An Exciting Collaborative Research Initiative for Anesthesiology Clinical and Translational Science: a Call for Letters of Intent

Introduction

We are pleased to inform you about an important new collaborative approach to Anesthesiology clinical and translational research. For several years, colleagues in Europe, Australasia and Canada have successfully conducted multicenter clinical trials in Anesthesiology, including perioperative medicine, pain management, peri-partum care, and perioperative critical care. These studies have enabled our field to address questions that are important to Anesthesiology and society, and have greatly advanced the quality of care we provide on a daily basis. Currently, no such clinical trials network exists in the United States. To remedy this, a consortium of academic anesthesiology organizations has launched an initiative. This effort has been conceptualized and endorsed by organizations, which have as a common goal the advancement of knowledge in Anesthesiology and the enhancement of care in perioperative medicine, critical care, pain management, and peri- and post-partum care. These organizations include the Association of University Anesthesiologists (**AUA**), Early Stage Anesthesiology Scholars (**eSAS**), Foundation for Anesthesia Education and Research (**FAER**), International Anesthesia Research Society (**IARS**), and Society of Critical Care Anesthesiologists (**SOCCA**). We have consulted with several program officers representing NIH institutes, and they have unanimously expressed enthusiasm regarding the process we have conceptualized. The proposed clinical trials network could naturally collaborate with other existing international networks.

The Process of Grant Selection

In order to launch this process, and to establish a proactive and dynamic agenda, we are embarking on a program to solicit, select, and refine clinical research proposals that will have a high probability of receiving support from the National Institutes of Health or another funding agency. We are therefore extending an invitation to investigators to submit letters of intent for pragmatic clinical trials in perioperative medicine. The trials could focus on any or all of the following areas: preoperative care/optimization, operating room management, postoperative management, perioperative critical care, peri- and post-partum care, and pain management. Outcomes should be clinically relevant and important to society. Letters of intent should no more than 2 pages in length, with 1 page being the Specific Aims Page. They should be single spacing, minimum of size 11 font (Arial or Times New Roman) with minimum borders of 0.5 inches.

1) Please send your letters of intent as Microsoft® Word or PDF documents to Meghan Whitbeck (mwhitbeck@iars.org) up to the deadline of December 31, 2017.
2) A study section has been established for this process, comprising representatives of the following organizations: AUA, eSAS, FAER, IARS, and SOCCA. Members of the study section will review the letters of intent, triage the proposals, and, on 15 January 2018, solicit expanded research proposals (specific aims page and 5 pages for research plan) from a subset of meritorious LOI submissions.
3) Expanded research proposals must be received by 15 March 2018.
4) The three selected grants will be announced on 15 April 2018.

The Process of Peer Feedback

On May 1 2018, following the AUA, SOCCA and IARS meetings, there will be a symposium in Chicago to launch this exciting initiative. This meeting will be advertised and will be open to those interested in anesthesiology-related clinical and translational science. The IARS has kindly offered to provide meeting space and information technology support for this event. The principal investigator or another representative of each of the three winning proposals will present their grants to peers, who will provide constructive feedback and suggestions. This will be a structured process in the form of a "Science Garage" or "Grant Boot Camp" and will serve two important functions. First, it will inform the community about the trials, and allow colleagues to become energized about the studies and sign their sites up for participation. Second, it will help to harness the collective intellectual expertise of members of the perioperative research community in order to refine and enhance the grant applications. Apart from the "Science Garage", there will be input from an NIH representative on the importance of this initiative and of the potential to work closely with NIH institutes in advancing this exciting agenda. Representatives of FAER and the IARS will present how such initiatives could provide opportunity to early stage Anesthesiology scholars, wishing to pursue clinical and translational research paths. Finally, organizations that could serve as data coordinating centers and provide other "core" support to clinical trials (e.g., Duke Clinical Research Institute [DCRI], Multicenter Perioperative Outcomes Group [MPOG]) would be invited to make brief presentations outlining how they could provide support to the perioperative clinical trials group and provide discussion of resources (and estimation of costs) available to assist in trial conduct.

