

Pediatric Emergency Care Applied Research Network (PECARN) Policies and Procedures



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Note: This document contains selected, relevant bylaws, policies and procedures necessary to apply for this funding opportunity announcement. For further information please contact Diane Pilkey at dpilkey@hrsa.gov



Pediatric Emergency Care Applied Research Network (PECARN) Bylaws

Document History

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Version September 1, 2006	Created 28 Feb 2006	September 1, 2006 by electronic vote October 1, 2015 by electronic vote
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I. Name: PECARN

II. Purpose

1. Mission Statement

The Pediatric Emergency Care Applied Research Network (PECARN) is dedicated to improving the health care for ill and injured children. PECARN will perform meaningful and rigorous multi-institutional research into the prevention and management of acute illnesses and injuries in children in order to promote their health in all phases of care. PECARN will also provide the leadership and infrastructure needed to support research collaboration among EMSC investigators and informational exchanges between EMSC investigators, providers, and the communities they serve in order to significantly improve EMSC care delivery.

2. Research Agenda

The research agenda of PECARN is focused on achieving the goals of the mission statement. In general, the research agenda follows that of pre-existing consensus-derived EMSC research agendas, including published EMSC/MCHB research priorities (PA-01-044, "Research on Emergency Medical Service for Children" release date January 25, 2001, <http://grants.nih.gov/grants/guide/pa-files/PA-01-044.html>) as well as the written PECARN research priorities established by consensus within the PECARN.

III. Structure

PECARN Steering Committee and Subcommittees
Research Nodes
Research Node Centers (RNC)
EMS Affiliates (EMSA)
Hospital Emergency Department Affiliates (HEDA)
Data Coordinating Center (DCC)
Working Groups

IV. PECARN Membership

1. Network Membership

Categories of PECARN membership include Active and Associate members.

- a. Active members are defined as individuals who are participating within the structure of PECARN as defined under item III. In addition, members of the federal government participating in PECARN will be considered Active members.
- b. Associate members are defined as individuals who are not members of the PECARN structure as defined under item III, but who are involved in the conduct of PECARN research projects in another capacity.

2. Steering Committee and Subcommittee Membership

Active members of PECARN may serve as members of the PECARN Steering Committee and Subcommittees.

a. Steering Committee

The voting members of the Steering Committee will consist of the RNC PIs and the EMSA PI, HEDA PIs or other representatives from each Research Node, and the PI of the PECARN Data Coordinating Center. All other representatives from each Research Node (mentioned above) will be appointed by the respective Nodal PI, or designated as an official proxy by any voting member absent during an official vote. Ex officio members from the HRSA/MCHB will be non-voting.

b. Subcommittees

The Subcommittees will consist of at least one representative from each Research Node, selected by the Research Node PI. Each subcommittee will vote to add additional members if deemed essential for functioning of the committee, and make additional appointments, subject to approval of the

Steering Committee. All subcommittee members have voting privileges within the subcommittee.

Subcommittee Chairs are appointed by the Steering Committee Chair subject to approval by majority vote of a quorum of the full Steering Committee (maximum of 19 voters). If it's an EMS related concept or protocol the maximum voters will be 22.

Role of External Investigators in Committees

In certain circumstances, external investigators who are not otherwise members of PECARN may be invited to participate as associate members of specific committees. This may occur when the Chair of that committee deems it necessary because special expertise is lacking in the committee. This invitation must be approved by vote of the Steering Committee. External investigators may be invited by a Research Node, a Subcommittee, a Working Group, or by the Steering Committee. Any sponsor of an external investigator assumes responsibility for the investigator within PECARN. No external investigators will be voting members of PECARN.

V. Officers of PECARN

1. Steering Committee and Subcommittee Officers

Steering Committee Officers

Officers of PECARN Steering Committee will include the Chair, Vice-Chair, and Secretary.

Duties of the PECARN Steering Committee officers:

- a. Duties of the PECARN Chair are primarily those of overseeing the operation of PECARN, which includes coordinating and running the Steering Committee meetings on a rotating basis with the other Nodal PIs, appointing Subcommittee Chairpersons to be later approved by the Steering Committee, maintaining ongoing communications with Nodal PIs and keeping all of PECARN updated with new/ongoing activities, and serving as liaison to HRSA/MCHB federal officials.
- b. Duties of the Vice-Chair include assisting the Chair with PECARN responsibilities, as deemed necessary. In addition, the Vice-Chair will assume the position of Acting Chair in the event the Chair becomes incapacitated, and will initiate an immediate vote by the Steering Committee to elect a new Chair from the RNC PIs. The Vice-Chair may officiate at meetings in the temporary absence of the Chair.

- c. The PECARN Secretary will work closely with HRSA/MCHB representatives to insure that careful and authentic records of Steering Committee proceedings are kept. These duties will include carefully reviewing Steering Committee minutes and summaries prepared by the HRSA/MCHB for their accuracy and integrity. The Secretary will also maintain an updated list of all committee officers and members and insure that a copy of the PECARN bylaws is available at all Steering Committee meetings. The PECARN Secretary will serve as the primary point of contact for the meeting logistics contractor, coordinating meeting hotels, venues, meeting equipment, etc. In addition, the Secretary will provide administrative support to the Chair of the Protocol Review and Development Subcommittee (PRADS). The Secretary will assume additional responsibilities as deemed appropriate by the Steering Committee Chair and Vice-Chair.

Subcommittee Officers

Each Subcommittee will be led by a Chairperson:

- a. The duties of these Chairs will be to oversee the operation of their subcommittees, which includes planning and coordinating the subcommittee meetings, maintaining ongoing communications with subcommittee members as well as serving as liaison to the PECARN Steering Committee. The Chairs will coordinate the generation and review of documents pertinent to their subcommittees, for ultimate approval by the Steering Committee. Subcommittee Chairs will maintain regular communications with the Steering Committee Chair.

2. *Terms of Office, Qualifications, and Elections*

Terms of Office

- a. Steering Committee officers will be elected by the voting members of PECARN. Elected officers will serve three -year terms. Any active member of PECARN, as defined above, may nominate individuals for an officer position.

Qualifications

- a. The Steering Committee Chair and Vice-Chair must be RNC or EMSA PIs. The Secretary position must be a PECARN Nodal Administrator.
- b. The Subcommittee Chair should typically be, but is not required to be, a member of the Steering Committee. If the Subcommittee Chair is not a member of the Steering Committee, s/he will nonetheless be expected to

attend Steering Committee meetings, albeit as a non-voting member, unless serving as an alternate for a voting member.

Elections

- a. Elections will be conducted by ballot vote either in person or on the voting eRoom. Steering Committee officers will be elected by majority vote.
- b. Subcommittee Chairs are appointed by the PECARN Chair and are subject to approval by a Steering Committee (majority) vote.
- c. PECARN officers can be removed from office by a vote of two-thirds of the PECARN Steering Committee.
- d. Nominations can be made by any active member of the PECARN.
- e. Removal of an officer before expiration of his or her term requires a 2/3 majority vote.

VI. Meetings

1. *Frequency of meetings*

Steering Committee

- a. In person Steering Committee meetings will be held up to four times annually, per HRSA/MCHB guidance and Steering Committee vote. There will also be provisions for electronic meetings, as necessary.

Subcommittees

- a. Subcommittee meetings will be held per HRSA/MCHB guidance and Steering Committee vote. Subcommittees should meet in person as often as necessary to conduct subcommittee business. The subcommittees will also be expected to communicate more frequently via conference call or other electronic means.

2. *Alternates*

Alternates for Steering Committee and subcommittee members who cannot attend a specified Steering Committee or subcommittee meeting must be designated by the Research Node PI. It is assumed that the alternate should have substantial knowledge of the PECARN issues to be discussed at the specified meeting.

3. *Voting*

Decisions are made by majority vote of those votes cast, one vote per member or alternate, with two-thirds vote required under special conditions (per Robert's Rules of Order and other PECARN bylaw guidance).

4. *Quorum*

Steering Committee

- a. Steering Committee quorum consists of at least two thirds of RNC PIs plus at least one half of voting HEDA PIs or alternates.

5. *Robert's Rules of Order, Meeting Confidentiality, and Open Meetings*

- a. Robert's Rules of Order will be used to conduct the business at PECARN Steering Committee and subcommittee meetings.

All members of PECARN and meeting attendees must abide by the confidentiality of research proposal materials presented at PECARN meetings and in PECARN communications. Research proposal review materials and meeting discussions are privileged communications prepared for use only by PECARN members and research program staff. Guest meeting attendees will be informed of the strict confidentiality issues in PECARN and must agree to them prior to attendance.

- b. PECARN Steering Committee meetings are open to all active members of PECARN, unless the Steering Committee decides by majority vote to keep a meeting closed. Due to the sensitive nature or confidentiality requirements of the deliberations on some topics and issues, the meetings of the Steering Committee may be closed to all except voting Steering Committee members and members of the federal government participating in PECARN.
- c. PECARN subcommittee meetings are open only to subcommittee members, alternates, consultants, Federal Liaisons, all RNC or EMSA PIs and other PECARN members approved by the Subcommittee Chair, due to the privileged nature of their communications.

VII. Committees

1. *Standing Committees*

There are five six Standing Committees. The PECARN Steering Committee and five subcommittees, including the Protocol Concept Review and Development, Safety, Regulatory & Quality Assurance, Feasibility and Budget, and Grant

Writing and Publications Subcommittees, and the Research Coordinator Subcommittee.

2. *Duties*

The descriptions and duties of the Steering Committee and Subcommittees are delineated in the Policies and Procedures manual.

3. *Ad hoc committees*

The Steering Committee and Subcommittees may establish ad hoc committees as necessary to carry out the work of the network.

VIII. Policies and Procedures

The PECARN Policies and Procedures manual is a separate document from the PECARN Bylaws, as delineated per HRSA/MCHB guidelines. The Policies and Procedures manual contains the descriptions and duties of the PECARN Steering Committee and subcommittees, as delineated per HRSA/MCHB guidelines, PECARN subcommittee recommendations, and Steering Committee approval.

IX. Code of Ethics

All PECARN members, Active and Associate, will be held to the highest ethical principles and standards consistent with the Federal Regulation for Protection of Human Subjects (HRSA Circular No. 96.05, Code of Federal Regulations Title 45 Part 46 (45 CFR Part 46), and the Belmont Report). This includes, but is not limited to, compliance with any and all federal, state or institutional regulations regarding the performance of research.

X. Conflicts of Interest

All PECARN members, Active and Associate, are subject to the conflicts of interest policies of their respective educational institutions' policies and applicable federal laws and regulations (per 42 CFR Ch. 1, Subpart F, 50.6), state laws and regulations, and local institutional policies. Potential conflicts of interest are situations which might not allow for impartial or objective determinations. These situations include, but are not limited to, relationships with products, devices, government or companies such as pharmaceutical, formula, or equipment manufacturers. This would also include the receipt of research support or lecture honoraria from such companies or organizations.

In addition to the mandated requirements listed above, Active and Associate PECARN members having any real, perceived or potential conflicts of interest in the development and testing of any drug, technique, methodology or technology are also

required to disclose these conflicts to the PECARN Steering Committee at the time the conflict is recognized. These conflicts will be reviewed by the Steering Committee, who may deem it necessary to limit the role of the member in specific research endeavors in order to insure scientific objectivity. Failure to disclose these conflicts of interest as required may result in the loss of the privilege to participate in PECARN.

XI. Bylaw Amendments

1. Adequate aging and prenotification

Adequate aging and prenotification of these bylaws will consist of providing written notification of proposed amendments one meeting in advance, with a provision for emergency circumstances as determined by the PECARN Steering Committee Chair. In emergency circumstances, written notice of proposed amendments one month in advance would be considered adequate.

2. Voting on amendments

Two thirds vote of the total Steering Committee membership is required to carry a motion when voting on bylaw amendments.

XII. Construction and Severability

1. If the Bylaws are in conflict with statute, the statute prevails.

2. If part of the Bylaws are judged illegal, the remainder prevails.



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- **PARLIAMENTARY PROCEDURES**
- **PECARN STEERING COMMITTEE DEFINITION**
- **EXPANDED PECARN SUBCOMMITTEE DEFINITIONS**
- **OTHER PECARN POLICIES, WORK FLOW, AND PROCEDURES**

PARLIAMENTARY PROCEDURES

Introduction

Parliamentary Procedure is a time tested method of conducting business at meetings and public gatherings that allows everyone to be heard and to make decisions without confusion. The PECARN Steering Committee has adopted Robert's Rules of Order Newly Revised as its basic handbook of operations.

The Basic Rules

1. ***The rights of the Organization supersede rights of individual members.*** The organization has the right to make it own rules, which then must be observed by all members. Should a conflict arise between the rights of a member and the right of the organization to do its business, the rights of the organization prevail.
2. ***All members are equal and their rights are equal.*** Those rights are to 1) attend meetings, 2) make motions and speak in debate, 3) nominate, 4) vote, and 5) hold office.
3. ***A Quorum must be present to do business.*** A quorum is the number of members who must be present to legally transact business. The number is stated in the Bylaws. The purpose of a quorum is to prevent an unrepresentative group from taking action in the name of the organization.

4. ***The majority rules.*** The minority has the right to be heard, but once a decision has been reached by a majority of the membership the minority must respect and abide by the decision.
5. ***Silence is consent.*** Those members who do not vote agree to go along with the decision of the majority by their silence.
6. ***Two-thirds vote rule.*** A two-thirds vote is necessary whenever you are limiting or taking away the rights of members or whenever you are changing something that has already been decided.
7. ***One question at a time and one speaker at a time.*** No motion is in order that does not directly relate to the question under consideration. In addition, once a member has been recognized, he or she has been granted “the floor” and another member may not interrupt him or her.
8. ***Debatable motions must receive full debate.*** The presiding officer may not put a debatable motion to vote as long as members wish to debate it. Debate can only be suspended by a two-thirds vote of the members present.
9. ***Once a question is decided, it is not in order to bring up the same motion or one essentially like it at the same meeting.*** Such motions should be ruled out of order.
10. ***Personal remarks in debate are always out of order.*** The presiding officer must rule all personal remarks out of order. Debate must be directed to motions and not motives, principles, or personalities.

Procedures for Making and Voting on Motions

The method used by members to express themselves is in the form of moving motions. A motion is a proposal that the entire membership take action or a stand on an issue. Individual members can 1) call to order, 2) make or second motions, 3) debate motions, and 4) vote on motions.

There are four basic types of motions:

1. ***Main Motions:*** The purpose of a main motion is to introduce items to the membership for their consideration. They cannot be made when any other motion is on the floor and yield to privileged, subsidiary, and incidental motions.
2. ***Subsidiary Motions:*** Their purpose is to change or affect how a main motion is handled and is voted on before a main motion
3. ***Privileged Motions:*** Their purpose is to bring up items that are urgent about special or important matters unrelated to pending business.
4. ***Incidental Motions:*** Their purpose is to provide a means of questioning procedure concerning other motions and must be considered before the other motion.

The following steps apply to the presentation, delivery, debate, and vote on main motions.

Other types of motions will follow a similar course, with exceptions made for seconding, debate, amendments, and the required vote for acceptance (see the attached chart).

STEP ONE: Presenting a Main Motion

1. Obtaining the floor

- a. Wait until the last speaker has finished.
- b. Rise and address the Chair.
- c. Wait until the Chair recognizes you.

2. Make your motion

- a. Speak in a clear and concise manner.
- b. State the motion affirmatively (“I move that we...” rather than “I move that we not...”)
- c. Stay on the subject

3. Wait for someone to second the motion

4. Another member will second the motion or the Chair will call for a second.

5. If there is no second, the motion is lost.

6. The Chair states the motion

- a. The Chair will say, “It has been moved and seconded that we..” This places the motion before the membership for consideration and action.
- b. The membership either debates the motion or may move directly to a vote.
- c. Once the Chair presents the motion to the membership, it becomes “assembly property,” and cannot be changed without the consent of the members.

STEP TWO: Expanding on the motion

1. Discussion

- a. At this point, the mover may speak in favor of the motion.
- b. The mover is always allowed to speak first.
- c. All comments and debate must be directed to the Chair.
- d. Speaking must be within the time limit that has been established.
- e. The mover may speak again only after other speakers are finished, unless called upon by the Chair.

2. Putting the question to the membership

- a. The chair asks, “Are you ready to vote on the question?”
- b. If there is no more discussion, a vote is taken.
- c. On a motion to move, the previous question may be adapted.

STEP THREE: Voting on the Motion

There are five common methods used to vote. The method of vote on any motion depends on the situation and the By-Laws and Constitution. The basic methods are:

1. By Voice—The Chair asks those in favor to say “aye,” those opposed to say “no.” Any member may move for an exact count.
2. By Roll Call—Each member answers “yes” or “no” as his or her name is called. This method is used when a record of each person’s vote is required.
3. By General Consent—When a motion is not likely to be opposed, the Chair says, “If there is no objection....” The membership shows agreement by their silence. However, if one member says, “I object,” the item must be put to a vote.
4. By Division—This is a slight verification of a void vote. It does not require a count unless the Chair so desires. Members raise their hands or stand.
5. By Ballot—Members write their vote on a slip of paper; this method is used when secrecy is desired.

