investigators and annual meetings with other investigators participating in the Centers. An ultimate product of this program will be the creation of a report on the challenges and results of active collaboration as well as on training in such a model.

Postdoctoral Fellowship Training Requirements:

- Each Center will provide a multidisciplinary training program to give fellows basic, clinical, population, and translational research experience.
- Each Center will train three (3) fellows during the period of the award (one two-year fellowship in years one and two; one two-year fellowship in years two and three and a final two-year fellowship in years three and four). Individual development plans for each trainee will be utilized.
- Each Center will provide professional, non-medical training to develop and enhance presentation and communication skills.
- Centers will be expected to utilize current principles of effective adult education in their programs.

#### COLLABORATION

One of the key objectives of this initiative is to encourage interaction among the Strategically Focused Research Network Centers, both in training and research efforts. An important component of the initiative is a multi-disciplinary approach both within and among Centers that comprise the Network. The structure of the Network will include sufficient components to maximize the interaction and collaboration among the Strategically Focused Children's Research Centers. The AHA Oversight Advisory Committee will monitor and encourage interactive and collaborative activities, and develop and implement a plan for regular dialogue among the Center participants. The entire network will operate as a team.

Once awarded, there is an expectation that the three to four (3–4) Centers will interact with each other to provide networking opportunities for trainees, to encourage sharing of commonly-useful knowledge and methods, to educate each other on unique knowledge and methods and to provide a stimulating atmosphere for research collaborations. Strategies for communication and interaction among the Centers should be addressed in the proposal and could include ways to encourage interaction, augment or expand study findings, share training opportunities for fellows and junior investigators, etc.

All key Center personnel will be expected to participate in annual meetings and other activities such as routine tele/videoconferences to facilitate interaction and collaboration. Annual progress reports describing each Center's efforts and financial commitments towards integration, as well as a report on successes/challenges of such efforts, will be required.

Centers selected for funding will be expected to interact and develop new hypotheses leading to collaborative projects. The collaborating Centers are expected to share everything from "samples to ideas." The Centers will be expected to work with the AHA Oversight Advisory Committee to define the strategies for leadership in training and interdisciplinary collaboration, as well as a clear commitment to collaboration with the other disciplines and other centers within the Network. Collaborations within the Network need not be limited to single projects, but could be transformative for the overall work of the Network if approved by the Oversight Advisory Committee.

Collaboration Requirements:

- Centers will be expected to meet and collaborate with each other through interactions and meetings to accelerate information exchange and ideas. Specifically:
  - Center Directors will participate in quarterly teleconferences
  - Training Directors (and fellows) will participate in monthly teleconferences
  - All key Center personnel (Center Director, Training Director, Project PIs and fellows) will attend Annual Scientific Meetings
  - All key Center personnel will participate in a teleconference to provide progress updates to the Oversight Committee at 6 month intervals.
- Directors and investigators are expected to provide and share in networking and crosstraining opportunities for postdoctoral trainees in conjunction with AT LEAST one other Center in the Network.
- Each center will be expected to collaborate with AT LEAST one other center in the Network to develop a new hypothesis or build off of currently funded hypotheses. This interaction should lead to at least one (1) collaborative publication, at a minimum.
- Centers will collaborate and participate in producing an end-of-award report about the challenges, mechanisms and successes of the Centers' collaborations;
- Centers will be expected to earmark percentages of their budgets to contribute to collaborative efforts and provide an annual collaborative report outlining and describing these expenditures.

 Centers will consider themselves part of the AHA Strategically Focused Children's Research Network.

#### ELIGIBILITY

#### INSTITUTIONS

Awards are limited to non-profit institutions in the United States, such as universities and colleges, public and voluntary hospitals, laboratories, research institutes, and other non-profit institutions that can demonstrate the ability to conduct projects and organize a center. Applications will not be accepted for work with funding to be administered through any federal institution or work to be performed by a federal employee, with the exception of Veterans Administration employees.

Broad collaborations for expertise are highly encouraged. A Center's application can consist of three (3) proposals from their one (1) institution; or they can reach out and bring in other projects from other institutions. For example: the basic project could come from laboratory X in Delaware; the clinical project from hospital Y in Texas and the population/ translational project from University Z in California.

