This article is the first in a series exploring all aspects of grant submissions. In it we explore some of the major required steps to submitting a successful grant application.

A key PECARN goal is to increase the number of extramurally-funded grants. Although we have PECARN funding, most research projects require outside funding to be successful. Our network has been successful thus far at obtaining extramural funding; however, it is always a monumental task to submit grants for projects that will use multiple sites.

Routing Applications: Introduction

Routing an application for government funding is an elaborate, time-consuming process—under the best of circumstances! If you are lucky, you will have access to an experienced savvy person within your department to take care of the entire process for you, as well as a Nodal Administrator to help manage the process both internally and externally.

Timing is key: for multi-site projects, the budgeting process MUST begin several months ahead of time. Luckily, the Feasibility and Budget Subcommittee is charged with making sure your project will work within PECARN and will assign an NA to work with you to help develop the budget. Generally, investigators greatly underestimate the amount of time and resources it takes to develop and submit external research proposals. The entire process may take up to a year for newly developed projects, down to a few months for resubmissions. It may help to discuss your research plan with your Nodal PI, NA, and other PECARN investigators to get a sense of how projects have been organized in the past. However, take note that the allocation of PECARN resources is dependent on a Steering Committee prioritization and vote.

For both the research plan and budget, it is critical to read the Program Announcement or RFP carefully each time you prepare an application. Requirements change all the time, application forms are revised frequently, so read the RFP even if you are preparing a resubmission.

Routing Submissions: Approvals

Your first goal in processing your grant application is to obtain required institutional approvals from participating hospitals. For multi-center studies, this process must start at least 45-60 days prior to your institution’s deadline for reviewing the grant application. Initiating this process involves sending each participating institution the following information: budget and budget justification for their site; the primary site’s budget and budget justification (in some cases), an abstract formatted on the appropriate...
Once you have obtained all necessary approvals, and have copies (original, faxed, or printed) of participating sites’ Face pages, you are ready to submit to your OGC Project Officer for review 21-30 days prior to the granting agency application deadline (or longer if your institution requires). You will compile a mock-up of your entire grant, including a table of contents, all application forms, bio-sketches, and the grant narrative. This packet will also include some indication of your institution’s prior required approvals, and a link to or copy of the RFP. The packet should be page-numbered and look as close to the final submission as possible. In most cases, you can do this easily, because the only portion of the grant that is being edited at the last minute is the narrative and you know exactly how many pages this will be.

Your Project Officer will resolve any corrections or modifications, sign the Face Page and give you the original to include with your submission. At this point, you have everything you need to submit your proposal.

**Routing Applications: Conclusion**

You can be guaranteed that everyone involved in submitted grants in your institution will be harried and pressed for time in the weeks immediately preceding the major agency deadlines. It will help your case greatly if you have good personal working relationships with everyone involved.
Availabiity of Pediatric Services and Equipment in Emergency Departments: United States, 2002-03.
http://www.cdc.gov/nchs/data/ad/ad367.pdf

Although most children requiring emergency medical care are brought to hospitals that have appropriate emergency care specialists and equipment, a significant number are treated at facilities that lack AAP/ACEP-recommended pediatric equipment and a fully-trained staff, according to a new CDC report. Children account for about 30 million visits a year to hospital EDs. The survey data, collected in 2002-03 through an interagency agreement with HRSA/MCHB/EMSC, showed that most children who need emergency care are brought to hospitals which see more than 10,000 pediatric patients each year. These larger hospitals are more likely to have a pediatric ward, a pediatric intensive care unit, and are also more likely to have a board-certified pediatric emergency physician on staff. The NHAMCS gathers detailed data from a sample of the Nation’s EDs. More information about hospital preparedness for pediatric emergencies will be gathered in the 2006 survey, which will include a larger number of children’s hospitals.

National EMS Information System (NEMSIS) Update
The NEMSIS is a national system designed to collect standardized EMS data in order to determine the clinical and operational contributions made by EMS, facilitating research efforts, evaluating outcomes, and providing valuable information for several areas of emergency care and disaster preparedness. Currently 48 State and 4 Territorial EMS offices have signed on to a Memorandum of Understanding, agreeing to promote and support NEMSIS implementation. NHTSA’s National Center for Statistics and Analysis (NCSA) has agreed to house national NEMSIS data. The NEMSIS Technical Assistance Center is a contract between NHTSA’s Office of EMS and the University of Utah, assisted by the University of North Carolina. For more information, go to www.nemsis.org

Economic Costs of Injuries
CDC’s NCIPC is pleased to announce the publication of The Incidence and Economic Burden of Injuries in the United States. The book provides a fresh look at the incidence and economic burden of injuries that occurred in 2000, including injury-attributable medical expenditures and the value of lost productivity resulting from these injuries. For more information on this publication, go to:

For more information and a fact sheet on this topic, go to:
http://www.cdc.gov/ncipc/factsheets/CostofInjury-Children.htm

Past Meetings
Interagency Committee on EMSC Research (ICER) Meeting
Hosted by the EMSC Program

Dan Kavanaugh, MSW, LCSW-C hosted the ICER meeting, which focused on presenters who described 3 research agendas related to EMSC: 1) the PECARN agenda presented by Mr. Kavanaugh; 2) The National EMS Research Agenda, published in 2001 (the Strategic Plan was published last year), presented by NHTSA’s EMS Specialist, Susan McHenry; and 3) the CDC/NCIPC’s new Acute Injury Research Agenda, presented by Richard Hunt, MD, Director of the Division of Injury Response. The discussion included advice from NIH and AHRQ representatives, who shared ideas about informing various federal agency leaders about EMSC and EMS research needs, and strategies for getting research gaps addressed in research announcements.

National Association of EMS Physicians Annual Meeting
EMSC Program & NAEMSP co-sponsored a Pediatric Prehospital Research Workshop

This Workshop, supported by the EMSC Program and organized by PI Kathleen Brown, MD, was again well-received by participants and provided a forum for participants on how to turn their research ideas into proposals for funding pre-hospital EMSC research.

John Templeton Jr., Pediatric Trauma Symposium
CHOP, Children’s Hospital of Pittsburgh, and St. Christopher’s Hospital for Children

This meeting highlighted advances in pediatric trauma assessment and treatment and evidence-based injury prevention initiatives. Two EMSC grantees, Mirna Farah and Dr. Nancy Kassam-Adams, presented their respective research on family presence and 48 State contributions made by EMS, facilitating research efforts, evaluating outcomes, and providing valuable information for several areas of emergency care and disaster preparedness. Currently 48 State and 4 Territorial EMS offices have signed on to a Memorandum of Understanding, agreeing to promote and support NEMSIS implementation. NHTSA’s National Center for Statistics and Analysis (NCSA) has agreed to house national NEMSIS data. The NEMSIS Technical Assistance Center is a contract between NHTSA’s Office of EMS and the University of Utah, assisted by the University of North Carolina. For more information, go to www.nemsis.org

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Has Anyone Seen the Study Protocol?
By Sally Jo Zuspan, RN, MSN, CDMCC Program Coordinator

How important is a well written protocol? A well written, scientifically sound research protocol is the foundation of a successful PECARN research study. In PECARN, we have learned that a complete, concise protocol will help sites carry out the study accurately, and will help assure valid data and patient safety. On the other hand, confusing statements and inconsistencies can result in those pesky protocol amendments, changes in data forms and the database. This is a painful process we want to avoid! Each change to the protocol or addition of data elements can delay your project for weeks or months.

Lessons Learned: We have learned several lessons about writing protocols. The protocol should be specific enough that sites should be able to find answers to most questions regarding “how to” conduct the study. However, we have also learned that too much detail can work against you when multiple sites are participating. It is a good idea to survey participating PECARN sites prior to writing the protocol to clearly understand how other ED systems work before specifying study procedures. For example, perhaps you wish to specify that the first study assessment must be done before triage. While this might work in some EDs, other centers may not be able to complete any sort of clinical activity prior to triage. A well-meaning site that cannot comply might even develop slightly varied procedures that could ultimately affect the data. Time frames for study procedures are another potential area of difficulty. Time limits should be as general as possible to avoid frequent protocol deviations. A rigid time frame, (say vital signs taken within a 15 minute interval) will likely be difficult for sites to attain and may result in so many protocol deviations that a protocol amendment will be required to lengthen the time frame. Regulatory agencies like to inquire about the number of protocol deviations in a study as an indicator of the simplicity of the study processes. Too many protocol deviations is not a good thing.

Grant vs. Protocol: The study description required for a grant application is not necessarily the same as the clinical protocol. The protocol guides describes the specifics of the study and must be able to stand up to the scrutiny of the IRB and regulatory agencies. This article will identify some of “Do’s and Don’ts” for writing the clinical protocol. The FDA regulations specify protocol elements for drug studies in more detail than what is described here. PECARN studies should contain most of the sections below to be compliant with GCP. The CDMCC will work closely with the investigator to advise on regulatory, safety, statistical, ethical and practical considerations in writing the study protocol. Once the protocol is drafted, the protocol should be transitioned to the CDMCC for finalization. It is essential that the final protocol is not changed once in its final form. Sites may not make any changes without approval from the CDMCC and the investigator.