OTHER POINTS

1. The Chair can require a long motion to be submitted in writing.
2. The maker of a motion has first right to speak to it.
3. A member can vote against his or her own motion, but cannot speak against it.
4. A member can modify her or his own motion before the Chair states it. The member can also offer an amendment after her or the Chair has stated his motion.
5. A member can withdraw his or her motion up to the time it has been stated by the Chair, and after that he or she must have permission from the group.

PECARN STEERING COMMITTEE DEFINITION

The PECARN Steering Committee (SC) is the primary governing body of the PECARN. In consultation with the federal project officer, it reviews and approves the research agenda, formulates and monitors policies and procedures guiding the research activities. All major scientific and operational decisions are made by majority vote with the concurrence of the federal project officer. The Steering Committee may appoint Subcommittees and Working Groups as needed to carry out specific tasks identified by the Steering Committee. All participating Nodes must agree to abide by the policies approved by the Steering Committee.

Purpose

The Steering Committee is the governing body of the PECARN. It will review and approve the scientific and administrative policies and procedures of the PECARN in consultation with the federal project officer.

Policy

The Steering Committee will function in accordance with the Terms and Conditions of the PECARN RFA and other applicable policies of MCHB and HRSA/DHHS.

Steering Committee Membership

The voting membership of the committee is to consist of a Principal Investigator from each of the Research NODES, and four HEDA representatives (i.e., one representative from each of four HEDAs) from each Research NODE, and the Principal Investigator of the Central Data Management and Coordinating Center. The federal project officer for PECARN will serve as liaison to the PECARN Steering Committee. Other (non-voting) memberships also include PECARN Officers, Subcommittee and Work Group Members, and other Active and Associate members, per the PECARN bylaws.

Responsibilities

The PECARN Steering Committee, in coordination with the federal project officer, will constitute the primary governing body of the PECARN network. This committee will establish bylaws, policies, and standard operating procedures to govern all aspects of the PECARN network. This committee will review and approve the collaborative research agenda as well as specific research proposals and concepts, formulate and monitor policies and procedures guiding the research activities, review and approve procedures for data acquisition, analysis and management, oversee communication within the PECARN as well as with the greater scientific community and the public.

The PECARN Steering Committee will be responsible for ensuring that there are well documented policies and operating procedures guiding all aspects of PECARN activities (e.g. protocol development, review, initiation, conduct, and closure, data collection, publication, etc.)

and bylaws delineating the requirements and expectations of collaborating institutions, membership criteria, review of research progress and performance, establish standards of performance, and procedures for removing institutions due to poor performance.

All major scientific decisions will be determined by vote of the PECARN Steering Committee. All participating Research NODES and their HEDAs must agree to abide by the study designs and policies approved by the PECARN Steering Committee.

The PECARN Steering Committee will, by majority vote, elect a Chair from among the NDDP Principal Investigators. The Steering Committee will establish subcommittees and workgroups to assist it in carrying out its functions. The PECARN Steering Committee may meet up to 4 times per year

EXPANDED PECARN SUBCOMMITTEE DEFINITIONS

PROTOCOL REVIEW & DEVELOPMENT SUBCOMMITTEE (PRADS)

The purpose of PRADS is to:

- a) Provide scientific review of research proposals after the research concepts have been approved by the sponsoring node and the PECARN steering committee. The goal of the review is to provide feedback to the investigator, which will strengthen the proposal, particularly in content areas of research design and data analysis.
- b) Inform the PECARN Steering Committee of its findings regarding pending research proposals to assist deliberations regarding proposal approval.

PRADS is established by the PECARN Steering Committee and its actions are advisory to the Steering Committee.

PRADS membership will be appointed by the Chair of the Steering Committee. Typically, membership will consist of two persons from each PECARN node including the CDMCC. A nodal PI can be an additional member of PRADS. The Chair of the Steering Committee will also appoint a Chair of PRADS.

PRADS will review research proposals that are developed after the research concept has been approved by the PECARN Steering Committee. The suggested format for submissions to PRADS can be found in Development and Approval of Research Concepts and Protocols in PECARN, Attachment B.

The Chair of PRADS will assign a primary and secondary reviewer to each proposal scheduled for review. The format for the primary and secondary reviews will follow the NIH study section review format. In addition, a representative of the CDMCC will provide a methods/statistics review. Other committee members will read the proposal and be prepared to discuss it; however, their written comments are optional.

Each assigned proposal will be discussed at the PRADS meeting. Presentations are made by the primary, secondary and methods/statistics reviewers. The PRADS Chair will prepare a summary of the key points raised by the reviewers and the committee deliberations. These will be approved by the committee.

PRADS Committee Output:

The investigator will receive the PRADS summary and all three written reviews verbatim. Only the PRADS summary will be posted in the eRoom and be made available to the PECARN Steering Committee. The minutes of the committee will contain only the PRADS summary. PRADS reports should be submitted within two weeks of the PRADS meetings.

The prescribed method of review includes an in person meeting of the PRADS Committee. Proposals are typically reviewed at the next PECARN Meeting scheduled after the meeting at

which the research concept was approved by the PECARN Steering Committee. At the direction of the Chair of the Steering Committee, PRADS may review research proposals electronically or by conference call in between scheduled meetings.

SAFETY & REGULATORY AFFAIRS SUBCOMMITTEE (SRAS)

Functions:

1. To help streamline the processing of network-wide IRB submissions at local nodes.
2. To aid in HEDA local IRB submission (e.g. to facilitate submission in advance of local deadlines).
3. To offer HEDA IRB support through:
 - a. Proposal flow, review and problem solving when requested
 - b. Anticipatory guidance
 - c. Project IRB template support
4. To make recommendations to the Steering Committee concerning specific safety and regulatory issues that arise

1. Streamlining the Process of IRB Submissions

SRAS' support role in this regard includes safety and regulatory review of proposals, to anticipate variation in IRB issues across the network and to assist in recommending policies which will aid PECARN researchers in trans-network IRB submissions.

2. HEDA Safety, Regulatory and IRB Technical Support

- a. The Subcommittee will review projects, along with the other subcommittees in order to offer recommendations to the investigators and to the Steering Committee in deciding on the merits of projects within PECARN.
- b. The Subcommittee will offer problem-solving support. For example, if two HEDA IRBs demand changes which are contradictory, the Subcommittee may offer to help the PI of the Proposal work with HEDA members and the members of the two IRBs.
- c. The Subcommittee will also assist in proposal submission by offering anticipatory guidance over ethical issues and IRB process issues. For example, the eRoom site of the Subcommittee has postings of federal guidelines for ethics and IRBs.
- d. A basic IRB template for each proposal which will go out to many or all of the HEDAs should be prepared by the proposal's PI. While responsibility for the contents of the template will be the responsibility of the proposal's PI, the Subcommittee can offer technical assistance in its creation.

3. Recommendations to the Steering Committee

- a. The subcommittee will provide feedback to the Steering Committee on regulatory issues.

- b. Project specific problems will be reviewed and recommendations made to the Steering Committee for resolution.
- c. Policy and Standard Operating Procedures (SOPs) related to regulatory concerns will be reviewed and recommendations made for refinement.

QUALITY ASSURANCE SUBCOMMITTEE (QAS)

The Quality Assurance Subcommittee (QAS), created by the PECARN Steering Committee, will function as an advisory group to review and endorse quality assurance practices of all proposed and ongoing PECARN research. The QAS is responsible for developing QA policy standards and criteria applicable to all PECARN research. These policy standards and criteria will be used to review QA plans and reports to ensure they are in accordance with the QA policy.

The quality assurance policy has these objectives:

- Ensure quality assurance procedures are included in protocol design, development, and implementation
- Establish procedures to ensure accurate data collection
- Assist the lead investigator with protocol compliance issues
- Encourage the culture of continuous quality improvement
- Develop and implement a PECARN wide performance report card

Responsibilities of the Quality Assurance Subcommittee (QAS)

- Serve as an advisory resource to the Steering Committee on policy related to QA
- Develop guidelines including a check list of requirements for QA procedures in each protocol
- Review all protocols for the presence of QA practices and make recommendations to the lead investigator on meeting the required elements.
- Report Card
 - Develop and maintain Report Card MOO that describes report card scoring, including
 - Selecting PECARN studies and their relevant weight that will be evaluated in the report card measures for each specific year.
 - Provide oversight and guidance to CDMCC regarding scoring of specific measures that are not covered in the existing MOO
 - Help mediate or resolve all report card scoring issues from sites, nodes or CDMCC

Collaborate with the steering committee and subcommittees within PECARN to ensure that relevant QA issues are addressed in all protocols

- Serve as an advisory resource to lead investigators during protocol development on QA issues

- Request and review QA activity reports as required by protocol from the nodes, and support or recommend plans of action as indicated
- Provide written or electronic minutes/reports to the Steering Committee including recommendations and action taken.

Assumptions

- The Study Principal Investigator has the ultimate responsibility to ensure that all necessary protocol specific QA plans are developed and in place prior to protocol implementation
- The node Principal Investigator (PI) has the ultimate responsibility to ensure adherence to all necessary QA plans for their node.
- MCHB provides periodic independent monitoring of the PECARN QA processes, with the assistance of Steering Committee.

Feasibility and Budget Subcommittee

Definition

The purpose of Feasibility and Budget subcommittee (FAB) is to review proposals submitted to PECARN in order to provide the Steering Committee with recommendations regarding the development of research proposals and provide a technical resource to investigators in preparing grants and study protocols.

The FAB is established by the PECARN Steering Committee, and its actions are advisory to the Steering Committee.

Role of the Subcommittee:

- 1) To assist investigators in developing protocols that can feasibly work within the confines of budget restrictions.
- 2) To provide the PECARN steering committee an input and review of the project budget with consideration of current PECARN resources and an assessment of whether the plan for implementation is feasible.

The subcommittee will develop guidance materials for investigators to assist them in developing budgets and determine the type and amount of resources that they may need.

Review of Research Protocols and Grant Applications:

The subcommittee will review the preliminary budget and general feasibility of the study at the time of the initial submission of the protocol to PECARN. The chair will assign a primary and secondary reviewer to review the protocol and budget; a representative from the CDMCC will review the CDMCC portion of the budget for all projects. The reviewers will prepare written reports that will be discussed by the FAB committee. After review by FAB and presentation to the Steering Committee, a formal written report with recommendations will be prepared and submitted to the RNC PIs for review. When finalized and approved by the RNC PIs, the recommendations will be sent to the investigator.

Budget Revision and Resubmission to PECARN

If budget revision is required, the study PI will work with the NA and assigned FAB member to amend the budget as needed. The revised budget will be resubmitted for review by FAB and the full Steering Committee prior to vote on the protocol. FAB will give input to the Steering Committee prior to this vote. (see FAB Policy)

**GRANT WRITING AND PUBLICATION SUBCOMMITTEE
(GAPS)
POLICY AND PROCEDURE (Adopted 4/23/02, Revised 7/20/04, 5/19/2008,
9/11/2008)**

The GAPS was created by the PECARN steering committee and serves as an advisory committee to the Steering Committee. This subcommittee assists Principal Investigators in developing research grant applications to be submitted for funding, reviews proposals for presentation and publication, and makes recommendation to the PECARN Steering Committee. The GAPS will utilize the operating procedures for the internal peer review process to promote PECARN publications and presentations and to ensure their scientific quality. In addition, the GAPS will assist with timely dissemination of PECARN findings to the scientific and non-scientific communities. Finally, the GAPS will review, critique and help PECARN Principal Investigators develop grant proposals to fund PECARN-related research proposals.

Publication, Presentation and Grant Definitions

The following are covered under this document:

1. Research manuscripts, methodological papers, monographs, book chapters and other PECARN related material to be published in scientific journals and other scholarly literature.
2. Presentations at scientific meetings (oral and poster).
3. Publications of PECARN materials (e.g. books, monographs, training manuals, therapist manuals, summaries of study protocols and trial progress reports).
4. Proposals for grant funding submitted to government or non-government agencies, to support PECARN research activities.
5. Other products for public dissemination including methodology and other know-how or information regardless of the form (e.g. research instruments, computer software, video and audio taped materials) that are produced from PECARN activities.
6. Exceptions:
 - a) Materials (e.g. posters, handouts, recruitment cards) or presentations used solely to promote enrollment or inform professional audiences of the PECARN structure, purpose, study design, or research proposals. Such presentations should not include discussion of previously unpublished data and must not result in publication.
 - b) Press releases: MCHB will provide the Steering Committee with its current policy and the Steering Committee will write a procedure for press releases that is independent of the

Publications policy and/or procedures. Press releases should be forwarded to GAPS for archiving and tracking.

c) Data collection instruments, including surveys, intended for use in PECARN studies but not for public dissemination.

General Principles and Procedures

1. Grant review. The GAPS will, at the request of investigators, review grant applications being submitted for external funding. The focus of the GAPS review of grant proposals will be on overall structure of the proposal and quality of the writing.
2. Manuscript review.
 - a. All presentations and publications, as defined above, based upon data collected or to be collected as part of the PECARN, shall be submitted to the GAPS for review and approval recommendation before submission to journals or professional organizations. Because of the short lead time typically available for abstracts submitted for scientific meetings, it is not expected that abstracts will be reviewed by GAPS prior to submission. Review of abstracts will follow an expedited process outlined in the Authorship Guidelines.
 - b. Active or associate PECARN members may propose publications or presentations related to PECARN. Participants are required to submit topics for publications and presentations in advance. The processes for proposing manuscript topics and writing teams are detailed in the Authorship Guidelines. Publication plans will be submitted for approval to the GAPS.
 - c. Manuscripts submitted for GAPS review should, in the opinion of the authors, be ready for journal submission, and should be accompanied by a statement that all authors have reviewed and approved the manuscript. Materials submitted for review will be circulated to all voting members of the subcommittee by the GAPS chair. The chair will assign a primary reviewer from the subcommittee. A methodology/statistics reviewer from the Central Data Management and Coordinating Center will also be assigned. These reviewers will provide a written critique of the presentation or publication, using a standardized review format to be developed separately. The written review will also be circulated among the committee at large. Following group discussion and comment, either in person or via electronic means, the primary reviewer will complete a summary evaluation for the lead author. The members of GAPS will also be asked to vote for approval, approval with minor revisions (subject to re-review by GAPS chair or designee), or approval with major revisions (subject to re-review by the full subcommittee). The lead author will be asked to respond to the critique, with manuscript revisions as appropriate. Once the author and GAPS chair agree the revisions are complete, the GAPS chair will forward a recommendation for approval to the Steering Committee for a vote, along with the original critique and responses. Where manuscript approval is by unanimous vote of GAPS, final approval will be by the nodal PIs. The final decision of the Steering Committee will be communicated to the lead author and writing team.

- d. It is expected that reviews will be completed in a timely fashion. The expected turn around time will depend on any deadlines, but generally should be within 2 weeks of receipt of the material by the chair.
- 3. Manuscript submission. Once a manuscript has been approved by the Steering Committee or Nodal PIs, it may be submitted for publication. The lead author shall notify the GAPS chair of the date of submission, and will provide updates on the status of the manuscript. Final versions of manuscripts should be sent electronically to the GAPS chair for archiving.
 - a. All NIH-funded studies must comply with the NIH Public Access Policy. Under a new federal law, the NIH is requiring that “all investigators funded by the NIH submit or have submitted for them to the National Library of Medicine’s PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication: Provided, That the NIH shall implement the public access policy in a manner consistent with copyright law.” (See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html>. Other information is available at <http://publicaccess.nih.gov/FAQ.htm#c2>, and <http://publicaccess.nih.gov/>)
 - b. If a manuscript is revised prior to resubmission (either to the same or a different journal), the revised manuscript must be reviewed by the GAPS chair or designee prior to resubmission. If the revisions are substantial, the GAPS chair may require re-review by the full subcommittee prior to resubmission. In the event of full subcommittee re-review, the Steering Committee or nodal PIs will be asked to make a final determination on the manuscript following the same procedure as described above for initial submissions.
- 4. Abstract submission and review.
 - a. Once an abstract is approved by a nodal PI, it may be submitted for the appropriate meeting. The lead author shall notify the GAPS chair of the date of submission, and will provide updates on the status of the abstract.
 - b. GAPS will provide lead authors of all abstracts a checklist of requirements for posters and presentations. GAPS will also develop and maintain templates for posters and presentations to maintain consistent PECARN branding.
 - c. Prior to the meeting where an abstract will be presented, one of the nodal PIs must review and approve the poster or presentation. The purposes of this review are to ensure:
 - i. consistent appearance to optimize PECARN “branding”
 - ii. proper accreditation for funding agencies
 - iii. no inappropriate political or other content

- d. Recognizing that last minute changes may be unavoidable, the presentation need not be in final form. However, sufficient material for meaningful review must be provided, including title slide/acknowledgments, results, and conclusions.
 - e. The deadline for submission of the poster or presentation to nodal PIs will be determined by the nodal PIs; GAPS recommends two weeks prior to the meeting. GAPS will send the nodal PIs a list of abstracts at least one month before the meeting to allow them to plan for the upcoming review, divide up the workload, and contact the authors.
 - f. The nodal PI approving a poster or presentation may be one of the listed authors. However, if a nodal PI is the first or senior author, another nodal PI must review and approve. GAPS members will be available to review posters or presentations at the request of the nodal PIs.
 - g. Final versions of abstracts should be sent electronically to the GAPS chair for archiving.
5. Studies where a group that is not formally part of the PECARN analyzes PECARN data over which the network retains control are subject to the same procedures unless another procedure is mutually agreed upon and codified in a letter of agreement.
6. In the case of pharmaceutical collaborators, the Clinical Trials Agreement between sites and the pharmaceutical collaborator(s) should specify that these guidelines would be followed. Alternative procedures may be followed if all parties (including the Steering Committee) mutually agree upon modifications to those guidelines.
7. In the case of collaborative studies with co-sponsoring agencies or other study groups, the letter of agreement must reflect that the guidelines of the PECARN Network will be followed unless all parties agree on the modifications.
8. Proper acknowledgment of PECARN and the funding agency(ies) is required in all publications and presentations.
9. Any decisions of the GAPS may be appealed to the Steering Committee.
10. These procedures will be reviewed on an ongoing basis and modified as necessary. Revisions may be approved by a majority vote of the subcommittee, and then forwarded to the Steering Committee for final approval.



