

Fisher & Paykel Healthcare/Emergency Medicine Foundation Research Grant

Nasal High Flow Therapy for Respiratory Compromised Patients in the Emergency Department

Request for Proposal

Please read these instructions carefully. Applications that do not follow these instructions with regards to type size, length, format, and supporting documentation will be summarily rejected. No extension of the deadline will be granted.

Before submitting your application, please be sure that the following items have been addressed:

- Information page is included as the first page of the application packet and is fully completed (sample attached).
- Type size is 12 pt. font, single-spaced and margins are 1 inch
- Evidence of IRB approval, or at least evidence of submission to IRB, from each institution, is included in application packet (for multi-centered studies, approval from or evidence of submission to IRB/AUC for all sites is required)
- Clearly stated research hypothesis
- Statement of Conditions is signed by **Principal Investigator** and **Institutional Official** and is included in application packet (see last page of this RFP)
- Letter of support from Emergency Medicine Chair is included in application
- Letter of support from a preceptor/mentor is included in application
- Other grant support for all investigators is included in application
- Submission via the on-line application system is required. Late applications will not be considered. Submit application at <https://emfoundation.aibs-scores.org>.

Fisher & Paykel Healthcare/Emergency Medicine Foundation Research Grant

Nasal High Flow Therapy for Respiratory Compromise in the Emergency Department

Application Deadline	February 7, 2020
Notification of Award	June 2020
Funding Period	July 2020 – June 2022
Funding Amount Per Award	\$180,000
Number of Awards	One

BACKGROUND

Undifferentiated breathlessness or dyspnea are common presenting symptoms of undifferentiated respiratory compromise in the emergency department (Hutchinson 2017). Patients with severe respiratory complaints account for about 12% of emergency department (ED) visits (McCaig 2002; Weiss 2014). To a large extent supplemental oxygen via a facemask has been pervasive as initial treatment; however, evidence demonstrates that hyperoxia may be detrimental when associated with various hypoventilatory and hypercapnic conditions (Stolmeijer 2018). In this case, interest has turned to alternatives such as nasal high flow therapy (NHF) due to both technology that has enabled reliable delivery of inspired oxygen fraction and therapeutic mechanisms that contribute to respiratory support (Baker 2019).

Similarly, acute respiratory failure (ARF) unspecified as to whether it is associated with hypoxia, hypercapnia or both, is a primary condition identified in the pre-hospital and emergency department settings requiring early intervention to improve outcomes (Behrendt 2000). It is often impossible to accurately define the pathogenesis of hypoxemia, especially in the severely ill or deteriorating patient (Fessler 2006). Early differentiation, identification and intervention is generally associated with improved outcomes where invasive mechanical ventilation can be averted, however, there are mixed evidence as to the most effective approach (Fessler 2006).

In patients with acute hypoxemic respiratory failure from COPD, pulmonary edema, or other causes, the need for mechanical ventilation is associated with high mortality, but data on the overall effects of NIV with respect to the prevention of intubation and improvement in outcome are conflicting as the literature does not conclusively support the use of NIV in patients with non-hypercapnic acute hypoxemic respiratory failure. Recent data demonstrate that NHF is noninferior to noninvasive positive-pressure ventilation (NIV) for the treatment of adult emergency department patients with respiratory failure from various causes (Doshi 2017). In this case avoidance of intubation and therapy failure rates for these patients suggest that NHF therapy may be an appropriate first-line therapy. There remains a need for examining optimal NHF as first line therapy for undifferentiated respiratory distress and respiratory compromise in the emergency department compared to NIV.

References

- Hutchinson A, Pickering A, Williams P, Bland J, Johnson M. Breathlessness and presentation to the emergency department: a survey and clinical record review. *BMC Pulm. Med.* 2017; 17: 53.
- Stolmeijer R, Bouma H, Zijlstra J, Drost-de Klerck A, ter Maaten J, Ligtenberg J. A systematic review of the effects of hyperoxia in acutely ill patients: should we aim for less? *Biomed. Res. Int.* 2018; 2018: 7841295.
- Baker K, Greaves T, Fraser JF. How to use humidified high-flow nasal cannula in breathless adults in the emergency department. *Emerg Med Australas.* 2019 Aug 6. doi: 10.1111/1742-6723.13372. [Epub ahead of print]
- McCaig LF, Ly N. National hospital ambulatory medical care survey: 2000 emergency department summary. *Advance Data.* April 22, 2002.