The Centers are not transferable to other institutions. AN INSTITUTION MAY SUBMIT ONLY ONE AHA STRATEGICALLY FOCUSED RESEARCH NETWORK APPLICATION FOR THIS COMPETITION. Individuals at the applicant institution who are not participating in their institution's center application (and/or its three project applications) may participate in another separate institution's center application. Individuals participating in their institution's center application, other than the Center Director may participate in a separate institution's center application. The application may include individuals and/or projects at more than one institution provided there is evidence for a successful close personal and geographical interaction among research and training personnel.

It is the responsibility of the *submitting institution* to ensure that only one proposal is submitted for the institution or to coordinate across several institutions to create a single application. The Center Director's institution will maintain fiscal responsibility for the entire award. The appropriate Institutional Officer should sign off on the proposal in AHA's online grants management system, Grants@Heart.

#### INVESTIGATORS

Directors and Principal Investigators of projects of the Centers

- Must possess an M.D., Ph.D., D.O., D.V.M., or equivalent doctoral degree at time of application, and
- Must have a faculty or staff appointment.
- May hold another AHA award simultaneously.
- Must demonstrate a 20% minimum effort requirement for the Director, a 5% minimum effort for the Training Director and a 10% minimum effort requirement for Principal Investigators (PI) of Center projects. These responsibilities are mutually exclusive.

\*Director and Project PI salary requested must be proportional to the percent effort devoted to the Center. The AHA does not impose a salary cap other than the caps noted in the <u>Budget</u> below.

Center Director

- Must demonstrate expertise in the area of children's research, with demonstrated ability to build a Center team.
- Should demonstrate a successful history of leadership in a research project team and in

career development. A clear demonstration of the Director's commitment to integration with the other Centers is required.

- May also serve as a Project PI on the Center application.
- May also serve as Training Director on the Center application.
- Experience in multi-institutional collaboration is encouraged.
- May not serve in a director capacity on another active or proposed Network.

**Training Director** 

• Should demonstrate a successful history of leadership in career development. A clear demonstration of the Director's commitment to integration with the other Centers is required. May also serve as a Project PI on the Center Application

The responsive application will demonstrate a history of successful post-doctoral fellowship training with a plan to continue the program or a strong plan to develop a successful program. In addition, training in clinical outcomes research and translational research concepts as well as collaborative research should be described in the application. Collaborative interdisciplinary training programs are encouraged.

A viable source for identifying and recruiting trainees must be presented in the application and while trainees are not required to be named at the time of the application submission, the first set of fellows must be identified within 90 days of award activation. The trainee fellows must possess an M.D., Ph.D. or equivalent doctoral degree at the time of participation in the program.

#### CITIZENSHIP REQUIREMENTS

Directors must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
- G-4 Visa family member of employee of international organizations and NATO

Principal Investigators of proposed projects must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
- E-3 Visa specialty occupation worker
- H1-B Visa temporary worker in a specialty occupation
- O-1 Visa temporary worker with extraordinary abilities in the sciences
- TN Visa NAFTA professional
- G-4 Visa family member of employee of international organizations and NATO

Named fellows of the Centers must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received

authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)

- E-3 Visa specialty occupation worker
- H1-B Visa temporary worker in a specialty occupation
- O-1 Visa temporary worker with extraordinary abilities in the sciences
- TN Visa NAFTA professional
- J-1 Visa exchange visitor
- F-1 Visa student
- G-4 Visa family member of employee of international organizations and NATO

\*All awardees must meet the citizenship criteria throughout the duration of the award.

#### FELLOWSHIP QUALIFICATIONS

Named fellows of the Centers at U.S. institutions must hold a Ph.D., M.D., D.O., D.V.M. or equivalent doctoral degree and commit 75% effort to research training. Center fellows may commit a minimum of 70% effort if justification is accepted by the AHA Oversight Advisory Committee. A named fellow may not hold another fellowship award, although the institution may provide supplemental funding. Fellows may not hold a faculty or staff appointment, with the exception of M.D.s or M.D./Ph.D.'s with clinical responsibilities. These fellows may hold a title of instructor or similar due to their patient care responsibilities, but must devote at least 75% effort to research training. A named fellow may have been a recipient of an AHA fellowship, but may not hold an AHA affiliate fellowship or AHA Fellow-to-Faculty Transition Award at the same time as an AHA Strategically Focused Research Network fellowship.