STANDARD OPERATING POLICY AND PROCEDURE FOR Development and Approval of Research Concepts and Protocols

Initial Draft: March 2007 Version No.: 2 Revised: 14Aug 2009	Development and Approval of Research Concepts and Protocols in PECARN	Original Steering Committee Approval: 22Oct07 Revised Steering Committee Approval: 18Dec09
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1. PURPOSE

1.1. The purpose of this policy is to provide guidance for PECARN investigators and others involved in PECARN research regarding the development, submission and approval process of a research concept and a research protocol.

2. POLICY

2.1. This document describes the approved method of initiating a PECARN research project. Any changes to this process must be approved by the PECARN Steering Committee or the Nodal PI group.

3. SCOPE

3.1. This document applies to all investigators, nodal administrators and others involved in PECARN-related research and to all participating sites.

4. DEFINITIONS

4.1. Nodal Principal Investigators: Investigators named on the HRSA cooperative agreements at each PECARN node and the CDMCC.

5. RESPONSIBLE PARTIES

5.1. A PECARN investigator or an external investigator is responsible for preparing the initial draft of the concept or protocol, in conjunction with participating PECARN nodal investigators, subcommittees, subject matter experts, the CDMCC, biostatisticians, information technology/database experts, and others, as appropriate.

5.2. The investigator who initiates the concept or protocol is responsible for assuring that the concept or protocol meets all regulatory requirements, and is ethically and scientifically sound.

6. PROCEDURES

6.1. Research Concept

6.1.1. An investigator with a research concept drafts an initial written concept proposal and, through the principal investigator of the submitting Node, requests review by the Federal Project Officer in order to:

- Assess the importance of the research question and its general appropriateness for PECARN
- Determine whether the research topic addresses an identified priority (e.g. PECARN research agenda)

6.1.2. Upon approval by the Federal Project Officer, the Nodal PI may then identify a mentor, subject matter expert or consultant as necessary to further develop the concept within the node. The Nodal PI's role is to oversee the nodal review of the concept and to:

- Determine, in consultation with the Federal Project Officer, the general feasibility of conducting the proposed study within PECARN
- Assist the investigator in refining the science of the concept proposal
- Assist the investigator in navigating the PECARN protocol development process

6.2. Concept Submission, Presentation and Review

6.2.1. After nodal review and approval, the investigator will submit a 2-page concept paper to the PECARN Steering Committee (SC). The deadline for concept submission will be two weeks prior to the next scheduled SC meeting. The investigator will attend the SC meeting (Meeting #1) and present the research concept in person. The 2-page limit was adopted in order to encourage brevity, clarity, and focus. Appendices and references may extend the 2-page limit. If the concept paper exceeds 2 pages, (excluding appendices and references) the PECARN Secretary will return the submission to the investigator for revision.

The concept paper should address the following:

- Why the proposed topic is important to EMSC
- Why the study requires the PECARN network
- Background in brief
- Specific aims
- Methodology in brief
- Subject population
- Sample size requirements

Note: Concept papers should be single-spaced using 11-12 point standard type and one-inch margins.

The concept proposal submission should include a face sheet. This face sheet must include the names of all project investigators and attestation that the concept proposal has been reviewed and approved by the submitting node. See Attachment A.

A cover page must also be submitted with the concept proposal. The cover page should identify a target external funding agency. The cover page should also include the institution of the lead investigator, along with the investigator's address, telephone and fax numbers and email address. An example of cover page is at the end of this document. See Attachment A.

- 6.2.2. The concept paper should be submitted electronically to the PECARN Secretary at least 2 weeks prior to the SC meeting in which it will be discussed. No budget is necessary at this step.
- 6.2.3. As a general rule, no more than four new concepts should be submitted for review at a given SC meeting. This limit may be exceeded if all Nodal PIs, in consultation with the Federal Project Officer, agree. Each node is guaranteed the option of forwarding one concept per meeting. If a node has more than one concept to submit, they must check with the PECARN Secretary to verify the number of expected submissions. The PECARN Nodal PIs have the right to refuse to accept more than one concept per node if the total number of submissions per meeting exceeds four.
- 6.2.4. The Investigator will present the research concept at the PECARN SC meeting. The purpose of the presentation, which may or may not use a PowerPoint format or equivalent, is to encourage scientific dialogue, to develop a broad understanding of the proposal among SC members, to review and consider the scientific merit, and to address questions not covered in the presentation, etc. This presentation will be approximately 10-15 minutes in length, with approximately 45-50 minutes of subsequent discussion.
- 6.2.5. After the conclusion of the presentation, the SC will vote by secret ballot to determine whether or not the concept should be endorsed for further development into a PECARN protocol. A 75% majority of the PECARN voting membership is required for concept endorsement. Abstentions will not count in determining whether a majority has been reached. The majority required will insure that there is not only recognition of scientific merit, but wide enthusiasm for developing the concept into a research protocol for implementation in PECARN. SC approval by 75% or more implies that the Investigator will proceed with protocol development. Concepts that receive 50-74% approval may be revised and resubmitted to the SC for discussion and reconsideration at a future meeting at the discretion of the Investigator. Concepts receiving less than 50% approval will not be reconsidered by the SC.

6.3. Protocol Development

- 6.3.1. Once the research concept is approved, the investigator will identify a group of co-investigators or collaborators, and with the help of this group, develop the concept into a research protocol. The protocol can take the format of a standard protocol as might be submitted to an IRB or as a grant. Irrespective of the format, the protocol/grant should contain sufficient detail about the proposed study such that the Protocol Review and Development Subcommittee (PRADS) and SC members may assess scientific merit and feasibility. The essential elements of a protocol to be submitted to the Steering Committee are described in Attachment B (*Protocol Template: A Guideline for Writing a Clinical Protocol for PECARN*). Investigators are required to discuss study design, protocol development and statistical methods with the CDMCC. The length of the protocol is not limited.

Throughout the rest of this policy, the word “protocol” is used with the understanding that the format to be submitted can be either in IRB-type protocol format or in grant format.

6.3.2. The protocol should also contain a preliminary budget and budget narrative. The investigators must work with a PECARN Nodal Administrator to develop the draft budget in accordance with the Feasibility and Budget (FAB) guidelines see FAB Protocol Review Policy). Investigators are required to consult FAB, and strongly encouraged to consult other PECARN subcommittees.

6.3.3. After the protocol is preliminarily developed by the study group, investigators are required to meet (preferably in person) with the CDMCC to further develop the protocol. While this should occur at least 6 weeks before submitting the protocol to the SC, it is important that the scientific details of the protocol be sufficiently developed prior to the CDMCC visit to enable the group to meet the goals of refining study details. The CDMCC will assist the investigator in formatting the protocol properly if in the format of an IRB-type protocol and will provide boilerplate material for certain portions of the protocol.

6.4. Protocol and Budget Review and Development by all Subcommittees

6.4.1. The protocol is then submitted to all members of the SC and all subcommittees for a scientific review at the next PECARN SC meeting (Meeting #2). The protocol must be submitted to the PECARN Secretary four weeks prior to the meeting. The Secretary will distribute the protocol to all subcommittees and SC members. Subcommittees and SC members will conduct a detailed review of the protocol. It is preferable, although not required, that the investigator present the protocol at Meeting #2.

6.4.2. After the PECARN meeting at which the protocol is reviewed, the chair of each subcommittee (PRADS, QAS, SRAS, and FAB as applicable) is required to submit **two** documents to the PECARN secretary. The first document should be a *confidential, detailed*, written summary of the subcommittee's commentary on the protocol. The subcommittee chair will submit this document to the PECARN Secretary within 2 weeks of the date on which the protocol was reviewed. The document will be distributed by the Secretary to the investigator only. The investigator may share the summary with other members of his/her team at their own discretion. Each subcommittee chair will also submit a shorter written summary of their subcommittee's commentary on the protocol. This document will be made available to all SC members to aid in reviewing the subsequent revised protocol, and in determining if the investigator has been responsive to subcommittee critique. The difference between the two documents is that one document has detailed commentary and is intended for the investigator; the other is a brief, general summary of the issues intended to assist the SC in determining whether or not to approve the protocol. These documents *could* be identical at the discretion of the subcommittee chair based on the sensitivity of the commentary. The Secretary will post the general summary of each subcommittee in eRoom and make it available for the SC in time for the next protocol review.

6.5. Protocol and Budget Refinement

6.5.1. After the subcommittee review, the investigator may opt to return to meet in person with the CDMCC to help revise and refine the protocol. A member from each of PRADS and FAB may be identified to work with the investigator as needed to address the subcommittee comments and further develop the protocol and/or budget.

After receiving the reviews, the investigator will make appropriate revisions to the protocol. While subcommittee recommendations are not binding, the investigator should give strong consideration to the comments that were provided. The investigator must submit the revised protocol 2 weeks prior to the next SC meeting. The investigator should highlight where substantive changes were made, particularly in regard to summary comments from the subcommittees. It is also required that the investigator(s) submit point-by-point responses to the major summary comments of subcommittees, as one would do in resubmission of a manuscript. It is the responsibility of each subcommittee chair to review the subcommittee's feedback as well as the investigator's response and be prepared to provide the Steering Committee with an assessment of the responsiveness of the revised protocol, and/or any remaining issues from the perspective of the subcommittee.

The SC will have the opportunity to review the protocol and related documents and assess the investigator's response to subcommittee comments before the vote on the protocol.

6.6. Steering Committee Approval

6.6.1. Investigators may submit a protocol for review at the meeting immediately following PRADS review (meeting #3), or may postpone until the next meeting (meeting #4). Investigators may not delay protocol submission later than two meetings after the PRADS review, unless special circumstances apply.

6.6.2. The investigator should present the revised protocol at the SC meeting, either in person or remotely. Protocol presentations should be 10-15 minutes in duration, using a Power Point presentation or equivalent, as appropriate. This presentation will be followed by approximately 45-50 minutes of open discussion. The investigator will clearly summarize the goals, aims, methods and other aspects of the protocol in detail. At the close of this discussion, a SC vote will be held by secret ballot. Protocols receiving 75% support would be approved for further development of a grant application or for internally-funded implementation. Protocols receiving 50%-75% approval should be revised and resubmitted at the following SC meeting. Protocols receiving less than 50% approval will not be considered further for PECARN implementation. Abstentions will not count in determining whether a majority has been reached.

6.6.3. If the protocol is approved, the FAB subcommittee will continue to help address any feasibility issues with the investigator. In addition, as indicated above, the protocol will likely require more detailed revision prior to study implementation if the study is ultimately funded.

6.7. Grant Application

6.7.1. Following development and approval of a PECARN protocol, unless the protocol will be implemented with internal resources, the investigator prepares a grant application. As noted prior, the protocol that is submitted for Steering Committee approval can take the form of a grant but must include the essential elements, as noted above, that are necessary to complete a thorough scientific review.

6.8. PRADS is available, as are all the subcommittees, to help develop and rigorously review the grant application following protocol approval by the SC.

6.9. Approval of Grant Application

- 6.9.1. Submission of the grant proposal to an external agency requires prior approval by a vote of the SC, with at least 75% approval. The grant application must be submitted electronically to the PECARN Secretary for posting to the SC voting eRoom at least two weeks before the external grant application deadline. It must be sufficiently complete that changes made during the last two weeks (following SC approval) are not scientifically or fiscally substantive.

6.10. Protocol Development: Expedited Review Process

- 6.10.1. Proposals that have not been endorsed previously by the SC may move through an expedited review process in exceptional circumstances such as short turn-around RFAs or other pressing grant deadlines. The expediency will be determined by the nodal PIs and Federal Project Officer. This process cannot be used to meet routine grant cycle deadlines. The expedited process should be conducted as follows:
- 6.10.2. Investigators must submit a 2-page concept paper for the Federal Project Officer review and Nodal PI review. Upon approval of concept by the Federal Project Officer and nodal PIs, the concept can be submitted to the SC for a vote as time allows. SC members will vote on these concepts electronically if the timing does not coincide with a PECARN meeting.
- 6.10.3. A 75% approval of the SC membership or unanimous approval by the Nodal PIs is required for concept approval..
- 6.10.4. If the concept is approved, investigators should immediately schedule opportunities to work with CDMCC and FAB representatives, and are encouraged to work with all subcommittees, on the development of a full protocol/grant and budget. It is understood that the submission will potentially take the format of a grant due to time constraints. However, the protocol/grant submitted must contain sufficient detail to thoroughly evaluate the science (particularly the methods) of the study. The protocol/grant must be submitted to PRADS and the SC for consideration electronically or at a PECARN meeting. The timing will be determined by the Nodal PIs.
- 6.10.5. PRADS will review the protocol/grant at the subsequent meeting if time allows, or electronically if necessary. A representative of PRADS will provide confidential feedback to the investigator after the subcommittee meets. This feedback will highlight concerns identified and suggestions for strengthening the scientific aspects of the protocol/grant application.
- 6.10.6. A SC vote will be conducted, either in person or electronically, to approve the protocol/ grant. Seventy-five percent approval by SC members is required for the protocol/grant to be endorsed. This is a vote to approve for the investigator to continue toward full grant submission to the SC.
- 6.10.7. Investigators will work with representatives of CDMCC, FAB and other relevant subcommittees to complete the full grant The full grant will be submitted for SC vote at least 2 weeks prior to the grant submission deadline. The SC vote will be

conducted, either in person or electronically. A majority (> 50%) approval by SC members is required for the grant to be endorsed.

6.10.8. In exceptional circumstances, parts of this process may be obviated, as will be determined and resolved by the Nodal PIs and Federal Project Officer.

Attachment A :

Concept Cover Page

Project Title

Principal Investigator: Name

Co- Investigators:

Name

Name

Name

Affiliate institution name

Corresponding address:

Street address

Phone number

Fax number

Email

Nodal Review completed ☐

Originating node-

Funding Plan: (*example*) If endorsed by PECARN, we anticipate developing extramural funding proposals to support the conduct of this study. We have preliminary interest from a corporate funding source from the automotive industry as well as the opportunity to request funds from the US Department of Transportation.

Attachment B: A Guideline for Writing a Clinical Protocol for PECARN

This document provides guidelines for protocol submission. It is only guidance, and the format in which you choose to present the information is up to you. You may choose to organize information in protocol form (as if the proposal were being submitted to the IRB) or in the form of a draft grant application. Regardless of the format, it is important that you address all appropriate components of this guidance in a level of detail that will allow the Protocol Review and Development Subcommittee (PRADS), the PECARN Steering Committee and other Subcommittees to fully review and give constructive input into the science and implementation of the project.

Furthermore, we encourage investigators to be in communication with PRADS, FAB and Subcommittee reviewers and the CDMCC to answer any questions and clarify any areas necessary (and revise the document if necessary) prior to full Committee/Subcommittee review.

Specific sections of the protocol:

Please note that there are sections or components that may not be applicable to your particular study.

There are some sections that the Central Data Management and Coordinating Center (CDMCC) can help complete (these sections are indicated in the guideline template).

You can discuss these items when you meet with the CDMCC.

1. Title Page

2. Introduction and Purpose

The basic work leading to the study should be reviewed. A clear statement of the specific aims (and hypotheses) of the research should be included. State primary/secondary study outcomes here.

3. Background and Rationale

Previous clinical work should be reviewed here and a description of how the current protocol extends existing work on the topic should be provided. The investigators should state how successful completion of this protocol will lead to improved emergency care of children. If the study is a drug or device study, relevant information might include pharmacological, toxicological and other biological properties of the drug/biologic/medical device, and previous efficacy and safety experience should be described. The investigators should discuss any preliminary studies performed by the investigational team.

Please note that this section does not need to provide the detail nor compelling style needed for a grant submission. This just needs to be enough to suffice for an IRB.