Do’s and Don’ts* for Protocol Development

These tips represent GCP, regulatory requirements and PECARN experience!

1. **Introduction and Objective(s):** The objective(s) should be clearly stated, and related to the design of the study. Primary and secondary endpoints should be clearly delineated.

2. **Study Design:** Clearly describe the rationale of study design (i.e., double-blind, placebo controlled, etc.), detail of treatment groups, subject description and duration of study period.

3. **Inclusion Criteria/Exclusion:** Criteria should be detailed sufficiently to make it easy for sites to determine who is eligible. Avoid criteria that are overly inclusive or exclusive.

4. **Study Plan and Methods:** Write a detailed plan of procedures, methods and timing of activities. All data elements should be explicitly listed. Describe in detail any laboratory or diagnostic tests. Describe circumstances for subject withdrawal or discontinuation (e.g., protocol violations, adverse events).

5. **Adverse Events:** Describe expected adverse events and how they are to be reported.

6. **Ethical Considerations:** Describe risk/benefit assessment, informed consent process, regulatory compliance, and maintenance of subject confidentiality. The IRB will want details of how sites will obtain informed consent/assent. Make sure you have consulted with the CDMCC or others to address all potential concerns that the IRB might raise.

7. **Study Monitoring:** Include a plan that details the frequency and type of site monitoring.

8. **Investigational Product Management:** Describe packaging, tracking, storage, and destruction of study drug.

9. **Data Analysis:** Details the statistical approach that includes how the sample size was determined, including the assumptions made in making this determination. Before the study begins, the endpoints need to be clearly and completely defined. Safety endpoints should also be defined before the study begins.

10. **Statistical analysis:** Describe how the results will be analyzed and reported; primary endpoint(s), statistical tests for analysis of the endpoints, a definition of the level of significance, statistical tests to be used, and methods used for missing data. Describe any interim analyses.

References:

PECARN Study UPDATE

Bioterrorism Surveillance:
Boston Children’s Hospital continues to gather biosurveillance data from Children’s National Medical Center and is working with UC Davis and University of Michigan IT groups to set up processes to collect historical data as well as daily data feeds. Technical discussions are about to begin with Howard County Hospital. A pre-proposal is under review at the Agency for Health Care Research and Quality. Ken is also in discussions about the proposal with appropriate personnel at the CDC. The proposal has two major objectives: 1. to take a leadership role and help coordinate current health information technology efforts among the American Academy of Pediatrics, the American Board of Pediatrics, the National Association of Children’s Hospitals and Related Institutions, the Child Health Corporation of America, and the Centers for Disease Control and Prevention. 2. to build a robust dataset for use by PECARN researchers. The completion of these two major objectives will accomplish the goal of establishing a Children’s node within NHIN. Optimally, the full demonstration of this capability should be ready by fall 2006, to coincide with other major national demonstration projects for the Office of the National Coordinator of Health Information Technology. The Biosurveillance group continues to hold monthly conference calls.

Bronchiolitis Study:
Active enrollment across all sites stopped on April 30, 2006. During season three, 197 subjects were enrolled for a total of 614 subjects. Site monitoring close out visits are being conducted at every site and will be completed by mid-June. The query and data cleaning process is underway and data analysis will begin once all data is cleaned.

C-Spine Injury in Children:
We currently have seventeen sites abstracting charts and anticipate all sites to be active by June. Though only a fraction of our total sample has been entered into the EDCS, we have amassed the largest case series of cervical spine injured children ever reported. A plenary meeting for the EMS focus group phase of our project will be held in association with the Fall PECARN meeting.

Diagnostic Grouping System:
Since our last meeting, diagnoses from DGS have been assigned severity ratings representing the intensity of ED resources required. Examples of the lowest severity diagnoses include contact dermatitis and diaper rash; moderate severity diagnoses include fever, asthma, and vomiting; and highest severity diagnoses include asphyxia and septicemia. Currently, study investigators are correlating these severity ratings with other measures of resource use from EM datasets.

Traumatic Brain Injury:
Traumatic Brain Injury: Participant enrollment for the derivation phase of the TBI study reached 34,000 by the end of April 2006. We will create our decision rule based on these data. However, we will continue to enroll an additional 10,000 participants through August 2006 in order to validate the decision rule. The CDMCC has started data cleaning and query generation in preparation for data analyses. Sites have maintained a steady 78% capture rate overall. Thanks to everyone for working so diligently to make TBI a success!

Hypothermia:
Hypothermia update data queries are finally complete and data cleaning is underway. Funding for the R21 grant ended in March. We are hoping that the R34 writing grant will be funded; we should be notified by the June meeting.