#### TEAM EXPERTISE

Multidisciplinary teams are appropriate and desired and can be broadly defined. Basic disciplines such as cell/molecular biology, biochemistry, bioengineering/biotechnology, immunology/virology, genetics/genomics, physiology, vascular biology, genetics and bioinformatics among others are all appropriate. Clinical disciplines, including general internal medicine, nutrition and dietetics; cardiology, pediatric cardiology, cardiovascular surgery, exercise physiology, nephrology, anesthesia, nursing, emergency medicine, kinesiology, endocrinology, neurology, psychiatry and behavioral science are all appropriate. In addition, public health disciplines including the fields of health communications, health marketing, informatics, individual and collective behavior science are all of interest. Epidemiological, interventional, and behavioral science, biostatistical, and health economic approaches are appropriate to the focus of this program as well as eHealth, mHealth and related technologies.

#### **OTHER RELEVANT POLICIES**

The Center awards are not transferable to other institutions. The projects described can have no scientific or budgetary overlap with other funded work. Any inventions, intellectual property, and patents resulting from this funding are governed by the AHA Patent, Intellectual Property and Technology Transfer Policy. The applicant/awardee and institution are responsible for compliance with all AHA research award policies and guidelines for the duration of any awards they may receive. Go to Policies Governing All Research Awards to review AHA policies.

#### **APPLICATION PROCESS**

Only one Center proposal, including multiple research project proposals, may be submitted from an institution. Each Center application should have only one (1) Center Director. Co-Directors will not be recognized on official documents or publications. The completed application must include the primary Center application, three individual research project applications, and the overall training plan. The components of the application are described below.

Application instructions for the AHA Strategically Focused Research Centers will be available on the AHA's <u>website</u>. Applications will only be accepted through AHA's online grants administration system: Grants@Heart.

#### LETTER OF INTENT

Prospective applicants are requested to submit a Letter of Intent for the AHA Strategically Focused Children's Research Network on or before **December 9, 2016.** The letter will be submitted through the Grants@Heart system and will include the following information:

- Name, institution, and contact information of proposed Center Director
- Name, institution, and contact information of proposed Center Training Director
- Names, institutions, and contact information of proposed Principal Investigators for Center Research Projects
- Brief summary of the Center, including reference to the three projects, and overarching goals of the Center.

While a Letter of Intent is requested, it does not enter into the review of said subsequent application nor is it required in order to submit an application. The information provided in a Letter of Intent allows AHA staff to estimate the potential peer review workload and to avoid potential conflicts of interest in the peer review process. It also allows AHA to provide applicants with updated information about the application process if necessary.

The Letter of Intent should be submitted electronically via Grants@Heart **December 9, 2016**. Instructions for the Letter of Intent are available online in the Supporting Documents section of the <u>Strategically Focused Research Network Website</u>.

#### **CENTER APPLICATION**

The Director of the proposed Center must submit an umbrella application which consists of the following components:

- 1) Center Science Vision and Synergy (a clear, unifying central theme to which each research project application relates); a center should be viewed as a group of interrelated research projects that are complementary and synergistic.
- 2) Information regarding the Director
- 3) Information regarding any current children's research programs and any history of successes in children's research.
- 4) A detailed description of the multidisciplinary training program for the AHA Strategically Focused Research Center two-year fellowships (basic, clinical and translational research exposure), including information regarding the selection of prospective fellows and how funded fellows' ongoing progress will be guided via an individual development plan (IDP) and evaluated at least annually.
- 5) Information on current training programs and training grants within the Center institution and affiliated institutions relative to the research being proposed (if appropriate)
- 6) Information regarding other faculty/staff members at the Center institution and affiliated institutions (if appropriate) who will be submitting research projects.
- 7) Information on research funding available to the Director and proposed Principal Investigators on Center research projects.
- 8) Information on existing collaborative research teams within the Center institution and affiliated institutions (if appropriate) and their ability to share information and methodologies with other institutions. Documented evidence that other collaborations have produced synergistic results.

- 9) Information on facilities available to support the Center and affiliated institutions' (if appropriate) research projects.
- 10) An overview of the estimated four-year budget for the Center.
- 11) Information regarding the identification of a faculty/staff member at the Center institution or affiliated institutions (if appropriate) with the leadership skills to bring team-building and professional/organizational development to the collaborative process.