The Process of Grant Refinement

The Association of University Anesthesiologists (AUA) has generously earmarked $45,000 to provide seed funding to the three chosen grants ($15,000 each) so that the grants can be refined, strengthened and streamlined prior to submission to an NIH institute or another appropriate funding agency (e.g., PCORI). These funds can be used to obtain statistical analysis review, preliminary data, grant writing support, or fill any specific need identified by the proposal PI. It has been clearly recognized that steps must be taken to ensure that this venture serves as a unifying force in our field, and supports academic Anesthesiology across the United States, as well as other countries. As such, participation in this endeavor does not require that principal or co-investigators must hail from specific institutions or that their trial will utilize any specific existing infrastructure. However, by participating in and conducting their research through one or several established network/s or institute/s, investigators will have access to additional expertise and resources, which will prove a massive boost to any clinical trial. Indeed a major emphasis for the NIH is that clinical research should be conducted efficiently, and utilizing existing reliable infrastructures and registries is viewed as a priority. Clinical Trial Support Units (CTSUs, CTCs, CTSCs, CRSUs, CRUs, CTUs, CTIUs, CTSIs, CRTUs) have been established at multiple academic centers and in the private sector, and conceptually allow investigators to focus on the science instead of the administrative tasks when conducting clinical trials. Brief information is provided below on the DCRI and MPOG. More information on these can be obtained from their websites, and information on other trial support mechanisms can often be obtained from research offices at academic institutions. It is our hope that at least one (if not all) of the three selected grants will be successful in garnering federal (or equivalent) funding.

Duke Clinical Research Institute (DCRI)

The inception of the DCRI dates from 1969 and the formation of the Duke Databank for Cardiovascular Disease, from this humble beginning, the DCRI has grown to be the world's largest academic research organization. The DCRI's mission is to develop and share knowledge that improves the care of patients around the world through innovative clinical research. The DCRI has a rich history of clinical trial experience and success, with completion of over 1,000 phase I–IV clinical trials, outcomes, comparative effectiveness, and implementation studies. These studies have enrolled over 1.2 million patients in 37,000 distinct sites. DCRI's faculty includes scientists, statisticians, and practicing physicians who see patients each day. Together with the DCRI's experienced and knowledgeable operations teams, clinical trial investigators can design and implement innovative clinical trials grounded in the realities of patient care. The DCRI expands the impact of clinical research beyond regulatory approval by designing trials that advance our fundamental understanding of health and disease and inform efforts to improve the quality of care. The DCRI's faculty and operational team's passion is setting new standards for clinical innovation that changes the way healthcare is delivered.

Every day, the DCRI works to address the challenges faced by patients, physicians, government agencies, and research sponsors. The DCRI achieves this by changing the way clinical trials are conducted, by putting knowledge into practice, and by designing educational programs that inspire and prepare the next generation of clinical researchers. Everything the DCRI does is based on collaboration. The DCRI researchers and operational teams work closely with each other and with peers and partners around the world. As an academic research organization associated with the Duke University School of Medicine, the DCRI is able to challenge conventional approaches and explore innovative ways to accelerate the translation of scientific discovery into better care for patients everywhere. What makes the DCRI unique from other clinical research organizations is that it is a non-profit research organization, focused solely on creating and implementing new knowledge in perioperative care and other disciplines. This includes a long history of successful large perioperative trial work.

<u>The DCRI offers the following specific services to investigators:</u>

- Full integration and close collaborations among diverse trial primary investigators at many sites and clinical trial operational leaders/coordinators
- Scalable and Fit-for-purpose trial design support and operations
- Collaborative approach to academic leadership
- Mature North American site investigator networks that can be leveraged for high-quality enrollment
- Streamlined data collection (including EMR based data collection) and adverse event reporting
- Focused, risk-based monitoring and predictive modeling to minimize costs of trial conduct
- Emphasis on study drug/procedure compliance and complete follow-up
- Shared endpoint adjudication activities
- Long standing clinical research education and fellowship opportunities to train the next generation of perioperative clinician-scientists
- DCRI commitment to cover upfront costs of clinical trial submission and planning by providing expert grant-writing assistance, budget creation, study manual of operation creation, site contracting and study material generation for the perioperative trial network

A key feature of the DCRI resource is that a clinical trial or trials network can use as much or as little of DCRI's many components as is needed. This can truly be tailored to an individual study or network's needs. This can include utilization of only data management, only clinical coordinating center resources, statistics, regulatory, or any other key trial support functions alone or in combination as needed**.** The DCRI has a rich experience in coordinating research networks such as the Perioperative Clinical and Translational Science Initiative described in this call for proposals. This includes a history of coordination of 34 distinct networks including the > 110 million patient record PCORnet, The NIH Health Care Systems Research Collaboratory, The Federally Funded Pediatrics Trial Network, and The NIH CTSA Trials Innovation Network.