A summer 2006 meeting is being discussed to develop the protocol for the RCT.

PECARN Core Data Project:
The CDMCC has created validation reports for 2003-5 PCDP submissions.

Please respond to any outstanding issues for your site. Questions should be directed to Libby Alpern at: Alpern@email.chop.edu. For preliminary analysis of PCDP data for study design development, you can access the cubes from eRoom, or complete a data request form. The request form can be found at https://www.nedarcssl.org/erroom/ndd/p/PECARNCoreDataProject/0 a670 The PCDP manuscript "Epidemiology of a Pediatric Emergency Medicine Research Network: The Pediatric Emergency Care Applied Research Core Data Project" was accepted by Pediatric Emergency Care.

Psychiatric Emergency Pilot Project:
This group is currently re-abstracting data and data queries have been developed. Data queries will be resolved over the summer.

Prehospital Working Group:
The prehospital working group has been working on the EMS survey for PECARN. Most sites have completed the survey and data cleaning is in process.

Seizure:
Lorazepam for the Treatment of Pediatric Status Epilepticus: The seizure study is completing enrollment for the pharmacokinetic portion of the trial. As of April 2006 the study had currently completed enrollment for approximately 53 patients. The original goal was to enroll 60 children in the pharmacokinetic trial. As the pharmacokinetic study nears completion, we are beginning to develop the protocol for study 2, a double blinded randomized controlled trial of Lorazepam and Diazepam for the Treatment of Pediatric Status Epilepticus. The current plan is to submit an IND under an exception from informed consent. If approved, this will be the first pediatric trial conducted under an exception from consent. Preparations for the IND application will continue through the summer of 2006.
Data Queries

Now that several PECARN studies are nearing completion, the process of cleaning up the data is a priority. Data must be “cleaned” to correct missing or inconsistent data before analysis. There are three ways to verify data during a research study or clinical trial: 1) During site visits as the site monitor reviews data from the source document (medical record, or other specified document) and compares each element to what is entered in the database. If the two do not match the monitor will ask the site to resolve the problem on site, if possible. 2) Data errors can be found by computer generated logic checks to catch data that are out of range, missing or illogical, such as entering a visit date that is earlier than the date of birth. 3) The data can also undergo a manual review at the CDMCC. This method offers a way to monitor the data without the expense of travel.

What is a data query?

A data query is a question directed to the site that identifies any apparent data errors or inconsistencies. If an error is found by a computer generated logic check or by manual review, a data query form will be directed to the site from the data center. For example, if a 4-hour vital sign check was recorded as having been done at 4:00 pm instead of 1600 hours, a query would be sent to the site to verify the time. Another example is if a subject had a Glasgow Coma Score recorded as “5” but was reported to be alert. These two variables are inconsistent and would likely result in a query to the site.

Resolving Queries

In some cases, it is possible that the data are actually correct but just appear to fall outside of an expected set of values. In this case, the site can inform the CDMCC that despite appearing erroneous, the value is actually correct. For example, a blood pressure may be outside the range of “normal” but was accurate for a critical patient. To respond to a query, the Research Assistant (RA) at the site checks the paper data collection form or may need to go back to the medical record to verify the data. Once a questionable element has been corrected or verified to be accurate, it is considered resolved. Unresolved queries will continue to be sent to the site until they are completed.

How clean is clean?

While there is no magic number to represent an acceptable error rate, researchers want the data to be as clean as possible. In industry, an acceptable error rate is considered to be less than 1.0%. Double and triple data entry, logic checking and other methods help minimize error, but data queries help resolve outstanding data errors before the data is analyzed. In PECARN, we want to keep our data error rate as low as possible, so queries must resolved accurately by the site.

The making of a query

Ideally, the CDMCC and the PI or working group will define and generate queries at the beginning of the study. However, it is difficult to anticipate all the queries that are necessary. Therefore, new queries may be added at any point in the enrollment period. This question from the head injury study was a good example: “Was the CRF 1 completed before the CT results were reviewed?” When it was determined that sites were possibly interpreting this differently, the CDMCC and the lead investigator decided to send out a specific query to evaluate the way this question was being answered. These types of queries can be valuable in assuring that data collection is consistent between sites. Sites will benefit from early queries by catching mistakes in data entry, or finding data that are erroneous due to a misinterpretation of the protocol. With each subsequent PECARN study, queries have been generated earlier in the data collection process. In future studies, we will generate queries beginning with the very first enrolled subjects. This approach reduces the need to do large numbers of queries at the end of the study.