How does this impact on health outcomes for children? What health outcome are you addressing? (HRSA Requirement)

4. Study Design

This *brief* overview of the study design indicates how the study objectives will be achieved. This section includes a description of the type of study (i.e., double-blind,

multicenter, placebo controlled, etc.), details of the specific treatment groups and number of study subjects (in each group) and number of investigative sites. A brief description of the methods and procedures to be used during the study are mentioned.

5. Study Outcomes

This section should include a description of primary and secondary outcomes or endpoints, how they will be measured and a schedule of assessments over time. This section should also justify any additional measures (not related to a primary or secondary outcome) to be addressed in the analysis.

6. Study Population / Subject Eligibility

This section states the number of subjects required to be enrolled in the study at all sites. There should be a brief definition of the nature of the subject population that is required. Accrual projections and duration of the study should be described.

Inclusion Criteria: This section describes the criteria each subject must satisfy to enter the study, including but not limited to: age, sex, race, diagnosis, method of diagnosis, diagnostic test result requirements, concomitant medication requirements, severity of symptoms and signs of the disease, the ability to perform study requirements and to give informed consent. The criteria should be detailed sufficiently to provide the investigative site the information needed to recruit appropriate subjects. Care should be taken to develop these criteria so that they include the desired target population and not be overly inclusive or exclusive.

Exclusion Criteria: The criteria that eliminate a subject from the study population should be listed. These may include but are not limited to: previous medical history, pregnancy, childbearing potential, current or past therapy, severity of disease, current medical conditions, a minimum of time since the last clinical study, drug or alcohol abuse, and upper limits of laboratory tests that will disqualify potential subjects.

7. Procedures and Data Elements

This section details the plan of action, procedures, and methods to be used during the study. The investigators should describe if and how the methods in this study are novel or innovative.

The activities for each phase of the study are described. Include a clear outline of the study activities and who (e.g. research coordinator, PI, Nurse, Other) will collect data, administer tests, and perform clinical measures that are a part of the study.

Note that for PECARN review purposes, this section does not need to reflect the final protocol that would be submitted to an IRB, but rather, sufficient detail for the Protocol Review and Development Subcommittee (PRADS) and other Subcommittees to provide meaningful feedback and advice to the investigator.

Screening, Enrollment and Randomization: Describe how patients will be identified, approached, screened, randomized, and enrolled. A flow diagram is helpful.

Diagnostic and Laboratory Tests: Detailed methodology is described for laboratory or diagnostic tests. Any unusual tests or tests required specifically for the study should be described. A description of pharmacokinetic or pharmacodynamic assessments tests, if applicable, should be provided.

Data elements: A list of essential data elements that will be collected should be included here. This list is necessary for PRADS to determine if the variables needed for endpoints are being collected, and for other committees to assess complexity of the study. Actual data collection forms are not required at this juncture – those will be developed in conjunction with the CDMCC at a later point.

Follow-up procedures (if applicable): Describe the follow-up procedures (e.g. telephone follow up calls, returns for evaluation), and their timing.

8. Study Treatment (if applicable)

All interventions for the study such as treatments, schedules, and specific guidelines for study subjects should be described. Specific information for drug studies includes:

Dosing schedule (or investigational device use): The details concerning dose, frequency, and duration of the experimental treatment should be provided here. If placebos are part of the treatment plan, the details of their administration are also described in this section. If applicable, the drug, doses, frequency, and duration of concomitant treatment required in addition to the experimental medication are listed here.

Study drug/device supplies and administration: The Lead Investigator should determine who is going to provide the study medication (e.g., pharmaceutical company, local laboratory) and note this here. The Sponsor must be able to assert that the experimental medication has been manufactured following all regulations (i.e., by Good Manufacturing Practice or GMP). This is especially important if the investigational product is manufactured in a local laboratory without the participation of a biotech or pharmaceutical company. Details of the product stability, storage requirements and dispensing requirements should be provided if there are unusual needs.

Dose modification for study drug toxicity: Rules for changing the dose or stopping the study drug should be provided. If the involvement of an Investigator and/or an Independent Data Monitoring Committee and/or the Sponsor is/are required prior to stopping the drug or changing the doses, this should be noted in this section. Possible drug interactions: The foreseeable interactions of the study drug with other medications or herbal preparations should be noted. Concomitant therapy: The drugs that are permitted during the study and the conditions under which they may be used are detailed here. Describe the drugs that a subject is not allowed to use during parts of or the entire study.

Discontinuation from study treatment: The specific reasons from early discontinuation and the definition of treatment failure should be defined. Discontinuation due to other causes (e.g., adverse events, withdrawal of consent, etc.) should also be described.

Blinding/Unblinding procedures: If the study employs a blind on the Investigator and/or the subject, describe how this will be accomplished. If the study is blinded, the circumstances and the mechanism for unblinding to occur should be given.

9. Data Management (The CDMCC will suggest a plan for this section)

This section will include details on the collection and submission of data to the CDMCC.

Data quality: A statement about data quality and what methods will be used to assure data accuracy should be included. Describe double data entry, validation plans and internal audits as applicable to the study.

10. Data Analysis (prepared in conjunction with CDMCC)

The details of the statistical approach to be followed in the study are described:

Sample size: Describes the sample size required and how the sample size was determined, including the assumptions made in making this determination.

Efficacy endpoints: Before the study begins, the endpoints need to be clearly and completely defined. These can be grouped as primary and secondary endpoints. Safety endpoints should also be defined before the study begins (if applicable).

Statistical analysis: Details of how the results will be analyzed and reported are described in this section; specifically, statistical tests to be used to analyze the primary and secondary endpoints that were defined above, a definition of the level of significance, statistical tests to be used, and the methods used for missing data. The method of evaluation of the data for treatment failures, non-compliance, and subject withdrawals is presented. If an interim analysis will be performed, the rationale and conditions are described. Any statistical concerns to correct for interim analyses should be presented.

Pharmacokinetic (PK) analysis: If applicable, the statistical considerations for analyzing PK data are described here.

11. Human Subjects

(To be used for review by the PECARN Safety and Regulatory Subcommittee)

Risk/benefit assessment: Provide a discussion of major known risks of the treatment(s) and testing procedure(s). Specific risks associated with the investigational product and any control(s) should be included. Details of how known risks will be mitigated or minimized should be provided. What benefits exist for the subjects should be discussed.

Consent Process: This section should detail the consent/assent process or its substitute.

12. Study Monitoring & Quality Assurance

CDMCC will assist with this section. (To be used for review by the PECARN Quality Assurance Subcommittee)

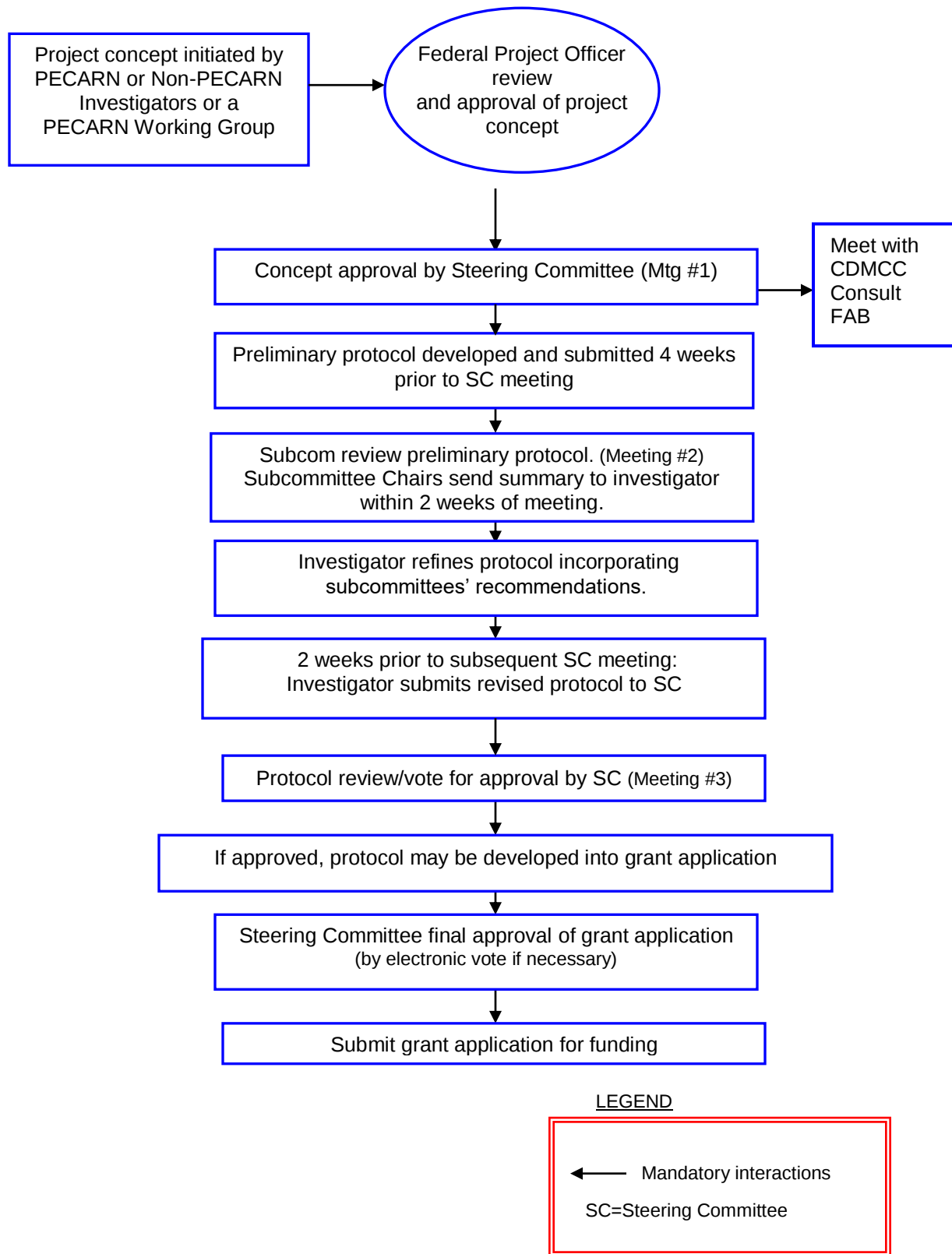
All clinical studies require monitoring commensurate with the degree of risk involved in participation as well as the size and complexity of the study. The plan provided in the protocol should be quite general, since funding resources may not be known. A general description will also help avoid amendments to the protocol if the monitoring plan requires changes. Detailed plans will be provided in the separate data management and site monitoring plans. The protocol should outline enough of a plan to display commitment in the areas of human subject protection and data quality without providing details that would not allow for flexibility. Describe the type of site monitoring and describe quality assurance plans in general. Include a general description of the type of study monitoring visits (initiation, interim, and close-out).

Describe record retention requirements including details of how long the study data and files need to be stored and how and when Investigators will be informed when the files can be destroyed. The right of the FDA, IRB, and representatives of the Sponsor to verify and inspect/audit the study data is presented here.

13. Organization of the project and capabilities of the investigators.

The investigators should briefly explain the organizational structure of the investigative team, including plans for mentorship, where appropriate. This section should briefly demonstrate the expertise of the team, including appropriate references, and should describe any special environments (e.g. basic science laboratory) needed to conduct the research.

PECARN Research Concept and Protocol Development Process





STANDARD OPERATING POLICY AND PROCEDURE FOR FINALIZATION AND AMENDMENT OF PECARN PROTOCOLS

Initial Draft: Aug 2006 Revision1 date: 8 Feb 2008 Revision 2 date: 14Aug2009 Revision 3 date Oct 2014;	Protocol Finalization and Amendments	Original SC approval: 10July 2007 Revised SC approval: 19Nov 2009 Exec Committee approval: 30 Sept 2015
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1 PURPOSE

1.1. The purpose of this policy is to provide guidance for PECARN investigators regarding the development of the final study protocol as well as describing the process for creating and submitting study amendments.

2. POLICY

2.1. An ethical and scientifically sound clinical research protocol is the foundation of all successful clinical research. A clinical protocol must clearly define the research population, the procedures that must be followed to ensure the collection of valid and trustworthy data, and outline the responsibilities of each member of the study team. A clinical protocol must incorporate all applicable regulatory requirements and guidances that are available to PECARN, as well as counsel from appropriate subject area and technical experts (clinicians, statisticians, database developers, etc.) including those outside the PECARN network, when appropriate.

2.2. The suggested format for writing an initial clinical protocol is detailed in *The Development and Approval of Research Concepts and Protocols* policy. The policy described here represents the steps in between endorsement of an initial protocol and implementation of a final protocol, as well as protocol amendments thereafter.

2.3. Protocol amendments may be required during the course of the study to accommodate changes in study design, subject inclusion criteria, and risk profile. The lead investigator will initiate protocol amendments. Protocol amendments may require substantial changes to data collection systems, and this should be considered whenever protocol amendments are indicated. Protocol amendments must be submitted to the DCC for approval prior to distribution to the network.

2.4. Protocol amendments must be reviewed by all involved IRBs. Changes to the protocol may not be implemented at an institution without approval of the lead investigator, the DCC and the IRB at each institution.

2.5. Compliance with the approved clinical protocol is essential in ensuring that the subjects' rights and well-being are protected. Any deviation from the approved protocol is a violation of the protocol, and must be reported to the DCC as described in the Manual of Operations for the study.

3. SCOPE

3.1. These policies and procedures apply to all PECARN-related research studies, to all investigators conducting and participating in PECARN research, and to all participating sites.

4. DEFINITIONS

4.1. The HEDA Investigator: The investigator identified in the PECARN cooperative agreement as the individual providing leadership and oversight of all PECARN related research at the respective site.

4.2. The Lead Investigator: The investigator who received official Steering Committee approval to oversee and provide leadership for the study, and who is the grant holder in studies receiving extramural funding.

4.3. The Site Investigator: The investigator who is identified by the lead investigator as being responsible for conduct of the study at a designated PECARN site.

4.4. Nodal Principal Investigators: Investigators for the HRSA cooperative agreements at each PECARN node and the DCC.

RESPONSIBLE PARTIES

5.1. The lead investigator is responsible for finalizing the protocol, in conjunction with participating investigators, subject matter experts, the DCC, biostatisticians, information technology/database experts, and others as appropriate. The DCC will finalize and version the protocol in a standard format.

5.2. The lead investigator is responsible for ensuring that all participating investigators comply with the approved clinical protocol.

5.3. The lead investigator is responsible for assuring that the protocol meets all regulatory requirements, and is ethically and scientifically sound.

5.4. The site investigator will generally be required to sign an investigator responsibility form which clearly outlines investigator responsibilities in the study.

5.5. The HEDA investigator is responsible for assuring that the site investigator provides adequate study-specific oversight and will assign a new site investigator if the original site investigator is unable to continue in his/her role.

6. PROCEDURES

6.1. Writing the final clinical protocol – If a grant, instead of a protocol, was written and approved by the PECARN SC, the final protocol will need to be developed after the grant has been funded. Usually, this will entail filling in details that may not have been worked out at the time of the grant submission.

If a clinical protocol was developed and approved by the PECARN SC, then the approved protocol may still need to be refined and augmented to create a final clinical protocol. This decision should be made by the Lead Investigator and the DCC. Protocol refinement at this stage, if required, may involve finalizing data elements and other fine details of the protocol. Specific elements of the final protocol template are attached in this policy. The final protocol may not be substantially different from either the grant or the original protocol that was approved by the SC without being approved by the Nodal PIs and in consultation with the Federal Project Officer.

6.1.2. If a grant was prepared instead of a protocol, the lead investigator and DCC will transform the grant into a clinical protocol. The DCC will assign the protocol a version number and effective date. This will become the final protocol.

6.1.3. Protocols for Investigational New Drug (IND) and Investigational Device Exemption (IDE) clinical studies may be submitted to the FDA for formal review as part of IND or IDE submissions. The protocol may also be sent informally to the FDA for preliminary review (pre-IND or pre-IDE) prior to an IND or IDE submission. The DCC will advise the investigator as needed.

6.1.4. The DCC will post the protocol in the study eRoom in pdf format.

Sites may not make any changes to the final protocol after this point without approval of the DCC. The DCC will maintain a copy of the IRB approval letter(s) from participating sites and place these documents in the IRB tracking system in eRoom. The participating site will maintain documentation of all IRB approvals and correspondence as well.

6.1.5. The site will not implement the protocol until final IRB approval is obtained, the protocol has been submitted to the FDA (if applicable), and the required 30-day response period has passed or an FDA approval letter has been received. Once FDA review is complete the protocol can be submitted to the IRB. Certain protocols must be submitted to other external and/or internal regulatory authorities for review before or concurrently with PECARN IRB/FDA submission.

6.1.6. The site will retain approved clinical protocols and their attachments, subsequent revisions and associated correspondences with regulatory authorities, as well as any other documents required, and keep them filed in the Essential Documents Binder.

6.2. Protocol Amendment Creation, Review and Approval

6.2.1. The lead investigator will make any necessary changes to the protocol in conjunction with the DCC, as necessary during the conduct of the study. Major changes may need to be approved by PECARN Steering- and/or sub-committees. Any revision to the original protocol or subsequent version of the protocol that substantially affects the scientific details of the study, safety of the subjects and/or significantly affects the scope of the investigation must be submitted to all site IRB(s) and the FDA (as applicable). The DCC will assist the lead investigator in this process. Protocol amendments must be written in the same format as the original protocol, highlighting the new elements. The DCC will amend the version number to reflect subsequent changes to the protocol after approval of the original version.