#### **PROJECT APPLICATIONS**

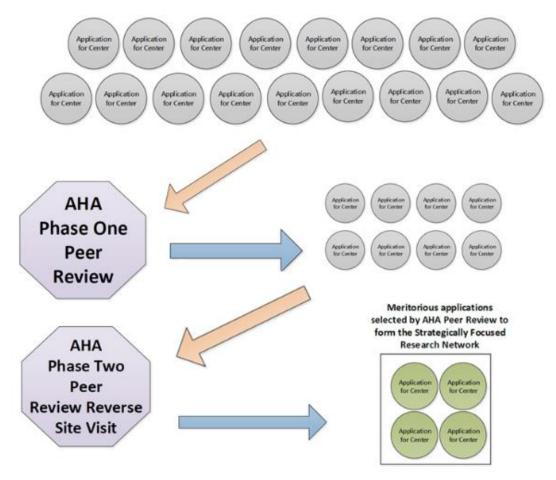
A Center research application must include three (3) synergistic research projects related to children's research topics described in the Topics of Interest section of this RFA. The three (3) projects from each Center should be from at least two (2) of these disciplines: Basic, Clinical, and Population (Translational) Research. Each project should demonstrate importance and relevance of the research to the field of children's. The projects proposed by a Center will be reviewed as a group. Successful applicants will structure their projects to include appropriate samples, cell lines, animal models, patients, cohorts or data points to draw powerful conclusions and further knowledge about children's. Submitted projects must be feasible within the budget described. AHA research funds will not be awarded to supplement or duplicate any work which is being supported by other funding agencies.

The Principal Investigator of each proposed research project must submit an application which consists of the following components:

- 1) Required application forms
- 2) Investigator's qualifications
- 3) Specific project aims
- 4) Background and significance
- 5) Preliminary data on same or related problems
- 6) Contemplated methods of approach to problem
- 7) Evidence of successful collaboration with other Center members
- 8) Ethical aspects, including human and animal subjects, if applicable.
- 9) An overview and plan of short- and long-term evaluation of metrics to support the Center's improvement in standard of care of patients with children's

Application Instructions for both Center Directors and Project PIs are available on the <u>SFRN</u> webpage.

#### PEER REVIEW PROCESS



Review of the applications will be conducted by the AHA and will occur in two phases. For the first phase, a peer review committee of volunteer scientists will be assembled to review all the submitted applications. Appropriate scientific expertise will be sought to review the applications received. Based upon the preliminary scores assigned to an application by the assigned reviewers, a streamlined review may be conducted for any application.

A second stage of the review will then be conducted with only the highest ranked Center applications, and will include a "reverse site visit" presentation to the AHA review group by each invited Center Director and select members of the Center team. A minimum number of participants, to be decided by the AHA, will be invited to the reverse site visit. Reviewers will score the Centers as a whole following the presentations, with the average of the reviewers' scores providing the final ranked list of applications. The ranked list will be reviewed by the AHA Research Committee. The three to four (3–4) Centers with the highest rank will be funded, contingent upon resolution of any policy concerns.

#### PEER REVIEW CRITERIA

The following major factors will be considered in the evaluation of each Center. These factors are intended to assist applicants in determining the appropriateness of candidacy. All of these factors will enter into the deliberations of the peer review committee. This process is weighted to reflect the interest of the AHA in funding highly collaborative and synergistic research and

training programs: The Center Application score will account for 50% of the Overall Center Score while Project Application scores will account for the remaining 50% of the Overall Center Score.

## This RFA should not be used as sole guidance when completing your application. Please reference the Application Instructions.

#### **Project Application Scoring Criteria**

**Projects** – Potential impact of the project on children's research; strengths of applicant investigators (qualifications, expertise and productivity); potential for collaboration or synergy of projects; scientific content; background; preliminary studies; detailed specific aims; approach detail; analytical plan; sample size; data management; significance; innovation; individual project scientific merit; and total project coordination (within and among projects). Projects will be rated on the following areas:

- **Approach**: Are the conceptual framework, design, methods and analyses adequately developed, well integrated, well-reasoned and feasible (as determined by preliminary data) and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? *For all applications that include vertebrate animals or human subjects, applicants must explain how relevant biological variables, such as sex, are factored into the research design, analysis and reporting. Furthermore, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.*
- **Innovation**: Is the project original and innovative? For example: Does the project challenge existing paradigms and address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
- **Investigator**: Is the investigator appropriately trained and well-suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?
- **Significance**: Does this study address an important problem broadly related to cardiovascular disease or stroke? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods and technologies that drive this field?
- **Environment**: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?
- **Impact**: How does the project relate to and support the mission of the AHA to *build healthier lives, free of cardiovascular diseases and stroke* and its commitment to work for health equity for *all Americans*?