The DCRI has recognized that there is a strong need to enhance perioperative clinical and translational research in the U.S. and around the world. For this reason, the DCRI recently recruited a Professor of Anesthesiology, Dr. Paul Wischmeyer, to be its Director of Perioperative Research. Dr. Wischmeyer is a highly accomplished clinical and translational researcher, and can be contacted by e-mail at: paul.wischmeyer@duke.edu. More information on the DCRI can be found at https://www.dcri.org/about/who-we-are/ and https://www.dcri.org/our-approach/.

Multicenter Perioperative Outcomes Group (MPOG)

MPOG is a group of passionate individuals from more than 50 hospitals across 18 states and 2 countries, working together to improve care for patients undergoing surgery. MPOG has evolved organically as a labor of love within Anesthesiology, and is committed to advancing the field academically and to providing growth opportunities for future leaders in Anesthesiology. MPOG's members include clinicians, quality improvement experts, software developers, statisticians, researchers, and administrators. Over the last decade, MPOG has built a comprehensive perioperative patient registry based on electronic healthcare data to improve quality of care, conduct research, educate caregivers and guide healthcare administration. MPOG is a collaborative venture that was made possible by the transition in hospitals to electronic medical records. Collaborating institutions contribute electronic data to MPOG, which the MPOG administrative team checks, cleans, and homogenizes. MPOG's mission is to benefit Anesthesiology and society through the generation of knowledge obtained from this valuable data repository. MPOG has a rotating Executive Board, which includes its Executive Director, Research Director, its Quality Improvement Director and 9 elected chairs, representing Anesthesiology departments in the United States and Europe. MPOG has a track record of successful and high impact observational research in perioperative medicine.

To increase the clinical impact of the existing infrastructure, MPOG founded a quality improvement initiative known as ASPIRE (Anesthesiology Performance Improvement and Reporting Exchange) three years ago, with more than $2M of external annual funding. ASPIRE sites work together build quality measures, review best practices, exchange ideas on how to improve patient outcomes. ASPIRE delivers measure performance information to participating sites via the ASPIRE dashboard and regular, automated provider specific feedback emails.

The logical next step for MPOG is the establishment of IMPACT (Initiative for Multicenter Perioperative Clinical Trials) as an arm that supports and empowers perioperative clinical and translational research. As a stepping-stone to prospective, pragmatic

clinical trials, MPOG recently embarked on an enhanced observational study. Chosen through a competitive process, the University of Utah and University of Virginia led a study conducted across 12 US and European medical centers focused on the Acute-to-Chronic pain transition in patients undergoing major surgery. Over the span of just 2 weeks in September 2017, more than 1100 patients were enrolled, consented, and phenotyped using robust, peer-reviewed pain, mood, affect, and opioid use instruments. Follow up 1 and 3 month phone calls have begun. A robust configurable electronic case report form (eCRF) tool, center-specific patient enrollment dashboard, registry-eCRF linkage, and competitive grant administration process have all been created to enable prospective enhanced observational studies and pragmatic randomized controlled trials.

MPOG can be contacted by email: anes-mpog@med.umich.edu. More information on MPOG can be found at https://mpog.org/about/.

Conclusion

We look forward to receiving letters of intent from a diverse range of investigators with projects spanning the many areas of perioperative medicine, critical care, and pain management. If you have questions regarding this initiative, please write to Vivian Abalama (vabalama@iars.org), and she will direct your query to an appropriate person on the ad-hoc coordinating committee.

This article / call for letters of intent has been endorsed by representatives of the following organizations:

- Association of University Anesthesiologists (**AUA**)
- Early Stage Anesthesiology Scholars (**eSAS**)
- Foundation for Anesthesia Education and Research (**FAER**)
- International Anesthesia Research Society (**IARS**)
- Society of Critical Care Anesthesiologists (**SOCCA**)