6.2.2. If changes to a protocol result in necessary changes to informed consent, the lead investigator will make associated changes to the informed consent form and will instruct participating sites to submit changes to their local IRBs.

6.2.3. Protocol changes made to eliminate an immediate hazard to subjects may be implemented immediately, provided that the FDA and the IRB are notified as soon as possible afterwards, but no more than 5 days after the change is implemented.

7. REGULATIONS

21 CFR 312.20 Requirements for an IND

21 CFR 312.21 Phases of an Investigation

21 CFR 312.23 IND Content and Format

21 CFR 312.30 Protocol Amendments

21 CFR 312.62 Investigator Recordkeeping and Record Retention

21 CFR 314.126 Adequate and Well Controlled Studies

21 CFR 812.25 Investigational Plan

21 CFR 860.7 Determination of Safety and Effectiveness

21 CFR 812.35 Supplemental Applications

21 CFR 812.140 Records

ICH E6 2.2, 2.4 –

2.6, 2.10, 2.11

The Principles of ICH GCP

ICH E6 4.5 Compliance with Protocol

ICH E6 4.9 Records and Reports

ICH E6, 5.1 Quality Assurance and Quality Control

ICH E6 5.4 Trial Design

ICH E6, 5.5 Trial Management, Data Handling and Record Keeping

ICH E6, 5.23 Multicentre Trials

ICH E6 6.0 Clinical Trial Protocol and Protocol Amendment(s)

ICH E8 General Considerations for Clinical Trials (December 1997)

ICH E9 Statistical Principles for Clinical Trials (September 1998)

ICH E10 Choice of Control Group and Related Issues in Clinical Trials
(May 2001)

8. REFERENCES

Supplement to the ***FINALIZATION AND AMENDMENT OF PECARN PROTOCOLS*** policy.

The following protocol finalization guideline describes what the lead investigator needs to include in the study protocol after a grant is approved to fund the study. This final protocol will be submitted to the IRB and is generally more detailed than the earlier version submitted to the PECARN Steering Committee. The goal of protocol finalization is to describe the study in a clear, concise, detailed written document that IRBs may review.

A. Elements of the final protocol

1. Title Page

2. Introduction and Purpose

The basic work leading to the study should be reviewed. A clear statement of the specific aims (and hypotheses) of the research should be included. State primary/secondary study outcomes here.

3. Background and Rationale

Previous clinical work should be reviewed here and a description of how the current protocol extends existing work on the topic should be provided. The investigators should detail how successful completion of this protocol will lead to improved care of children. If the study is a drug or device study, relevant information might include pharmacological, toxicological and other biological properties of the drug/biologic/medical device, and previous efficacy and safety experience should such exist. The investigators should discuss any preliminary studies performed by the investigational team. This section may be shortened from what is in the grant and reduced to the essential elements that an IRB needs to know.

4. Study Design

This section provides a thorough overview of the study design, including how the study objectives will be achieved. This section will describe the type of study (i.e., double-blind, multicenter, placebo-controlled, etc.), the specific treatment groups and number of study subjects (in each group) and number of investigative sites. A brief description of the methods and procedures to be used during the study will be provided, but will be expanded upon in the Procedures section.

5. Study Outcomes

This section should include a description of primary and secondary outcomes or endpoints, how they will be measured and a schedule of assessments over time. This section should also justify any additional measures (not related to a primary or secondary outcome) to be addressed in the main analysis.

6. Study Population / Subject Eligibility

This section states the number of subjects required to be enrolled in the study at all sites. There should be a brief definition of the nature of the subject population that is required. Accrual projections and duration of the study should be described.

Inclusion Criteria: This section describes the criteria each subject must satisfy to enter

the study, including but not limited to: age, sex, race, diagnosis, method of diagnosis, diagnostic test result requirements, concomitant medication requirements, severity of symptoms and signs of the disease, the ability to perform study requirements and to give informed consent. The criteria should be detailed sufficiently to provide the investigative site the information needed to recruit appropriate subjects. Care should be taken to develop these criteria so that they include the desired target population and not be overly inclusive or exclusive.

Exclusion Criteria: The criteria that eliminate a subject from the study population should be listed. These may include but are not limited to: previous medical history, pregnancy, childbearing potential, current or past therapy, severity of disease, current medical conditions, a minimum of time since the last clinical study, drug or alcohol abuse, and upper limits of laboratory tests that will disqualify potential subjects.

7. Procedures and Data Elements

This section details the plan of action, procedures, and methods to be used during the study. The investigators should describe if and how the methods in this study are novel or innovative.

The activities for each phase of the study are described. Include a clear outline of the study activities (collecting data, administering tests, performing clinical measures, recording data) This section should be sufficiently detailed for PECARN sites to understand the specific procedures associated with the study. Very specific details will likely go into the Manual of operations, but in general, the procedures should be outlined in enough detail that a person could conduct the study from the protocol. For example, “the research coordinator will abstract the data from the chart and enter it into an electronic data collection system”. This is sufficient for the protocol. Additional information that might be in the Manual of Operations would be: time of ED admission will be abstracted from the triage note. The DCC can assist with the amount of detail that should be included.

Screening, Enrollment and Randomization: Describe how patients will be identified, approached, screened, randomized, and enrolled. A flow diagram is helpful.

Diagnostic and Laboratory Tests: Detailed methodology is described for laboratory or diagnostic tests. Any unusual tests or tests required specifically for the study should be described. If the tests are part of standard of care, this should be described. If the tests are not part of standard of care, this should be explained in detail.

Data elements: A general description of essential data elements that will be collected should be included in this section. It is important to be thorough yet not too specific as data elements may change slightly over the course of a study, and overly specific information may require formal amendment. The goal is to describe to the IRB the main types of data that will be collected, knowing that there will be more specifics inside the Manual of Operations. For example, “we will collect demographics, ED laboratory results, all CT scan findings, admission information, a brief medical history, treatment received in the ED, medications administered in the ED, LOS, and follow up information for patients who were discharged from the ED.”

Follow-up procedures (if applicable): Describe the follow-up procedures (e.g. telephone follow-up calls, returns for evaluation), and their timing.

8. Study Treatment (if applicable)

All interventions for the study such as treatments, schedules, and specific guidelines for study subjects should be described. Specific information for drug studies includes:

Dosing schedule (or investigational device use): The details concerning dose, frequency, and duration of the experimental treatment should be provided here. If placebos are part of the treatment plan, the details of their administration are also described in this section. If applicable, the drug, doses, frequency, and duration of concomitant treatment required in addition to the experimental medication are listed here.

Study drug/device supplies and administration: The Lead Investigator should determine who is going to provide the study medication (e.g., pharmaceutical company, local laboratory) and note this here. The Sponsor must be able to assert that the experimental medication has been manufactured following all regulations (i.e., by Good Manufacturing Practice or GMP). This is especially important if the investigational product is manufactured in a local laboratory without the participation of a biotech or pharmaceutical company. Details of the product stability, storage requirements and dispensing requirements should be provided if there are unusual needs.

Dose modification for study drug toxicity: Rules for changing the dose or stopping the study drug should be provided. If the involvement of an Investigator and/or an Independent Data Monitoring Committee and/or the Sponsor is/are required prior to stopping the drug or changing the doses, this should be noted in this section. Possible drug interactions: The foreseeable interactions of the study drug with other medications or herbal preparations should be noted. Concomitant therapy: The drugs that are permitted during the study and the conditions under which they may be used are detailed here. Describe the drugs that a subject is not allowed to use during parts of or the entire study.

Discontinuation from study treatment: The specific reasons from early discontinuation and the definition of treatment failure should be defined. Discontinuation due to other causes (e.g., adverse events, withdrawal of consent, etc.) should also be described.

Blinding/Unblinding procedures: If the study employs a blind on the Investigator and/or the subject, describe how this will be accomplished. If the study is blinded, the circumstances and the mechanism for unblinding to occur should be given.

Conditions for a subject to withdraw from the study should be described here.

9. Data Management (The DCC will suggest a plan for this section)

This section will include details on the collection and submission of data to the DCC.

Data quality: A statement about data quality and what methods will be used to assure data accuracy should be included. Describe double data entry, validation plans and internal audits as applicable to the study.

10. Data Analysis (prepared in conjunction with the DCC statistician(s))

The details of the statistical approach to be followed in the study are described:

Sample size: Describes the sample size required and how the sample size was determined, including the assumptions made in making this determination.

Efficacy endpoints: Before the study begins, the endpoints need to be clearly and completely defined. These can be grouped as primary and secondary endpoints. Safety endpoints should also be defined before the study begins (if applicable).

Statistical analysis: Details of how the results will be analyzed and reported are described in this section; specifically, statistical tests to be used to analyze the primary and secondary endpoints that were defined above, a definition of the level of significance, statistical tests to be used, and the methods used for missing data. The method of evaluation of the data for treatment failures, non-compliance, and subject withdrawals is presented. If an interim analysis will be performed, the rationale and conditions are described. Any statistical concerns to correct for interim analyses should be presented.

Pharmacokinetic (PK) analysis: If applicable, the statistical considerations for analyzing PK data are described here.

11. Human Subjects

Risk/benefit assessment: Provide a discussion of major known risks of the treatment(s) and testing procedure(s). Specific risks associated with the investigational product and any control(s) should be included. Details of how known risks will be mitigated or minimized should be provided. What benefits exist for the subjects should be discussed.

Consent Process: This section should detail the consent/assent process or its substitute. If the lead investigator is requesting a waiver of informed consent, this should be stated and justified.

12. Study Monitoring & Quality Assurance (DCC will suggest a plan for this section). All clinical studies require monitoring commensurate with the degree of risk involved in participation as well as the size and complexity of the study. The plan provided in the protocol should be quite general, since funding resources may not be known. A general description will also help avoid amendments to the protocol if the monitoring plan requires changes. Detailed plans will be provided in the separate data management and site monitoring plans. The protocol should outline enough of a plan to display commitment in the areas of human subject protection and data quality without providing details that would not allow for flexibility. Describe the type of site monitoring and describe quality assurance plans in general. Include a general description of the type of study monitoring visits (initiation, interim, and close-out).

Describe record retention requirements including details of how long the study data and files need to be stored and how and when Investigators will be informed when the files can be destroyed. The right of the FDA, IRB, and representatives of the Sponsor to verify and inspect/audit the study data is presented here.

13. Organization of the project and capabilities of the investigators.

The investigators should briefly explain the organizational structure of the investigative team, including plans for mentorship, where appropriate. This section should briefly demonstrate the expertise of the team, including appropriate references, and should describe any special environments (e.g. basic science laboratory) needed to conduct the

research. Names should be omitted unless absolutely necessary because any subsequent investigator name changes will require an amendment.

Informed consent process: This section should describe the consent/assent process. It should include a statement that the elements of informed consent comply with FDA regulations, the ICH Guidelines for Good Clinical Practice (GCP) and/or other guidelines.

14. Adverse Events (DCC can assist with language for this section)

Describe procedures for reviewing and reporting adverse events (expected and unexpected) that occur during the study. Include a detailed description of expected adverse events from previous experience with the investigational product, if available. Include a description of the procedures used to evaluate an adverse event and the time constraints for reporting the different types of adverse events.

Reporting serious adverse events: The details of serious adverse event reporting should be described including contact information for telephone and/or fax reporting.

15. Investigational Product Management

Investigational product description and packaging: All ingredients and the formulation of the investigational drug/biologic and any placebos that are used in the study are described. The precise dosing that is required during the study and method of packaging, labeling, and blinding is described. The method of assigning treatments to subjects and the subject identification code numbering system is detailed. If applicable, the method of blinding to make the test treatments indistinguishable should be explained. The method of drug/biologic coding, code storage, and code access is described. If a third party such as a pharmacist will be dispensing or blinding the investigational product, specific instructions should be supplied.

For investigational medical devices, the device specifications and appropriate clinical use are discussed. The method of packaging, labeling, and blinding (if applicable) is described. The method of assigning treatments to subjects and the subject identification code numbering system is detailed.

Stability and storage requirements: These should be detailed enough so that the pharmacist or other designee who stores and dispenses the investigational product knows what is required. Explicit instructions for the storage of the investigational products are listed here.

Investigational product accountability: Instructions for the receipt, storage, dispensation, and return shipping of the investigational products are described here. FDA regulations require a complete accounting of all investigational products received, dispensed, and returned/destroyed.

16. Appendices

This section includes copies of the informed consent form/assent form; and any other documents referenced in the clinical protocol.



Initial Draft: March 2007 Version No.: 2 Revised: 14Aug 2009	Feasibility and Budget Subcommittee Process for Review of PECARN Proposals	Original Steering Committee Approval: 22Oct07 Steering Committee Approval: 19Nov09
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1. PURPOSE

- 1.1. The purpose of this policy is to provide guidance for PECARN investigators and others involved in PECARN research regarding the development, submission and approval process of a project budget

2. POLICY

- 2.1. This document describes the approved method of developing a budget for a PECARN research project. Any changes to this process must be approved by the PECARN Steering Committee or the Nodal PI group.

3. SCOPE

- 3.1. This document applies to all investigators, nodal administrators and others involved in PECARN-related research and to all participating sites.

4. DEFINITIONS

- 4.1. Nodal Principal Investigators: Investigators named on the HRSA cooperative agreements at each PECARN node and the CDMCC.

5. Subcommittee Quorum:

- 5.1. A quorum of the subcommittee will be considered when at least one member or alternative from each node and the CDMCC are represented.

6. RESPONSIBLE PARTIES

- 6.1. A PECARN investigator or an external investigator is responsible for preparing the initial draft of the budget, in conjunction with participating PECARN nodal investigators, subcommittees, subject matter experts, the CDMCC, and others, as appropriate.

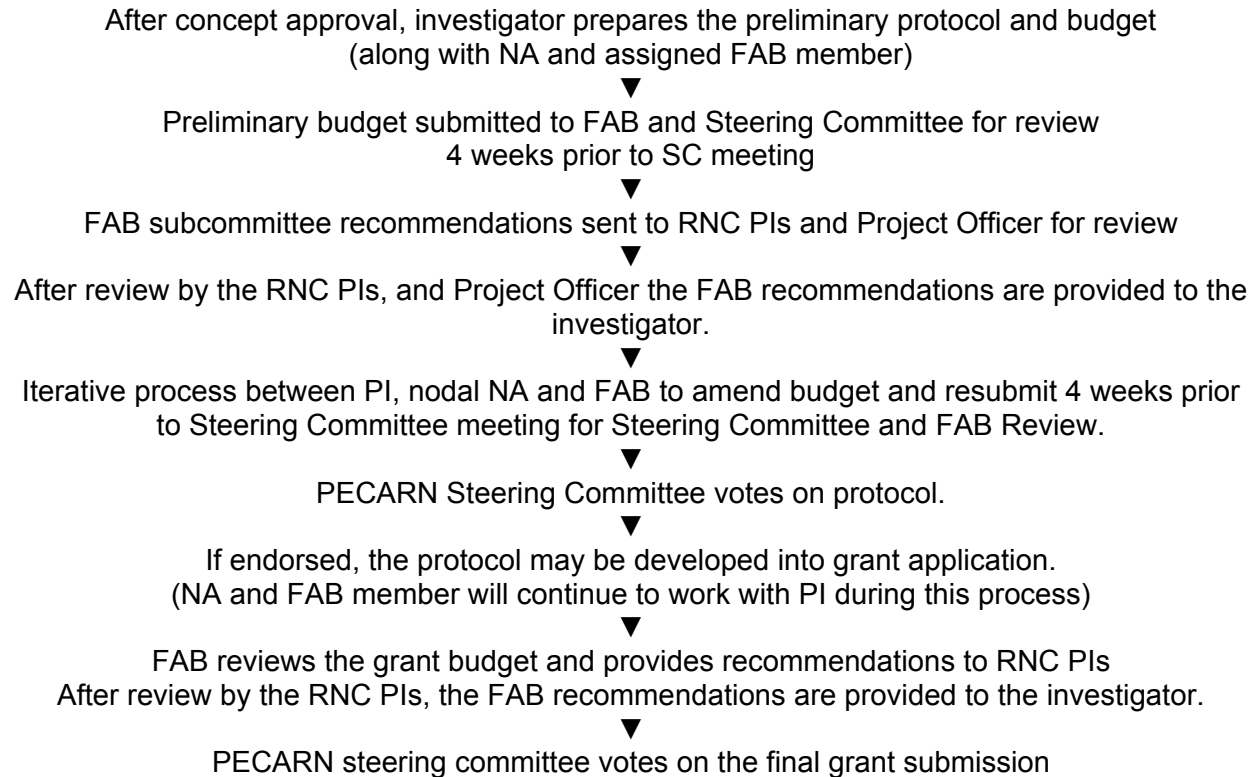
7. PROCEDURES

7.1. Developing the Proposed Budget :

Investigators will work with FAB subcommittee representatives throughout the protocol and grant development process. The preliminary budget will be completed by the PI, in cooperation with the nodal administrator of his/her sponsoring node, and a selected member of FAB.