(Project Applications will be scored individually according to the criteria above. Projects will account for 50% of the Overall Center Score.)

#### **Center Application Scoring Criteria**

**I. Synergy –** A clear vision of scientific direction is expected. A Strategically Focused Research Center should be viewed as a group of interrelated research projects, each of which is not only individually scientifically meritorious, but also complements the other projects and contributes to an integrating theme. Describe the rationale for the total program. Explain the strategy of achieving the objectives of the overall program and how each individual project relates to the strategy. Describe the synergies and interactions among projects and their investigators. What collaborations do you envision between investigators working on individual projects? Is there evidence of synergy among the projects and training

component of the Center? **PROJECTS THAT DO NOT DEMONSTRATE SYNERGY WILL NOT MOVE FORWARD TO PHASE 2.** (30% of Center Application Score)

**II. Collaboration –** History of collaboration, as well as the ability and commitment to collaborate with other institutions, investigators and within the applicant institution as well as within the awarded Network. Defined and detailed process for collaboration with other sites in addition to within and among the proposed projects; plans to actively participate in a collaborative network. Evidence of formal training in leadership skills with an emphasis on collaborative leadership will be favorably reviewed.

**Interaction Plan within and among this Network and other AHA Networks** (if appropriate) – Plan for and commitment to sharing knowledge and methods, providing a stimulating atmosphere for research collaborations, and providing networking opportunities for trainees. Cited strategies for communication and interaction among the Centers.

(25% of Center Application Score)

**III. Training component** – A detailed plan for developing and implementing a postdoctoral training program that includes clinical (M.D.) or Ph.D. training in children's research; qualifications and characteristics of current and anticipated trainees; didactic and practicum training opportunities; plan for the selection of prospective fellows and how funded fellows' ongoing progress will be guided via an individual development plan (IDP) and evaluated at least annually. Plan for involving fellows in annual Center meetings and Center-to-Center visits, along with identifying opportunities for fellows to work with established investigators at other network Centers; ability to track trainees; conferences and meeting participation for trainees; documentation of a ready supply of fellows; and history of successful fellowship training for children's researchers.

(20% of Center Application Score)

**IV. Center Team** – Qualifications of the Director to provide scientific and administrative leadership for the Center; experience and commitment of the nominated Director; quality of research team; qualifications of investigators and co-investigators; experience with children's-related studies; training experience.

**V. Center Director** – Demonstrated ability to lead others, along with experience and commitment to the success of the Center, the projects contained within, and the Network as a whole. Documented evidence of willingness to collaborate with others outside their institution to share ideas, science, etc. to progress the field of children's research.

(10% of Center Application Score)

**VI. Investigator team** – Qualifications of each PI to provide scientific and administrative leadership for their respective projects; demonstrated commitment of each PI, and experience with children's studies; quality of interdisciplinary research team; qualifications of co-investigators; training experience.

(10% of Center Application Score)

**VII. Environment** – Institutional commitment, resources and facilities to sustain the Center; institutional resources available to complete the project; analytical resources available to the project; letter from Center Director's Department Head assuring the department and institution's support of the Center along with confirmation that the Center Director will devote at least 20% effort towards the Center. Other Center personnel may be appointed to assist the Director in the administration of the Center. However, the Director will be required to devote 20% effort to the Center.

(5% of Center Application Score)

#### REVERSE SITE VISIT

If a Center application is selected to move to the 2<sup>nd</sup> phase of review, the applicants will receive critiques from Phase One review as well as instructions for the reverse site visit. The Center Director and key personnel will have approximately 3-4 weeks to prepare for the reverse site visit; presentation should focus on the Center review criteria and response to specific issues raised in Phase One critiques. The actual presentation should not be more than 30 minutes, followed by 15 minutes of responses to follow-up questions from the panel. The entire reverse site visit will last approximately 45 minutes. Note: Each invited Center Director and key personnel will be expected to travel to attend the reverse site visit at their own expense.

#### HUMAN SUBJECTS & ETHICAL CONSIDERATIONS

All applications must adhere to AHA research <u>program policies and standards</u> including those regarding the ethical treatment of animals and human subjects, as well as the policy addressing inclusiveness of study populations relative to gender, race, age and socioeconomic status. Institutional review board approval will be handled on a "just in time" basis and will be required before the date of the first quarterly payment made to the institution. Funding is contingent upon institutional review board approval initially and for the duration of the award. Any ethical concerns identified via the review process shall be forwarded to the AHA Research Committee for consideration.