Weiss AJ, Wier LM, Stocks C, et al. Overview of Emergency Department Visits in the United States, 2011. Agency for Healthcare Research & Quality. 2014.

Behrendt C.F. (2000). Acute respiratory failure in the United States: Incidence and 31 - day survival. Chest, Volume 118, Number 4, p 1100 - 1105.

Fessler MB, Welsh CH. Mechanical ventilation: invasive and noninvasive. In: Current Diagnosis & Treatment in Pulmonary Medicine, Hanley ME, Welsh CH (Eds), McGraw-Hill, New York 2006.

Doshi P, Whittle JS, Bublewicz M, Kearney J, Ashe T, Graham R, Salazar S, Ellis TW Jr, Maynard D, Dennis R, Tillotson A, Hill M, Granado M, Gordon N, Dunlap C, Spivey S, Miller TL. High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial. Ann Emerg Med. 2018 Jul;72(1):73-83.

RESEARCH TOPICS

Priority topics for this funding opportunity include addressing the role of NHF in the emergency department to determine adult (older than 18 years) patient outcomes and use of healthcare resources and patient satisfaction with the use of NHF therapy (~50-60 L/min) as first-line approach in undifferentiated respiratory compromise.

Secondary priorities areas in undifferentiated respiratory failure include:

- Effect of level of NHF flow rate on clinical and physiological predictors of success
- Optimization of NHF implementation
- ED discharge/admission pathway for patients with NHF
- Factors associated with pre-hospital to emergency room transition to NHF
- Differential diagnosis of respiratory failure pathogenesis with NHF
- Therapeutic cost effectiveness and healthcare resource utilization

Fisher & Paykel will provide, at its cost and on terms and conditions to be provided by Fisher & Paykel Healthcare, a reasonable amount (as determined by Fisher & Paykel Healthcare in its sole discretion) of loaned Nasal High Flow Therapy equipment for the awarded research, if it is not already at the institution where the research is being conducted. Equipment must be returned to Fisher & Paykel in good working condition at the end of the grant term. Fisher & Paykel will be responsible for all associated shipping and set-up costs.

ELIGIBILITY AND QUALIFICATIONS OF THE INVESTIGATORS

The principal investigator must have a primary faculty appointment in Emergency Medicine. The principal investigator will make all arrangements for conduct of the proposed research projects and assumes responsibility for conducting the research projects and supervising the work of all associate investigators.

INSTITUTIONAL SUPPORT

The applicant is required to demonstrate that the project will be successfully completed at their institution. The applicant must demonstrate that access to a suitable caseload, patient population or database will be available for study during the funding period. **Research must be approved by the institutional review board (IRB), or its equivalent, and a copy of the approval or pending approval sent with this application. IRB approval must be documented prior to dispensation of EMF funds.**

The applicant must also submit a letter from the Chair/Director of Emergency Medicine stating that adequate funds and time will be available to the applicant to complete the proposed project.

EVALUATION OF APPLICATIONS

Each application will be reviewed by the Scientific Review Subcommittee (SRS), emergency medicine specialists who are actively involved in basic science and clinical research. Each application will be judged primarily on: (1) the significance of the project to improve emergency medicine, (2) the soundness of the research methodology, (3) the likelihood the project will be completed, and (4) innovation. The final funding

decision will be made by the Emergency Medicine Foundation Board of Trustees and all decisions are final.

Both scientific review and awarding decisions will be made independent of Fisher & Paykel Healthcare.

TERMS OF THE AWARD

The grant funds will be disbursed semi-annually over the two-year cycle. Disbursement of payments will be contingent upon satisfactory progress reports.

The contribution of Fisher & Paykel Healthcare set out in this RFP constitutes the total amount of Fisher & Paykel Healthcare's contribution to the program. However, Fisher & Paykel Healthcare may, at its sole discretion, if it deems appropriate, provide additional support as it sees fit.