- 7.2. A preliminary budget and brief budget narrative will be submitted to FAB at the time of the initial submission of the protocol to PECARN. This will occur 4 weeks prior to the Steering Committee meeting.
 - 7.3. The template for this preliminary budget is attached (Appendix 1). The preliminary budget must include an accurate accounting of all costs necessary to complete the study.
 - 7.4. If there is a known cap on total grant dollars at the time of preliminary budget submission (e.g. already queried the NIH and were not given permission to exceed the cap), the preliminary budget must also identify areas where the full budget could potentially be trimmed. This will allow FAB to make productive recommendations.
 - 7.5. If it is not known at the time of the submission but later determined that the grant dollars available are capped, the budget will require additional FAB review. The investigator may request consideration for the use of internal PECARN resources to supplement the study budget. FAB will determine if internal resources are available and, along with the Executive Committee, will determine if and at what level internal resources can be allocated to the project.
 - 7.6. In addition to reviewing the budget, the committee will also assess and make recommendations regarding the general feasibility of the project.
- 8. Subcommittee Process for Review of Preliminary Budget:**
- 8.1. The subcommittee will review the preliminary budget at a breakout session during a PECARN Steering Committee meeting. Prior to the meeting, the chair will assign a primary and secondary reviewer and a representative from the CDMCC to review the budget for all projects. The reviewers will prepare written reports. At the time of the subcommittee meeting, the study PI will be available to answer questions. This question-and-answer period will generally occur later in the meeting, and after the subcommittee has reviewed the preliminary budget. In case of a short turnaround RFA or as approved by the Executive Committee, the subcommittee may also convene an electronic review.
- 9. Format of Subcommittee Recommendations:**
- 9.1. The FAB subcommittee will review the preliminary budget and project feasibility and send their written recommendations to the Research Node Center (RNC) Principal Investigators (PIs) and the Federal project officer. After consultation with the RNC PIs, the FAB subcommittee will send the final recommendations to the investigator electronically. This document will also detail specific action items and instructions/timeline for responding.
- 10. Budget Amendment and Resubmission to PECARN**
- 10.1. The PI will work with the NA, assigned FAB member, and federal project officer to amend the budget as needed. This will be an iterative process. Input from specific sites involved in the study should be solicited.
 - 10.2. The amended budget will be resubmitted for review by FAB and the Steering Committee four weeks prior to the Steering Committee meeting.
 - 10.3. PECARN will vote on the protocol at this Steering Committee meeting.

Schematics of Review Process:



Appendix 1 – Preliminary Budget Template

Preliminary Budget Planning Document (Updated May, 2009)							
This spreadsheet may be used to develop your preliminary study budget and to compare your funding requirements to the funding agency limits. This document can be used to determine if you need to request internal PECARN resources for your project. Columns 2, 3 & 4 are the actual support you expect to require and columns 5, 6 & 7 are support you wish to request from the PECARN infrastructure or hospital in-kind support. This document may be used for your initial FAB submission.							
1	2	3	4	5	6	7	8
Description	Total \$ Amount	Percentage Support Requested	Amount of Funding Required	Funding to be requested from PECARN Infrastructure	Funding to be requested from CDMCC Infrastructure	In-Kind Support from Participating Institution	Funding Required less Infrastructure and In-Kind Support Requested
Project Research Budget				PECARN Site Infrastructure	CDMCC Infrastructure	Hospital in-kind	Grant Needed
Primary Site Personnel	<u>Salary/Benefits</u>	<u>% FTE</u>	<u>Amount</u>				
Principal Investigator	\$ 196,700	30%	\$ 59,010	\$ 40,000	\$ -	\$ 5,000	\$ 14,010
Site Research Coordinator	\$ 40,000	100%	\$ 40,000	\$ 25,000	\$ -	\$ -	\$ 15,000
Other persons	\$ 43,000	30%	\$ 12,900	\$ 12,900	\$ -	\$ -	\$ -
	<u>Cost per Trip</u>	<u># Trips</u>	<u>Amount</u>				
Travel	\$ 1,350	6	\$ 8,100	\$ 5,000	\$ -	\$ -	\$ 3,100
Other Expenses			<u>Amount</u>				
Expense One	\$ 3,200		\$ 3,200	\$ -	\$ -	\$ -	\$ 3,200
Expense Two	\$ 45,000		\$ 45,000	\$ -	\$ -	\$ -	\$ 45,000
Expense Three	\$ 3,600		\$ 3,600	\$ -	\$ -	\$ -	\$ 3,600
Primary Site Direct Cost			\$ 171,810	\$ 82,900	\$ -	\$ 5,000	\$ 83,910
Site Personnel	<u>Salary/Benefits</u>	<u>% FTE</u>	<u>Amount</u>				
Site Investigator	\$ 196,700	30%	\$ 59,010	\$ 10,000	\$ -		\$ 49,010
Site Research Coordinator	\$ 40,000	100%	\$ 40,000	\$ 10,000	\$ -	\$ -	\$ 30,000
Site Other persons	\$ 43,000	30%	\$ 12,900	\$ 5,000	\$ -	\$ -	\$ 7,900
	<u>Cost per Trip</u>	<u># Trips</u>	<u>Amount</u>				
Site Travel	\$ 1,350	6	\$ 8,100	\$ 2,000	\$ -	\$ -	\$ 6,100
Other Site Expenses			<u>Amount</u>				
Expense One	\$ 3,200		\$ 3,200	\$ -	\$ -	\$ -	\$ 3,200
Expense Two	\$ 45,000		\$ 45,000	\$ 15,000	\$ -	\$ -	\$ 30,000
Expense Three	\$ 3,600		\$ 3,600	\$ 1,000	\$ -	\$ -	\$ 2,600
Cost per Site			\$ 171,810	\$ 43,000	\$ -	\$ -	\$ 128,810
Number of Sites	4						
Total Site Direct Expenses			\$ 687,240	\$ 172,000	\$ -	\$ -	\$ 515,240
CDMCC Personnel	<u>Salary/Benefits</u>	<u>% FTE</u>	<u>Amount</u>				
CDMCC Investigator	\$196,700	10%	\$ 19,670	\$ -	\$ 19,300	\$ -	\$ 370
CDMCC PhD Statistician	\$125,000	15%	\$ 18,750	\$ -	\$ 18,750	\$ -	\$ -
CDMCC Program Manager	\$100,000	15%	\$ 15,000	\$ -	\$ 15,000	\$ -	\$ -
CDMCC Study Coordinator	\$60,000	100%	\$ 60,000	\$ -	\$ 30,000	\$ -	\$ 30,000
CDMCC Data Manager	\$70,000	100%	\$ 70,000	\$ -	\$ 35,000	\$ -	\$ 35,000
CDMCC Master Statistician	\$75,000	50%	\$ 37,500	\$ -	\$ 20,000	\$ -	\$ 17,500
CDMCC Other Persons	\$40,000	40%	\$ 16,000	\$ -	\$ 16,000	\$ -	\$ -
	<u>Cost per Trip</u>	<u># Trips</u>	<u>Amount</u>				
CDMCC Travel	\$ 1,350	6	\$ 8,100	\$ -	\$ 8,100	\$ -	\$ -
Other CDMCC Expenses			<u>Amount</u>				
Expense One	\$ 3,200		\$ 3,200	\$ -	\$ 3,200	\$ -	\$ -
Expense Two	\$ 45,000		\$ 45,000	\$ -	\$ 45,000	\$ -	\$ -
Expense Three	\$ 3,600		\$ 3,600	\$ -	\$ 3,600	\$ -	\$ -
Site Monitoring			\$ 50,000	\$ -	\$ -	\$ -	\$ 50,000
CDMCC Direct Cost			\$ 346,820	\$ -	\$ 213,950	\$ -	\$ 132,870
Total Project Direct Costs			\$ 1,205,870	\$ 254,900	\$ 213,950	\$ 5,000	\$ 732,020



STANDARD OPERATING POLICY AND PROCEDURE FOR INSTITUTIONAL REVIEW BOARD APPROVAL

Initial Draft: Sept 06 Revision: 14Aug09 Reviewed October 2014 Revision Sept 2015	Institutional Review Board Approval	Original Steering Committee Approval Date: 1Sept2006 Revision SC approval: 19Nov09 Exec Committee Approval: 30 Sept 2015
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1. POLICY

- 1.1 Obtaining Institutional Review Board (IRB) approvals for all research conducted by the investigative site is required by the Pediatric Emergency Care Applied Research Network (PECARN) before the site may begin a specific study.
- 1.2 Maintaining continuous IRB approval for each specific study throughout the study period is required.
- 1.3 The DCC must obtain and maintain documentation of continuous IRB approval for each specific study in order to collect data from the network sites.
- 1.4 Written documentation of original approval, all amendments and continuous IRB approval is required.

2. PURPOSE

- 2.1 Obtaining IRB approval for a proposed study at the investigative site is the first critical process in the protection of human subjects who volunteer to participate in clinical research.
- 2.2 This policy is intended to meet the requirements of federal regulations that all research involving human subjects be approved and reviewed at least annually by a qualified IRB.
- 2.3 It is the intent of PECARN to comply with federal regulations and guidelines and follow the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP).

3. SCOPE

This document describes the policy, procedures and responsibilities of PECARN members with regard to obtaining and maintaining continuous IRB approval

throughout the duration of each specific research study. It applies to all PECARN investigators and designated staff with delegated applicable roles.

4. RESPONSIBILITY

- 4.1 Selection of a qualified IRB to review PECARN research protocols will be at the discretion of the Investigator based upon the site's institutional requirements.
- 4.2 The investigator is responsible for assuring that the IRB reviewing each research study is in compliance with the relevant regulations, guidelines and requirements
- 4.3 The Investigator is responsible for submitting PECARN research protocols to the IRB within the time frame specified by the Steering Committee.
- 4.4 The Investigator is responsible for obtaining IRB approval for the protocol, amendments, advertisements and informed consent/assent/parental permission form(s) prior to enrolling patients or collecting data for the study.
- 4.5 The Investigator is responsible for submitting initial IRB renewal materials within the PECARN determined timeline and to update the DCC regarding documentation and actual lapses in IRB approval.
- 4.6 The investigator is responsible for submitting renewals in the time frame required by the site's IRB, in order to maintain continuous IRB approval for the study.
- 4.7 The Investigator is responsible for direct communications with the IRB and for informing the IRB of any protocol changes, deviations, violations, adverse events (AEs) or serious adverse events (SAEs).
- 4.8 The Investigator or documented designee is responsible for ensuring that copies of the IRB applications, IRB approvals of the protocol amendments, advertisements and consent/parental permission/assent form(s) are maintained in the site's Essential Documents Binder (EDB). This includes documentation that all AEs and SAEs have been reported to the local IRB in accordance with study recommendations and local site requirements and applicable regulations.
- 4.9 The Investigator is responsible for sending to the DCC documentation of all IRB approvals (original approval, amendments and renewals). This may be done by electronic format or by fax or mail. Documentation consists of a letter from the IRB chair or minutes from the IRB meeting that formally document approval of the protocol or amendment.
- 4.10 The IRB is responsible for providing written documentation of review and approval of the protocol, advertisements, amendments, consent/assent/parental permission form(s) and for timely continuing review of the research and submitted AEs and SAEs.
- 4.11 The IRB is responsible for documenting that personnel involved in the study do not vote on the protocol.

5. PROCEDURES

- 5.1 Operations of a qualified IRB or ethics committee:
- 5.1.1 An IRB is the board, committee or other group formally designated by an institution to review, to approve the initiation of and to conduct periodic review of biomedical research involving human study subjects in order to assure the protection of the rights and welfare of human research volunteers.
- 5.1.2 IRB approval means that the IRB has reviewed the proposed clinical research study and it may be conducted at the investigative site within the constraints set forth by the IRB and by other institutional, local and federal regulations, requirements and guidelines.
- 5.1.3 Required membership of a qualified IRB consists of at least 5 members, both men and women of diverse backgrounds and expertise with at least 1 member having scientific expertise, 1 member who is not a scientist and 1 member who is not affiliated with the institution.
- 5.1.4 An IRB that regularly reviews research involving a vulnerable category of subjects (children, prisoners, pregnant women, handicapped or mentally disabled persons) must consider including one or more individuals who are knowledgeable about and experienced in working with such subjects. As PECARN is a pediatric network, it is preferable that each site's IRB has pediatric expertise available when reviewing network protocols.
- 5.1.5 The IRB notifies the Investigator in writing of its decision to approve or disapprove the protocol or of modifications required to secure IRB approval. If the protocol is disapproved, the IRB provides a statement of the reasons for the decision and gives the investigator an opportunity to respond.
- 5.1.6 The IRB conducts continuing review of the protocol at intervals appropriate to the degree of risk, but not less than once a year.
- 5.1.7 An IRB expedited review may be carried out by the IRB Chairperson or one or more experienced reviewers designated by the IRB Chair from among the members of the IRB when appropriate
- 5.1.8 PECARN investigators or staff members who are members of the IRB will not review or vote on PECARN protocols (at their local site) in which they are involved. The site investigator will document this in writing as specified by the DCC.
- 5.1.9 IRB approval and renewal notices must include the title, the most current version number and date of the protocol and any consent/assent/parental permission form(s). If the IRB does not provide the version number of the protocol in its written approval, the site must provide documentation (email acceptable) from the IRB chair or designate that specifies which version of the protocol was approved. A letter from the PI is not sufficient to confirm the version number.
- 5.2 Investigative site procedures:
- Note: Activities in this section may be delegated to other appropriate personnel, but ultimately remain the responsibility of the Investigator at the local site.

- 5.2.1 The Investigator submits the protocol, advertisements, amendments, informed consent/parental permission, assent form(s) and Investigator's Brochure (as applicable), and any additional documents as may be required, to the IRB for review and approval prior to starting the study at the investigative site. The study materials should be submitted within the time frame determined by the principal investigator of the study.
- 5.2.2 The Investigator maintains a copy of the complete initial IRB submission in the EDB. The investigator obtains a copy of all subsequent IRB approvals and maintains copies in the EDB.
- 5.2.3 The Investigator maintains copies of all correspondence with the IRB in the EDB. During the study, the Investigator informs the IRB of AEs, SAEs, changes to the conduct of the research, submits amendments, progress reports and any protocol deviations that occur at the investigative site.
- 5.2.4 The Investigator submits renewal applications to the IRB at periods specified by the IRB but not less than once a year. Timely submission of renewal requests is required in order to maintain continuous IRB approval. For example, IRB renewals may need to be submitted 2-3 months before IRB approval expires to ensure that the study does not lapse at the site.
- 5.2.5 The Investigator may be requested to provide additional material to the IRB for renewal such as a summary of adverse events or summarized patient accrual information. The DCC will provide this information upon request. The IRB will not be provided with blinded or unblinded outcome data, but for blinded studies, reports by the Data Safety and Monitoring Board (DSMB) will be provided, if requested.
- 5.2.6 Upon study conclusion, the Investigator prepares a final report for the IRB following the local IRB requirements.
- 5.3 Procedures for lapse of continuous IRB approval.

There are two definitions for a lapse of continuous IRB approval. A discontinuity of documentation of continuous IRB approval at the DCC is considered a documentation lapse. A discontinuity of continuous IRB approval, as documented in the IRB approval and renewal dates, is considered an actual lapse of IRB approval. If the DCC does not receive documentation of IRB renewal of a continuously approved study by the date of expiration of the latest documented IRB approval, the site will be considered to have a documentation lapse.
- 5.3.1 The DCC will not accept data from an investigative site when a documentation lapse or an actual lapse has occurred. The DCC will notify the site Investigator and research assistants to cease patient enrollment until documentation of IRB approval is received by the DCC. The DCC will also inform the Research Node Center Principal Investigator and Nodal Administrator that there has been a documentation lapse at an investigative site in their Node.
- 5.3.2 Patient enrollment is not permitted during a documentation lapse, regardless of reason for the lapse.
- 5.3.3 Prior to resuming patient enrollment or data collection in a study, the Investigator must submit documentation of IRB renewal in writing to the

DCC. Documentation should be the IRB minutes, or letter from the IRB indicating approval. If the formal IRB letter is not available, the site must send a letter or email from the IRB chair or IRB administrative staff that states that the protocol has been reviewed and approved. Upon receipt of appropriate documentation, the DCC will notify the site Investigator and research assistants that study participation may resume. The DCC will also inform the Research Node Center Principal Investigator and Nodal Administrator that the investigative site may resume participation in the study.

- 5.3.4 If there is an actual lapse of IRB approval between expiration and renewal, based on the dates of approval noted by the site IRB documentation, any and all patients who were inadvertently enrolled during that lapse will be removed from the study. The same pertains to any patients enrolled prior to IRB approval. Note that neither of the above situations should occur, because sites should cease patient enrollment if the DCC does not have documentation of IRB approval. For patients who were enrolled prior to the lapse of approval but had follow up or other data collected during the lapse, the local IRB will be notified. Unless the local IRB disagrees, follow-up data collected during the lapse will be used in the study.
- 5.3.5 DCC will notify sites regarding the status of studies after data collection and queries are complete. DCC will also notify sites when data analysis is complete. Each site IRB will determine the need for renewal from this point forward. Each site is responsible for sending documentation to the DCC of their renewal status for studies that have completed enrollment and data queries.

6. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50	Protection of Human Subjects
21 CFR 56	Institutional Review Boards
21 CFR 312.66	Assurance of IRB Review
21 CFR 312.62	Investigator Recordkeeping and Record Retention
21 CFR 812 - D	IRB Review and Approval
21 CFR 812.42	FDA and IRB Approval
21 CFR 812.47	Emergency Research Under 50.24 of This Chapter
45 CFR 46	Protection of Human Subjects
45 CFR 46.107	IRB Membership
45 CFR 46.109	IRB Review of Research
ICH E6, 2.0	The Principles of ICH GCP
ICH E6, 3.1.4	IRB/IEC Responsibilities
ICH E6, 3.3	IRB/IEC Procedures
ICH E6, 3.4	IRB/IEC Records
ICH E6, 4.10	Progress Reports
ICH E6, 4.4	Communication with IRB/IEC
ICH E6, 5.11	Confirmation of Review by IRB/IEC
HHS Guidance	Guidance on 45 CFR 46.407 Review Process (Aug 2005)

HHS FAQs	FAQs on Human Research IRB Registration Process (Sep 2005)
HHS FAQs	FAQs on Human Research Regulations (Jan 2006)
HHS FAQs	FAQs on Research Involving Children (Jan 2006)

7. REFERENCES TO OTHER APPLICABLE SOPs

PECARN SOP&P: Adverse Event Recognition and Reporting
PECARN SOP&P: Human Subject Protection
PECARN SOP&P: Informed Consent Process



STANDARD OPERATING POLICIES AND PROCEDURES FOR THE INFORMED CONSENT PROCESS

Initial Draft 28 Feb 2006 Initial	The Informed Consent Process	Original Approval Version 1.0 September 1, 2006 by electronic vote
Revised 23 June 2006, May 2012		Nodal PI approval 10July 2012

1. POLICY

- 1.1 Obtaining Institutional Review Board (IRB) approval for all Informed Consent (IC) documents, Parental Permission (PP) forms and pediatric Assent forms is required by the Pediatric Emergency Care Applied Research Network (PECARN) Steering Committee before the site may begin enrollment in a study to which these documents are applicable.
- 1.2 Maintaining continuous IRB approval for IC/PP/Assent documents throughout the duration of the study is required in order for the site to continue enrolling subjects.
- 1.3 Written documentation of original and continuous IRB approval is required.
- 1.4 PECARN studies will use written documentation of informed consent to obtain IC/PP/Assent (as applicable) from all subjects in accordance with federal, state and local regulations, guidelines and IRB requirements, unless this requirement has been waived by the IRB.
- 1.6 Monitoring and/or auditing of PECARN investigative sites will include verification of written IC/PP/Assent (as applicable).

2. PURPOSE

- 2.1 Documentation of a clear and complete informed consent process is a critical step in the protection of human subjects who volunteer to participate in clinical research.
- 2.2 It is the intent of PECARN to comply with federal regulations and guidelines and follow the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP).
- 2.3 For applicable research protocols, this policy is intended to meet the requirement that all investigators involved in research on human subjects have obtained the legally effective informed consent of the subject or the subject's legally authorized representative.
- 2.3.1 This policy is intended to meet the requirement that, when applicable, IC shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of the consent.

3. SCOPE

This document describes the policies, procedures and responsibilities of PECARN members with regard to obtaining and documenting written informed consent from each human subject, or the subject's legally authorized representative, for all applicable PECARN protocols. It applies to all PECARN investigators and designated staff with delegated applicable roles. Please note that certain PECARN studies will not require written informed consent, as determined by the local IRBs. This document does not pertain to these studies.

4. RESPONSIBILITY

- 4.1 The Investigator is responsible for submitting IC/PP/Assent documents to the IRB and obtaining IRB approval for these documents, when applicable, prior to consenting or enrolling any subjects.
- 4.2 The investigator or an appropriately trained associate or staff member is responsible for obtaining informed consent on all research subjects, with the understanding that the ultimate responsibility of insuring adequate consent lies with the site investigator.
- 4.3 The IRB is responsible for providing written confirmation of approval of IC/PP/Assent documents submitted by the investigator and designating the version or version date of the approved document/s.
- 4.4 The Investigator is responsible for ensuring that IC/PP/Assent is obtained from each subject, or the subject's legally authorized representative, as necessary, for each applicable PECARN protocol, using the most recent IRB-approved version of these documents.
- 4.5 The Investigator is responsible for assuring that all elements of IC are discussed with the subject or the subject's legally authorized representative in terms that are understandable, answering any questions and allowing sufficient time for considering participation.
- 4.6 The Investigator is responsible for assuring documentation of the informed consent process and maintaining the original, signed copies of all IC/PP/Assent forms in the subject's study file, or the site's Essential Documents Binder (EDB) or a reasonable alternate location that is specified and documented in the EDB. A selected alternate location must provide easy access for a site monitor or auditor.
- 4.7 The Investigator or an appropriately trained associate or staff member is responsible for ensuring that each subject or legally authorized representative receives a copy of the applicable IC/PP/Assent form/s. Again, the ultimate responsibility for insuring that this occurs rests with the site investigator.
- 4.8 The investigator is responsible for ensuring that time of consent is documented in some location other than the consent form (e.g., an investigator note to file), when applicable as determined by the investigator or DCC.
- 4.9 The Investigator is responsible for ensuring and documenting that no study procedures or interventions are performed on a subject prior to obtaining IC/PP/Assent (as appropriate).

5. PROCEDURES

5.1 Procedures for Standard Written Informed Consent

- 5.1.1 The Investigator submits IC/PP/Assent forms (as appropriate) to the IRB for review and approval prior to use.

- 5.1.2 When a template is provided, the Investigator and/or Research Coordinator (RC) reviews and revises it to ensure that it contains all required elements and any additional elements required by state or local authorities and the investigative site's IRB.
- 5.1.3 Each IRB-approved IC/PP/Assent form will have an approval date or version date to ensure that the most current form is used.
- 5.1.4 The Investigator or RC discusses all elements of the IC/PP/Assent form/s with the potential subject or legally authorized representative in lay language that promotes understanding. Note: If the subject and/or legally authorized representative speak a language other than English, a certified translation of the IC/PP/Assent forms in the subject's native language with documented IRB approval must be used and must meet all of the requirements listed above for the English documents.
- 5.1.5 The potential study subject or legally authorized representative should be given as much time as s/he deems necessary to read the consent document, consider study participation and have questions answered prior to signing the IC/PP/Assent form. Note: Determining that research subjects and/or parents understand the information presented is part of the IC process. The presenter should ask questions in an attempt to validate that there has been understanding.
- 5.1.6 The subject and/or legally authorized representative must sign and date the appropriate IC/PP/Assent document prior to the performance of any study-related procedures in compliance with the each site's IRB requirements. Note: If in the course of routine medical care, certain examinations, procedures or tests were performed that could be used to assess eligibility, these assessments, done prior to the informed consent process, would not be considered study procedures even though the results could be used for the study (if allowed by the protocol and the IRB).
- 5.1.7 The person presenting the IC/PP/Assent for each subject should also sign and date the appropriate documents at the time consent is obtained from the subject or legally authorized representative.
- 5.1.8 Additional signatures must be obtained (for example signatures from a witness, witnesses or both parents) if required based on sponsor, institutional, IRB or other applicable requirements.
- 5.1.9 The study individual performing the consent process must ensure and documents that the subject or legally authorized representative has received a copy of the appropriate IC/PP/Assent form/s as specified by the site IRB.
- 5.1.10 The Investigator ensures that all active study subjects and/or legally authorized representatives are provided with updated study information as soon as possible and sign IRB-approved amended IC/PP/Assent forms, when necessary, retaining the original and providing a copy to the subject or legally authorized representative.

5.2 Recommended Consent Process for Studies with More Than Minimal Risk

- 5.21 Informed consent involves parent/subject understanding of: the pathophysiology of the disease/injury studied, the proposed research treatment option and alternative treatments, details of the study protocol including, but not limited to, therapy, randomization, laboratory tests, outcome measures, duration of study, compensation, required follow up, potential risks and benefits of the study, and

- the consent process including, but not limited to, voluntary nature, right to withdraw, and HIPAA protection.
- 5.22 Informed consent may require iterative discussions with the attending of record, research coordinators, and principal investigators or co-investigators. For both minimal risk and more than minimal risk studies, it is important for clinicians in the ED to have knowledge of the project and, if possible, be trained in Human Subjects Research Protection (HSRP)
- 5.23 **At least one person in the informed consent process must be formally trained in HSRP. The person obtaining the signature on the informed consent form *must* have this training.** HSRP training must comply with local institutional regulations.
- 5.24 **All PECARN Research Coordinators must have HSRP training.**
- 5.25 Research Coordinators are encouraged to obtain membership in a professional organization such as the Association of Clinical Research Professionals or the Society of Clinical Research Associates.
- 5.26 PECARN recognizes that a research coordinator, PI, HEDA PI or Co-investigator (the research team) trained in HSRP is likely to be the most knowledgeable in the details of the study design and the regulatory requirements of informed consent whereas the attending or fellow in charge of the patient's clinical care is likely to be most knowledgeable in the details of the study subject's clinical condition.
- 5.27 **Thus, member of the research team *and* the licensed independent practitioner* (clinician) in charge of the patient's care should be involved in the informed consent process for studies with more than minimal risk to assure that regulatory requirements are followed and to assure that clinical questions are answered.**** If the LIP is a member of the study team and has HSRP, then this person may obtain consent on their own. Either team member can obtain the signature of informed consent, but in either circumstance, a checklist for the study consent process (when there is more than minimal risk) must include an item stating that the family was offered an opportunity to speak with the treating clinician and/or a study investigator to answer any additional questions.
- 5.28 For studies that are greater than minimal risk, there must be documentation of the informed consent process for each subject. The documentation must summarize basic aspects of the consent process including (but not limited to) questions from participants, what the participant understood, and the involvement of the licensed independent practitioner (LIP). The documentation may be a PECARN informed consent checklist, or a site specific checklist.

* Licensed independent practitioner refers to a credentialed nurse practitioner, physician assistant, fellow or attending

** The licensed independent practitioner can delegate this role to a study PI or co-investigator

5.3 Procedures for Alternative Written Informed Consent

- 5.3.1 In certain circumstances, IC may be obtained in an alternative manner to that described above. In an effort to standardize study activities throughout PECARN, alternatives may be suggested when appropriate, but the Investigator and the local IRB must determine if this is allowable.
- 5.3.2 An IRB may, for some or all study subjects in a given study, waive the requirement that the study subject and/or legally authorized representative to

sign a written IC/Assent form in accordance with federal regulations as delineated in 45 CFR 46.

- 5.3.3 When the standard written IC cannot be obtained, the IRB may permit a written summary document that embodies the elements of informed consent to be read to the study subject or legally authorized representative. The oral presentation must be witnessed and the IRB must approve the written summary and/or oral presentation. A "short form" stating that the elements of IC have been presented orally to the subject, must be signed by the study subject or legally authorized representative. The witness and the Investigator (or presenter) must also sign the short form and the summary. Copies must then be provided to the subject or legally authorized representative.

5.4 Procedure for Obtaining Assent

- 5.4.1 Assent is required in writing for all subjects ≥ 7 years old. Note: "Asking a child for a decision, then disregarding that decision if it conflicts with what the Investigator or parent/guardians wish, is not acceptable" (SACHRP 11/1/05).
- 5.4.2 If assent is not obtained, the subject may participate in the study only if the following 3 conditions are met and documented:
- The study offers potential direct benefit to the child;
 - Treatment is available only in the context of the research project; and
 - The child is not considered mature enough to act in his/her own best interests.
- 5.4.3 The age, maturity and psychological state of the child should be taken into account when determining whether children are capable of assenting.
- 5.4.4 If verbal assent is obtained from a child younger than 7 years of age, this should be documented and should state the information provided to which the child verbally agrees.

6. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50 Protection of Human Subjects
21 CFR 50.20 General Requirements for Informed Consent
21 CFR 50.27 Documentation of Informed Consent
21 CFR 56 Institutional Review Boards
21 CFR 312.62 Investigator Recordkeeping and Record Retention
21 CFR 312.66 Assurance of IRB Review
21 CFR 812 – D IRB Review and Approval
21 CFR 812.42 FDA and IRB Approval
21 CFR 812.47 Emergency Research under 50.24 of This Chapter
45 CFR 46 Protection of Human Subjects
45 CFR 46 - D Additional Protections for Children Involved as Subjects in Research
45 CFR 46.116 General Requirements for Informed Consent
45 CFR 46.117 Documentation of Informed Consent
45 CFR 46.408 Requirements for Permission by Parents or Guardians and for Assent by Children
ICH E6, 4.8 Informed Consent of Trial Subjects
ICH E6, 5.11 Confirmation of Review by IRB/IEC
ICH E6, 5.18 Monitoring

ICH E11 Clinical Investigation of Medicinal Products in the Pediatric Population
HHS FAQs FAQs on Research Involving Children (Jan 2006)

7. REFERENCES TO OTHER APPLICABLE SOPs

PECARN SOP&P: Human Subject Protection PECARN SOP&P: Institutional Review Board Approval PECARN SOP&P: Site Monitoring



STANDARD OPERATING POLICY AND PROCEDURE FOR ADVERSE EVENT RECOGNITION AND REPORTING Interventional Clinical Trials

SOP: Adverse Events Initial Review: November 2013 Secondary Review: October 2014 Version No.: 2 Effective Date: 30 Sept 2015	ADVERSE EVENT RECOGNITION AND REPORTING Interventional Clinical Trials	Supersedes Document: SOP 03-18-2005 Exec Committee Approval 30 Sept 2015
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1. POLICY

Good Clinical Practice (GCP) requires the investigation and reporting of adverse events that occur during the conduct of a clinical study. Such reporting requirements place different responsibilities on the clinical investigator, the Institutional Review Board (IRB) and the Study Principal Investigator. An adverse event (AE) can be broadly defined as any untoward medical occurrence experienced by the subject. An event constitutes a disease, a set of related signs or symptoms, or a single sign or symptom. These may be temporally associated with the use of a medicinal product or device, whether or not considered related to the medicinal product or device. The Study Principal Investigator and all other participating Investigators and their key study personnel must be familiar with protocol-defined adverse events for products under investigation or for procedures being performed. All participating Investigators and key study personnel must be familiar with the natural history of the disease or disorder being treated, the parameters to judge that a therapy is successful, and the parameters to judge that a therapy is not successful. Any new or worsening sign or symptom that may be attributable to the investigational product or to the subject's involvement in the study must be recognized, documented and reported according to applicable regulations and guidelines. Prompt reporting of serious and unexpected AEs that occur during an interventional clinical study is a major health and safety priority.

2. SCOPE

This SOP defines the responsibilities of PECARN members with regard to the managing and reporting of adverse events occurring in PECARN clinical trials in order to ensure compliance with applicable adverse event reporting requirements and to provide uniformity in the management of adverse events.

It is the intent of PECARN to follow the International Conference on Harmonization (ICH) Guidelines for the management and reporting of adverse events.

This SOP applies to all investigators and research coordinators (RCs) / assistants (RAs) and others involved in PECARN clinical research.

This SOP is to apply to all clinical research performed in the PECARN network that has the requirement of adverse event reporting.

If the PECARN Data Coordinating Center (DCC) is not the data center for a particular protocol, the applicable data center would be expected to comply with the PECARN SOPs.

3. RESPONSIBILITY

The Study Principal Investigator is responsible for ensuring that a Data and Safety Monitoring Plan is written into the study protocol. This plan will include, among other things, the mechanism for assessing and reporting adverse events.

All participating Investigators are responsible for recognizing and reporting all serious adverse events or experiences (SAE) any other expected, unexpected and non-serious or routine AEs, and any unanticipated problems, according to applicable regulations and guidelines and the requirements of the protocol.

All participating Investigators are responsible for the appropriate medical management and follow-up of subjects who have experienced an AE while on study, irrespective of relationship to study treatment or investigational product.

All participating Investigators or their designees are responsible for documenting AEs as described in the study protocol.

The Study Principal Investigator is responsible for expedited reporting to appropriate regulatory authorities if required.

The Study Principal Investigator is responsible for clearly describing the plan for reporting of AEs and SAEs in the study protocol in compliance with all applicable regulations.

If Data and Safety Monitoring Board (DSMB) oversight is specified in the protocol Data and Safety monitoring plan, the DCC is responsible for collecting data for evaluation by the DSMB unless another data center is designated.

The DCC is responsible for forwarding applicable Safety Reports to participating Investigators as required by the study protocol. The participating Investigators

are responsible for forwarding Safety Reports to the IRB(s) of record as required by the local IRB.

The Medical monitor will perform SAE review as specified in the study protocol.