#### **OVERSIGHT ADVISORY COMMITTEE**

Once the Centers are selected, the AHA Strategically Focused Children's Research Network Oversight Advisory Committee will provide external oversight for the Centers and serve in an advisory capacity to the Centers. Anyone who applies to the Program and is funded will not be considered for membership on the Advisory Committee. Center Directors and project PI's will report to and meet with the Advisory Committee regularly. The Oversight Advisory Committee also will offer advice to the AHA Research Committee on the progress of the Centers and any issues that arise in their administration.

Responsibilities of the Oversight Advisory Committee include:

- Monitoring the scientific progress of the Centers and Center Projects
- Overseeing and annually evaluating the program, including an evaluation of the progress of the trainees, making recommendations regarding continuation to the AHA Research Committee
- Monitoring and encouraging interaction efforts within and among Centers. The Advisory Committee will encourage Centers to change traditional culture by rewarding interaction and will request an annual report on the successes and challenges resulting from efforts to interact
- Making recommendations to the AHA Research Committee regarding management of the program

#### PROGRAM EVALUATION

Each Center will be required to provide an annual interim report, as well as a final written scientific report of progress. Progress made and plans for the coming year shall be addressed in these annual reports. Preliminary measures of the success of the initiative have been identified, and each Center will be required to provide a milestones-to-success timeline at the time of funding and each subsequent year in conjunction with the annual progress report. Centers will be asked to report on the following measures:

- Productivity of Centers track publications and citations; document outcomes of research projects; document other funding resulting from the current initiative
- · Transfer of intellectual property to the marketplace
- Impact of the fellowship training experience on career development: track trained fellows over a five-year period for such measures as percent of time in research, publications, other funding, and promotions
- Report on the interaction among the Centers and lessons learned, including measures of level of collaboration, such as heterogeneity of co-authors of papers (number of academic departments represented among co-authors)
- Report on each project and center's progress as defined by the milestones to goal timeline.

#### BUDGET

The Program will have a total budget of approximately \$15 million. The funding will be allocated as follows assuming four (4) Centers are funded:

	Network Totals	Center Totals
<b>Projects</b> Three projects at each of three to four (3–4) Centers for four years <i>Maximum</i> of \$2.844 <i>M</i> to be divided among the 3 Projects funded at the Center over the 4 years. To accommodate various situations, the money does not need to be spent equally between projects or years.	\$11,376,000	\$2.844M/Center
Fellows Three Fellows at each Center for two years each	\$ 1,200,000	\$0.3M/Center
<b>Center Director</b> One Director at each Center for four years A maximum of \$50,000 per year for each Director. Center Director must commit at least 20% effort. If a separate Center Training Director is desired, this \$50,000 per year may be split to accommodate additional percent effort of this individual.	\$ 800,000	\$0.2M/Center
<b>Center Travel Costs</b> Covers travel for Center personnel to Center network meetings and other integration activities. <i>\$7,000 per year must be allocated to Center Travel.</i>	\$ 112,000	\$28,000/Center
Direct Costs (Total)	<b>*</b> 4 0 0 0 0 0 0	<b>4</b> 0.0701/0
Research Dollars	\$13,488,000	\$3.372M/Center
Indirect Costs AHA Policy allows for a maximum of 10% for indirect costs	\$ 1,348,800	\$0.3372M/Center
Total	\$14,836,800	\$3.7092M/Center

- It is expected that each Center will earmark a percentage of their award (% of direct costs) to use toward collaborative efforts according to the schedule below:
  - Year 1: 5% (\$42,150)
  - Year 2: 7% (\$59,010)
  - Year 3: 7% (\$59,010)
  - Year 4: 10% (\$84,300)

- Collaborative efforts must be detailed in each annual scientific progress report. Money can be set aside as a specific budget line item, or line items may be earmarked or tagged as collaborative expenses (for example, travel funds can be considered collaborative efforts).
  - Examples of collaboration include but are not limited to:
    - o sending a fellow or PI to another center in the network to learn a technique or skill
    - collaborating with an investigator from another center in the network on a new or tangential project or publication
    - hosting fellows from the network for a relevant symposium, course or training bootcamp

The total amount requested per Center, *including* 10% indirect costs, may not exceed approximately \$3.7 million for the 4-year award.