Limitations on Awards

Funds may be used for materials and supplies and to provide salary support. Capital equipment expenditures (costing more than \$5,000 and a life of over one year) must be justified in the budget. Payments will be made to the principal investigator's institution that will be responsible for administering the funds. **The Emergency Medicine Foundation will not be responsible for institutional overhead, cost for publications, travel, renovations, or secretarial support.** Detailed audited financial reports may be required. The EMF is not fiscally responsible for funds necessary for the project's completion.

Change of Status of Principal Investigator

If the principal investigator changes affiliations or ceases research in the field for which the award was made, the award will terminate, and the remaining balance will be returned to the Emergency Medicine Foundation.

Liability of Fisher & Paykel and Emergency Medicine Foundation

Fisher & Paykel and EMF assume no financial liability if patient care responsibilities of any kind are undertaken by the program faculty or investigator. The principal investigator and his or her institution acknowledge that Fisher & Paykel and EMF are not legally liable for the conduct of the institution, the principal investigator, the program faculty, or any associate investigators.

Patent Policy

The principal investigator and institution acknowledge that, though unlikely, if a patentable invention or discovery is conceived, or conceived and reduced to practice by EMF-supported personnel during the award year, EMF must be apprised of the invention and the institution's plans for protecting such invention under existing institutional patent policy. EMF will defer to institutional policies when they are in compliance with those of the Federal government. EMF reserves the right where the organization has no patent policy, or policies not in compliance with those of the federal government, to claim rights and interests in the invention or discovery.

SUPPORT FACILITIES

The applicant must submit letters of support if the proposed project uses facilities not routinely available to or directly under the supervision of the sponsoring program.

PUBLICATIONS

All discoveries resulting from work supported in part by Fisher & Paykel and EMF should be made available to the public and scientific community through scientific and/or public policy channels such as national meetings and peer-reviewed publications. Publications will acknowledge the support of Fisher & Paykel and the Emergency Medicine Foundation. Two electronic reprints of each publication will be forwarded to the Emergency Medicine Foundation.

PROGRESS REPORTS AND MONEY MANAGEMENT

The principal investigator will submit 3 six-month progress report and a final progress report within thirty days of the conclusion of the award year. Additional reports may be required. Failure to provide the reports will delay transmission of funds. Furthermore, failure to provide interim and final reports to EMF may negatively impact your institution's ability to apply for future EMF awards. EMF will maintain the copyright of all such reports. Progress reports must include an accounting report using Generally Accepted Accounting Procedures showing the distribution of funds with a signature from an institutional official (e.g., accountant, grants manager, administrator from the Office of Sponsored Research). EMF reserves the right to withhold release of interim funds if >25% of the previous cycle remains unspent. The EMF allows up to 25% of funds to be carried over from one cycle to the next.

SURVEYS

The principal investigator and the institution will be surveyed periodically following completion of the award regarding career paths, subsequent grants/contracts obtained, and publications. The principal investigator and the institution will be expected to respond to these surveys as EMF will rely on such information to support continuation of the award program.

ABSTRACT PRESENTATION – ACEP RESEARCH FORUM

Awardees are required to present their work at the American College of Emergency Physicians (ACEP) Scientific Assembly/Research Forum immediately following the completion of the award. At the time of submission, abstracts must not have been accepted for publication in any journal. Also, abstracts may not be presented at any U.S. nationwide emergency medicine meeting or major international emergency medicine meeting prior to the ACEP Scientific Assembly. Presentation at non-emergency medicine meetings is allowed after presentation at ACEP. Funds cannot be requested to cover the travel cost to attend the Research Forum.

EMF GRANTEE WORKSHOP

Awardees are expected to attend a grantee workshop in Bethesda, MD. The workshop is designed to bring together EMF grant recipients to present their progress and discuss any problems they may be facing. Senior researchers and faculty will be available to help solve problems, such as enrollment efforts, managing staff and life-work balance. NIH program officers participate in this workshop to discuss funding opportunities, provide research career advice and network with the grantees. Travel expenses will be reimbursed by the Emergency Medicine Foundation.

CONTACT INFORMATION

Please address questions to Cynthia Singh, MS, Deputy Executive Director at csingh@acep.org.