Continued on next page
The principal investigator of the Great Lakes EMSC Research Network, Ronald Maio, D.O., M.S., has accepted a position as Director of the Office of Human Research Compliance Review for the University of Michigan. Dr. Maio will begin his new position on May 1, 2006. Dr. Maio will continue in his role as the principal investigator of the Great Lakes Node of PECARN.

ACORN
The Academic Centers Research Node (ACORN) would like to congratulate two of its members on their recent promotions. Nate Kuppermann was promoted to the Bo Tomas Brofeldt Chair of Emergency Medicine at UC Davis in January, 2006. Nate has already made great strides in this new role, and the department is thrilled to have such a strong leader. Evie Alessandrini was promoted to Associate Professor of Pediatrics at the University of Pennsylvania School of Medicine- a well deserved promotion. Congratulations to you both on a job well done!!

PEDNET
In the Pediatric Emergency Department North East Team (PEDNET) CHOB enrollers Osman Farooq and Zeb Memon were both admitted to the Pediatric Residency program at the Women and Children’s Hospital of Buffalo (WCHOB). They will start their residency in June. We are excited for this great news! Both Osman and Zeb have done a wonderful job as research assistants for PECARN studies at CHOB. We wish them the best at their career.

Margaret Boyle, RA from Upstate Medical University, will be leaving this summer to pursue a nursing degree at Pacific Lutheran University in Tacoma, WA. She will earn her Master of Science in Nursing and plans to work in the Seattle area as a Family Nurse Practitioner.

CARN
CARN (Chesapeake Applied Research Network) had a nodal retreat on April 1, 2006 where we discussed new research ideas, brainstormed ways to improve enrollment in research studies and discussed strategies for improving nodal and PECARN infrastructure.
New Faces

GLEMSCRN welcomes four new researchers. **Alexander Rogers, M.D.,** an Instructor in the departments of Emergency Medicine and Pediatrics, is serving as the site principal investigator at the University of Michigan for the study *Predicting Cervical Spine Injury (CSI) in Children.*

**Ramin Mortarjemi,** who holds a Doctor of Medicine Diploma from Azad Medical University, Tehran School of Medicine, will serve as the research associate at Hurley Medical Center for the study *Predicting Cervical Spine Injury (CSI) in Children.*

**Kristine Ciesiak, M.D.,** an Assistant Professor of Pediatrics at the Northwestern University Feinberg School of Medicine, will serve as the site principal investigator at Children’s Memorial Hospital in Chicago for the study *Clinical Decision Rule to Identify Children with Intra-abdominal Injuries.*

**Nirupama Kannikeswaran, MBBS,** an Assistant Professor of Pediatrics, Division of Emergency Medicine, will serve as the site principal investigator at Children’s Hospital of Michigan for the study *Safety of Emergency Department Pediatric Procedural Sedation and Analgesia.*

**Brandon W. Perry** was born 11/7/80 in Tulsa, Oklahoma and moved to Pennsylvania in 1995. Attended University of Maryland at College Park, and received a B.S. in Biology in 2003. Member of Kappa Alpha Psi Fraternity Inc.

**Sara Mazzuto** started working at CNMC in February. Hailing from New Jersey, she came to the DC area for graduate studies at George Washington in Health Policy. She has a BA in Art History and Psych from Rutgers and an MPH from NYU. Her previous research experience was in cardiology. She is very excited to be a part of PECARN.

**Aaron Donoghue** is Assistant Professor of Pediatrics and Anesthesia in the University of Pennsylvania and is an attending physician in the Divisions of Emergency Medicine and Critical Care Medicine at CHOP. He holds an M.S. in Clinical Epidemiology from the Center for Clinical Epidemiology and Biostatistics at Penn Med. His research interests include pediatric cardiac arrest and resuscitation, pediatric airway management, and the use of high-fidelity simulation in pediatric medical education. He is a Fellow in the American Academy of Pediatrics.

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**CDMCC Site Monitoring Visits**

**February-June 2006**

**CDMCC Bronchiolitis Site Visits**

- Bellevue Hospital Center
- Boston Children’s Hospital
- Children’s Hospital of Buffalo
- Children’s Hospital of Michigan
- Children’s Hospital of New York
- Children’s Hospital of Philadelphia
- Children’s National Medical Center
- DeVos Children’s Hospital
- Howard County General Hospital

**Hurley Medical Center**

- Johns Hopkins Medical Center
- Primary Children’s Medical Center
- University of Rochester Medical Center
- Upstate Medical University
- University of Maryland
- Cincinnati Children’s Hospital
- Washington University /Saint Louis Children’s

**CDMCC C-Spine Site Visits**

- University of Maryland
- Washington University /Saint Louis Children’s