Center Directors, Training Directors, all Project PIs and fellows will be required to attend the Annual Network meeting each year. Please be sure that your budget accommodates enough funding to cover travel to these Annual Meetings.

The Center Director will be responsible for overseeing the total budget for his/her Center within the Network. If awarded, the Director and the institution assume an obligation to expend grant funds for the research purposes set forth in the application and in accordance with all regulations and policies governing the grant programs of the AHA, Inc.

The AHA is currently paying all research payments quarterly on or around the 17th of the month following the end of the calendar quarter. Payments are made to institutions on behalf of the Director. If activated on April 1, the first payment to the Center would be sent on or around July 17th (and in October, January, April and July thereafter).

#### **CONTACT INFORMATION**

Inquiries regarding this RFA may be sent to:

General Questions (214) 706-1441

(214) 706-1441 <u>sfrn@heart.org</u> Technical Assistance (214) 360-6107 login@heart.org Institutional Additions institutions@heart.org

Basic Science	The study of fundamental life processes. This type of research is often purely theoretical with the intent of increasing our understanding of certain phenomena or behaviors but is not directly aimed at solving a specific prevention or treatment issue in the short term.
Center	A Center is comprised of a Center Director, Center Training Director and multiple Project PIs. These individuals may be located at the same or separate institutions as long as there is evidence of past and/or current collaboration. Centers will work together to move research forward in the area of study.
Center Director	The Director serves as the leader of his/her Center. This individual is renowned as an expert in the science topic being proposed and provides leadership, training and collaboration experience.
Center Fellow	A Center Fellow has a post-baccalaureate doctoral degree (MD, PhD, DO, DVM, PharmD). These individuals will be highly involved in the work being proposed by the Center and will be encouraged to collaborate with fellows across the network. The Center Fellows will work closely with the Center Training Director and Center Director on their individualized multidisciplinary training plan.
Clinical Science	Addresses important questions of normal function and disease using human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) wherein an investigator or colleague directly interacts with human subjects. It includes research on mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, but does not include in vitro studies using human tissues not linked to a living individual.
Collaboration	Collaboration is defined as a process where two or more individuals or organizations work together to complete a task and achieve shared goals - a deep, collective, determination to reach an identified objective — by sharing knowledge, learning and building consensus.
Letter of Intent	The Letter of Intent is used by the AHA to gather information on prospective applicants – quantity of expected applications, projects being proposed, etc.
Multidisciplinary Research	Multidisciplinary Research brings different disciplines together to explore a topic from different perspectives. Collaboration across the disciplines is key to create new approaches, ideas, knowledge base, etc.
Oversight Advisory Committee	A group of scientific volunteers in the named strategic area tasked with supervising the progress and direction of the Centers in the Network to ensure that the goals of each project, each training program, cross-center collaboration, etc. are met and accomplished during the life of the Network.
Population Science	The science and art of studying the distribution and determinants of health status as influenced by social, economic and physical environments, human biology (including genetics and genomics), health policy and services and of preventing disease, prolonging life and promoting health at the population level. Population

	health research may include epidemiologic and behavioral
	studies, outcomes research, and health services research.
Project PI	A Project PI is an independent investigator responsible for
-	carrying out the scientific research project proposed in their
	application. They must provide evidence of successful research
	accomplishments and their ability and commitment to collaborate
	and share knowledge with others.
Reverse Site Visit	A reverse site visit occurs during the second phase of peer
	review for the Strategically Focused Research Network
	applications. The visit consists of an in-person presentation by
	the proposed Center Director and Project PIs, to the AHA Peer
	Review Committee. The reverse site visit is held at a neutral
	location and will consist of a brief oral presentation followed by a
	question and answer period.
Stratagically Featured	
Strategically Focused Research Network – aka	A Network is composed for multiple Centers, each at different
	institutions, coming together to study a common topic determined
Network	by the AHA to encourage collaboration and move the science
	community forward.
Synergy	Synergy is the ability of a group to produce something greater
	than the sum of its parts; the ability of the group to outperform
	even its best individual member.
Training Director	The Training Director is responsible for the direction and
	execution of the training program of the center postdoctoral
	fellows. This program should include multidisciplinary approach
	to training and developing the fellows in the area of research
	being proposed by the Center.
Translational Research	A multidisciplinary type of research that involves turning
	observations in the laboratory, clinic and community into
	interventions that improve the health of individuals and the
	public.
	11