APPLICATION INSTRUCTIONS

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

The application consists of the following sections:

1. INFORMATION PAGE

Name the **one** person responsible to the applicant organization for the scientific and technical direction of the project. Choose a title that is descriptive and specifically appropriate, rather than general. List the mentor and any associate investigators. (See sample below)

2. ABSTRACT (limit 1 page)

Provide a summary of research proposal and career development plan. Include rationale, research hypothesis, specific aims, and significance.

3. TABLE OF CONTENTS

4. RESEARCH PROPOSAL (limit 10 pages)

Please use the following subheadings:

Specific Aims

- State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will exert on the research field(s) involved.
- List succinctly the specific objectives of the research proposed, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.

Specific Aims are limited to one page.

Significance

- Explain the impact of the condition on the health of individuals and populations.
- Explain the potential for the study to improve healthcare and outcomes.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

Innovation

- Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation, or interventions.

Approach

- Describe overall strategy, methodology, and analyses to be used to accomplish specific aims of project.
- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high-risk aspects of the proposed work.
- Include information on Preliminary Studies. Discuss the PI's preliminary studies, data, and or experience pertinent to this application. Preliminary data can be an essential part of a research grant application and help to establish the likelihood of success of the proposed project.

5. PERSONAL STATEMENT (limit 1 page)

The applicant should compose and submit a personal statement that addresses:

- a. the applicant's interest in the topic and this project
- b. the applicant's perception of his/her role in the project
- c. any additional pertinent experience or interests the applicant wishes the reviewers to consider

6. ROLE OF PARTICIPANTS (limit 1 page)

List the principal investigator, co-investigator, mentor and others involved in the research. Include a brief description of how and to what extent each will be involved in the proposed project.

7. BIOGRAPHICAL SKETCHES

Use the NIH Biographical Sketch Format Page available on the internet at <https://grants.nih.gov/grants/forms/biosketch.htm> Information is requested for the applicant, mentor and any associate investigators who will be involved with the projects.

8. RESOURCES AND ENVIRONMENT

Describe the research facilities (laboratory space, clinical population, etc.) available for fellowship training. If computer access or statistical support is available, it should be described in this section.

9. BUDGET

Use the NIH Form Detailed Budget for Initial Budget Period available at www.grants.nih.gov/grants/funding/phs398/phs398.html# Indicate how the money will be spent. Justify all major expenditures. Use the current NIH salary cap. **Institutional overhead is not allowed.**

10. OTHER SUPPORT

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

11. ETHICS

Human subjects. For all research involving human subjects, a part of the peer review process will include careful consideration of protections from research risks, as well as the appropriate inclusion of women, minorities, and children. The EMF Scientific Review Subcommittee (SRS) will assess the adequacy of safeguards of the rights and welfare of research participants, and the appropriate inclusion of women, minorities, and children, based on the information in the application. This evaluation will be factored into the overall score. The information on the protection of human subjects that you are required to provide in this section is identical to information that you will be required to provide for IRB at your own institution and are required by most Federal agencies. This section must address the following items. These can be copied and pasted directly into your application.

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

1. RISKS TO THE SUBJECTS

- a. Human Subjects Involvement and Characteristics

Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. Note that 'prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins. List any collaborating sites where human subjects research will be performed and describe the role of those sites in performing the proposed research.

b. Sources of Materials

Describe the research material obtained from living human subjects in the form of specimens, records, or data.

Describe any data that will be recorded on the human subjects involved in the project.

Describe the linkages to subjects and indicate who will have access to subject identities.

Provide information about how the specimens, records, or data are collected and whether material or data will be collected specifically for your proposed research project.

c. Potential Risks

Describe the potential risks to subjects (physical, psychological, social, legal, or other), and assess their likelihood and seriousness to the subjects.

Where appropriate, describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research.

2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and Informed Consent

Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.

Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. Protection Against Risk

Describe planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects.

Studies that involve clinical trials (biomedical and behavioral intervention studies) must include a description of the plan for data and safety monitoring of the research and adverse event reporting to ensure the safety of subjects.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

Discuss the potential benefits of the research to the subjects and others.

Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

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

5. DATA AND SAFETY MONITORING PLAN (if applicable)

If your research includes a clinical trial, create a heading entitled "Data and Safety Monitoring Plan." Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring.

Vertebrate Animals. For all applications involving vertebrate animals, the applicant must address the following five items. These five points may be copied and pasted directly into the application.

1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Design and Methods section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.
2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
3. Provide information on the veterinary care of the animals involved including the name of the supervising veterinarian. Include information from the Association for Assessment and Accreditation of Laboratory Animal Care International: the name of the accredited parent organization (e.g., University of X) and the certificate number and date of last inspection.
4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.
5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If not, present a justification for not following the recommendations

12. LITERATURE CITED

13. APPENDIX

Include letters of support from the department chairs, and associate investigators (required). No page numbering is necessary for Appendix. Do not use appendix to circumvent page limitations for research plans. Do not include experimental methods, protocols or figures that should be incorporated within the research project description.

14. SIGNED STATEMENT OF CONDITIONS (see below)

Principal Investigator (*Last, first, middle*): _____

Table of Contents

_____	Information Page
_____	Abstract
_____	Table of Contents
_____	Research Proposal
_____	Personal Statement
_____	Role of Participants
_____	Biographical Sketch
_____	Resources and Environment
_____	Detailed Budget
_____	Other Support
_____	Ethics
_____	Literature Cited
_____	Appendix
_____	Signed Statement of Conditions

Information Page Sample

Principal Investigator Full Name with Titles:

Mentor Full Name with Titles:

Name of Institution:

Grant Category:

Project Title:

Amount Requesting:

Principal Investigator (*Last, first, middle*) _____

STATEMENT OF CONDITIONS GOVERNING THE EMERGENCY MEDICINE FOUNDATION GRANT

It is understood that any Emergency Medicine Foundation Research Grant approved by the Emergency Medicine Foundation will be made with the following conditions:

1. Institutional overhead is not allowed.
2. The principal investigator's institution is organized for humanitarian purposes and is not a profit-making organization.
3. All reports of work achieved with this grant will acknowledge the support of the Emergency Medicine Foundation and any co-sponsors.
4. Any discovery that arises from work supported by the Emergency Medicine Foundation will be submitted for publication. Two electronic reprints of each electronic publication will be forwarded to the Emergency Medicine Foundation.
5. Independent progress reports by the applicant will be submitted to the Emergency Medicine Foundation mid-project, and within thirty days of completion of the funding period. Additional reports may be required. The Emergency Medicine Foundation will maintain the copyright of all such reports.
6. Participation in the Emergency Medicine Foundation Grantee Workshop is expected. The Emergency Medicine Foundation will reimburse travel expenses.
7. Grantees must submit the abstract of the funded project to the ACEP Research Forum at the end of the project. Research Forum is held each year during the American College of Emergency Physicians Scientific Assembly. Grant funds may not be used for travel to the Research Forum.
8. If the named principal investigator leaves the institution or terminates research in the designated field, all remaining funds revert to the Emergency Medicine Foundation. If unused funds exist at the completion of the project, all remaining funds revert to the Emergency Medicine Foundation.
9. Patent rights will conform to institutional standards. If none exist, the Emergency Medicine Foundation reserves the right to protect such interests.
10. No research proposal will be funded unless the Principal Investigator and the Institutional Official of the sponsoring institution affirm:
 - a. That the investigation(s) proposed in this application are endorsed by the Animal and/or Human Subjects Committee or other designated body of the preceptor's institution.
 - b. That any research involving human subjects conforms with the principles of the Helsinki Code of the World Medical Association.
 - c. Research involving animals or human subjects must be approved by the institutional review board (IRB), or its equivalent, and a copy of the approval or pending approval sent with this application. IRB approval must be documented prior to dispensation of Emergency Medicine Foundation funds.
 - d. That research involving vertebrate animals will conform with the "Guiding Principles in the Care and Use of Animals" as approved by the Council of the American Physiological Society.
 - e. Research involving vertebrate animals must have approval from the Institutional Animal Care and Use Committee.

Date Signature of Principal Investigator

Type Name of Principal Investigator

Date Signature of Mentor, if applicable

Type Name of Mentor, if applicable

Date Signature of Institutional Official

Type Name of Institutional Official