The DSMB is responsible for preparing Safety Reports or other appropriate notifications as a result of SAEs that are reported to the DCC.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32	IND Safety Reports
21 CFR 312.50	General Responsibility of Sponsors
ICH E6	Good Clinical Practice: Consolidated Guidance
ICH E2A	Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (March 1995)

5. REFERENCES TO OTHER APPLICABLE SOPs (TBD)

6. TERMINOLOGY

Adverse Event (AE): Any untoward medical occurrence experienced by a subject. An event constitutes a disease, a set of related signs or symptoms, or a single sign or symptom. These may be temporally associated with the use of an investigational drug product or device whether or not considered related to the investigational drug or device.

Data and Safety Monitoring Board (DSMB): An independent data monitoring committee that may be established by PECARN to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to PECARN whether to continue, modify, or stop a trial. The DSMB is responsible for monitoring accrual of study subjects, adherence to the study protocol, assessments of data quality, performance of individual clinical sites, review of serious adverse events and other subject safety issues, and review of formal interim statistical analyses of treatment efficacy as outlined in the Charter.

Disability: Substantial disruption of a person's ability to conduct normal life functions.

Investigator: A person responsible for the conduct of the clinical trial at a PECARN site. If a trial is conducted by a team of individuals at a particular site (i.e. the Emergency Medicine staff of a hospital), the investigator is the responsible leader of the team.

Study Principal Investigator: The Investigator who initiates the research protocol within the network.

Serious Adverse Event (SAE): Any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly/birth defect or
- Any other event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition.

A SAE may occur in other situations that may not be immediately life threatening or result in death or hospitalization, but which may jeopardize the patient or require intervention to prevent one of the above outcomes. These should also usually be considered serious.

Unexpected Adverse Event: An adverse event, the nature or severity of which is not consistent with the applicable product information supplied by the drug manufacturer or as defined in the protocol.



Appendix A: Adverse Event Reporting Terminology

1. Intensity of the Event

Severity rating of the AE may not necessarily correspond with the participant's experience of them. Ratings depend upon the intervention taken to alleviate symptoms and the level to which symptoms interfere with usual activities.

Mild:	Participant is aware of the signs or symptom(s) and/or event(s), but they are easily tolerated and require no intervention.
Moderate:	Participant's normal routine is affected by one or more signs or symptoms. Discomfort is enough to interfere with usual activities and possible need for intervention. For example, the participant rested in bed, went to the doctor, left work/school early, etc.
Severe:	Symptoms are incapacitating, affecting the participant's ability to perform usual activities, significantly affecting clinical status, and there is a definite need for clinical intervention. Participant feels symptom is sufficiently severe that it cannot be tolerated. For example, participant will drop out of the study if symptoms persist.

2. Outcome:

Do not specify the outcome of the AE until the AE ends or the participant completes or leaves the study (whichever comes first).

Possible outcomes are:

- Death
- Recovered and the patient returned to baseline status
- Recovered with permanent sequelae (effects)

Symptoms persist/continue

3 Relationship to the Protocol or Intervention: An assessment of the relationship between the adverse event and the research intervention.

Adverse event probably related to a research intervention: An adverse event, which follows a reasonable temporal sequence from the time of beginning the assigned study intervention, and cannot be reasonably explained by other factors such as the subject's clinical state, therapeutic interventions, or concomitant drugs administered to the subject.

Adverse event possibly related to a research intervention: An adverse event, which follows compatible temporal sequence from the time of beginning the assigned study intervention, but could have been

produced by other factors such as the subject's clinical state, therapeutic interventions, or concomitant drugs administered to the subject.

Adverse event unrelated to a research intervention: An adverse event, that is clearly related to other factors, such as the subject's clinical state, therapeutic interventions, or concomitant drugs administered to the subject.



STANDARD OPERATING POLICY AND PROCEDURE FOR SITE MONITORING IN PECARN RESEARCH STUDIES

SOP: Site Monitoring PECARN Version No.: 2 Effective Date: Approved by Steering Committee electronic vote-June 14 2012		Supersedes Document: Version 1
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1. SITE MONITORING POLICY OVERVIEW

Site monitoring is an important aspect of a clinical study, whether a double blind randomized drug trial or an observational investigation. The overall objectives of site monitoring are to:

- Verify that the site is correctly following the study protocol.
- Verify that all regulatory documents exist and are current
- Document and report on clinical study progress
- Document that the protocol and other items are current and IRB approved
- Update the site team of any changes in study conduct/documentation
- Ensure that Sponsor requirements and Investigator obligations are met
- Ensure continued acceptability of the Site Investigator, team and facility
- Obtain and review current clinical data, reports and source documents
- Ensure adequate investigational product inventory and accountability
- Assure compliance with Good Clinical Practice
- Assure patient safety
- Assure data quality

Site monitoring generally consists of an on-site meeting of the Monitor, the Study Investigator and his/her research staff. Certain aspects of monitoring may also be conducted remotely via phone and mail or electronic communication when travel to the site is impractical. Monitoring visits may occur during several phases of the study. A site initiation visit is conducted prior to the start of a study, and this may be an onsite visit, a training session in which study site preparation is discussed or a remote visit. One or more ongoing monitoring visits may be conducted during the study, and a close out visit usually occurs after the study termination. Additionally, follow up visits may be conducted, as needed, based on the study protocol, the site's

progress and if determined by the research node center (nodal PI), DCC, or PECARN steering committee.

The type of study being conducted will affect the monitoring plan. Observational studies will generally require a higher level of monitoring than retrospective studies, and clinical trials or other interventional studies will require a specific site-monitoring schedule. Size of the study, number of subjects, study population characteristics and other aspects of the study protocol should be considered when devising a monitoring plan.

2. SCOPE

This policy applies to research conducted within the PECARN network.

3. DEFINITIONS

- a. Monitor: The Monitor refers to an individual contracted to perform site monitoring by the DCC or Investigator. The Monitor may also refer to a Nodal Administrator, or other person designated by the DCC to perform quality monitoring.
- b. Nodal Principal Investigators: Investigators named on the HRSA cooperative agreements at each PECARN node and the DCC.
- c. QUASI: Quality Safety and Regulatory Subcommittee
- d. Study Principal Investigator (PI): the investigator who is identified by the lead investigator as being responsible for conduct of the study at a designated PECARN or PECARN related site.

4. RESPONSIBILITY

The Study PI is ultimately responsible for the quality of a study and budgeting for implementation of Site Monitoring. The study budget will be reviewed by the Budget and Feasibility Committee prior to PECARN approval.

Implementation

The Study Investigator is responsible for including a general study monitoring plan in the study protocol that describes the major aspects of how the study will be monitored. The DCC can assist with this process as requested. A supplemental study-specific monitoring plan must be drafted prior to the start of the study that outlines criteria for site monitoring. This plan may include the number of planned site visits, criteria for focused visits, or additional visits, a plan for chart review, and a follow up plan for

non compliant sites etc. If there is no plan for site monitoring, the Investigator must address the reasons why monitoring is not needed. In nearly all PECARN studies, site monitoring should be anticipated by the investigator. Site monitoring can potentially be performed remotely, depending on the nature of the monitoring needs.

The Study Site Investigator (in coordination with the HEDA PI) is responsible for providing the monitor prompt and adequate on site access to necessary regulatory documents, medical records, source documents as required for the monitoring visits. The Study Site Investigator is also responsible for ensuring an adequate response to all site monitoring findings and rectifying all protocol deviations or other issues identified on the monitoring report.

The nodal administrator and DCC project managers are responsible for ensuring that each site is visited according to the monitoring plan. The Site Monitor is responsible for reporting the results using a DCC formatted report and letter of the visit to the site PI and the DCC.

The QUASI subcommittee will review monitoring reports or summaries of the reports compiled by the DCC. Reports will be submitted to the QUASI subcommittee, in order to both inform and educate QUASI regarding ongoing safety and regulatory challenges occurring in PECARN and to help identify trends needing intervention. In cases of serious regulatory or safety issues, reports will be shared with the Chair of QUASI and QUASI will, as necessary, make recommendations to the Steering Committee. The PECARN steering committee will vote on any recommendations of the subcommittee.

For serious infractions of the protocol, patient safety or other serious concerns, the site monitor would report details to the DCC and the Medical Monitor/DCC PI of the study. The Medical Monitor will make immediate recommendations to, the study PI, the nodal PIs, the Chair of the QUASI subcommittee, and the Project Officer about probationary enrollment suspension at the site in question. If an emergent decision about suspension is required, this would be determined by the DCC PI, the Study PI and the Project Officer.

The DCC will maintain records of all site monitoring reports. The DCC will provide advice on site monitoring and will assist nodal administrators and monitors in conducting and coordinating site visits when necessary.

The Monitor is responsible for conducting the monitoring visit at the clinical site(s) and completing a DCC formatted report and letter to the Site Investigator summarizing the findings. The DCC Principal Investigator is responsible for following up with non-compliant sites and decisions

regarding on going visits. If monitoring visits reveal serious protocol deviations that have not been rectified by the HEDA after the site visit, the DCC will make a recommendation to the Study Principal Investigator, the project working group, and the Steering Committee regarding site termination.

5. SPECIFIC PROCEDURES

A. Study Protocol Development

The Investigator will include a brief description of the plan for site monitoring in the study protocol. The monitoring plan must include (but is not limited to) the frequency and type of monitoring (Site initiation, ongoing, site close out) that will be required. It is generally recommended that all sites receive a monitoring visit. However, if specific sites are to be visited, the plan must address how sites will be selected for visitation. The study plan must comply with Good Clinical Practice guidelines and any applicable federal regulations.

B. Evaluation of Monitoring Plan

The DCC will assess the site monitoring plan based on several factors: study design complexity, phase of development, Investigator's experience, previous site compliance, rate of subject enrollment, site experience, study type, regulatory issues and any other unique attributes of the study and the site. The investigator, with help from the DCC will estimate the number of anticipated monitoring visits based on study complexity, length of study, and other factors. The investigator *must* follow the recommendations of the PECARN Steering Committee (which will be based on subcommittee and DCC recommendations).

C. Budgeting for Site Monitoring

If the project is externally funded, the investigator is required to obtain funding to support monitoring visits. Site monitoring costs should be included in the study budget, following the DCC site monitoring guidelines, taking into account any available DCC resources dedicated for site monitoring. Any funding issues should be addressed with the nodal administrators or PECARN subcommittees. If the DCC is expected to fund site monitoring visits, the investigator must obtain approval from the DCC Principal Investigator before the protocol will be approved by the Steering Committee.

D. Implementation of the Monitoring Plan

The DCC will work with the Investigator regarding scheduling and conducting monitoring visits. The DCC will implement a monitoring plan with the Nodal

Administrators or other identified qualified study monitors. The DCC will also provide a report to the investigator summarizing the monitor's findings.

E. Responding to Monitoring Reports and Documenting Appropriate Response.

The site investigator is responsible for responding to and rectifying any issues identified as follow up items. All items identified in the report must be corrected to the satisfaction of the DCC and the Study Investigator. Failure to resolve crucial issues will be reported to the study Principal Investigator, the project working group, and the Steering Committee, who will consider HEDA suspension from the study until resolution is accomplished.

6. APPLICABLE REGULATIONS AND GUIDELINES

ICH E6, 2.0	The Principles of ICH GCP
ICH E6	Good Clinical Practice: Consolidated Guidance
ICH E6, 4.5	Compliance with Protocol
ICH E6, 5.3	Medical Expertise
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.7	Allocation of Responsibilities
ICH E6, 5.15	Record Access
45 CFR Part 46	Protection of Human Subjects
21 CFR Part 50	Protection of Human Subjects (FDA trials)
ICH E11	Clinical Investigation of Medicinal Products in the Pediatric Population
ICH E6, 5.23	Multicenter Trials
FDA Guideline	The Monitoring of Clinical Investigations (January 1988)

See also:

- The Nuremberg Code (1949)
- The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research
- The World Medical Association Declaration of Helsinki (last revision 2002)
- Guidance for Industry Oversight of Clinical Investigations-A Risk-based approach to monitoring.
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
August 2011



STANDARD OPERATING POLICY AND PROCEDURE FOR Archiving Study Records

Initial Draft: August 2006 Secondary Review: March 2011 Version 2: Revised July 2011 Version 3: Revisions November 2013 version 4: October 2014	ARCHIVING STUDY RECORDS	Original Steering Committee Approval-July 2010 Executive Committee Version 2 Approval- Oct 2011 Executive Committee Version 3 Approval 30 Sept 2015
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1. POLICY

- 1.1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual patient enrolled in any Pediatric Emergency Care Applied Research Network (PECARN) research study. This is required for all applicable studies conducted by PECARN.
- 1.2. The investigator is required to save all documents pertaining to a PECARN study for the time duration specified by the study protocol, by federal regulations, by individual site's Institutional Review Board (IRB), or by this policy, whichever period is longest.

2. PURPOSE

- 2.1. This document describes the policy, procedures and responsibilities of PECARN members with regard to archiving study records for each PECARN research study.

3. SCOPE

- 3.1. This Standard Operating Policy (SOP) applies to all PECARN investigators and designated staff with delegated applicable roles, and to all clinical trials and research studies conducted in the network.

4. DEFINITIONS

- 4.1. *Study Principal Investigator / Lead Investigator*: The investigator who received official Steering Committee approval to conduct the study and who provides leadership of the conduct of the study.
- 4.2. *Site Investigator*: The investigator who is identified by the lead investigator as being responsible for conduct of a particular study at a designated PECARN or other study site.
- 4.3. *Hospital Emergency Department Affiliate (HEDA) Investigator*: The investigator identified in the PECARN cooperative agreement as a HEDA Principal Investigator. This includes EMSA Investigators as applicable.
- 4.4. *Nodal Principal Investigator*: The investigator identified in the PECARN cooperative agreement as the Principal Investigator for the cooperative agreement. This includes EMSA Investigators as applicable.

5. RESPONSIBILITY

- 5.1. The Site Investigator is responsible for maintaining applicable case history records, the study protocol and related documentation, including IRB documents, during all aspects of active study and after the conclusion of the study.
- 5.2. The HEDA Investigator is responsible to assure that the Site Investigator fulfills the responsibilities detailed in this SOP.
- 5.3. The Nodal Principal Investigator is responsible to assure that the HEDA Investigator and Site Investigator fulfill their responsibilities detailed in this SOP.

6. PROCEDURES

- 6.1. There are two types of records that are kept regarding a clinical investigation: (1) case history records and (2) the study protocol and related documentation, including IRB documents (Essential Documents).
 - a. Case history records include data collection forms and documents that support data in those forms and may contain:
 - i. Basic study subject identification information

- ii. Information confirming that each study subject meets the eligibility criteria or justification for enrolling the subject
 - iii. Sufficient information to support data in the case report form as submitted to the sponsor
 - iv. Information on each study subject's exposure to the test or control article, including the date (and time, if relevant) of each administration and the quantity administered
 - v. Copies of case report forms submitted to the sponsor, if required
 - vi. Signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes as applicable.
 - b. Case history records should be retrievable in such a fashion that all information regarding each individual participant in a study is attributable to that individual. Case history records also include information obtained from tests and examinations, such as physical examinations, lab results, radiographs, progress notes, consultations, and correspondence; information and data on the study subject's condition before, during, and after the clinical investigation; all diagnostic test results, diagnoses made, concomitant or concurrent therapy; and, factors that might alter the test article's effects (e.g., development of an intercurrent illness). [FDA Information Sheets] [21 CFR 312.62(b)]
 - c. The study protocol, IRB records, study correspondences and other study documentation constitute the "essential documents" of the study, and may be stored in the Essential Documents Binder (EDB). Reference to secure electronic storage of files should be noted in the physical EDB.
- 6.2. The Site Investigator, Lead Investigator, and the Data Coordinating Center (DCC) must maintain all applicable study records in accordance with federal guidelines, protocol requirements and the investigative site IRB requirements.
- 6.3. All records shall be accessible for inspection and copying by authorized representatives of the regulatory authorities at reasonable times and in a reasonable manner [45 CFR 46.115(b)] [ICH E6 (3.4)].
- 6.4. Study completion (i.e. Study Closure) occurs after subject enrollment has ended at all sites, including all research interventions and follow-up activities (e.g. follow-up visits, surveys and evaluations), and the study data queries have

been resolved or as outlined in the study protocol or grant, whichever is longer..

- 6.5. Case history records will be retained at each clinical site for three (3) years after study completion (45 CFR 46.115b), as defined in previous clause (or longer if required by the study site IRB). If the study involves an IND or IDE and a marketing application, the records must be retained for two (2) years after the marketing application has been filed (21 CFR 312.62(c)). If there is no marketing application, the FDA should be notified when study completion has been accomplished (as defined in previous clause), and records retained for three (3) years, similar to other PECARN studies. This record retention is required whether or not a site remains in PECARN for the time period.
- 6.6. Essential documents will be retained at each clinical site for three (3) years after study completion (or longer if required by the study site IRB). If a HEDA site stops participating in PECARN, its records may be retained by the respective PECARN node. If a complete node stops participating in PECARN, the records may be retained by the DCC.
- 6.7. The required retention of records is not affected by the timing of publication of the results of the respective study.

7. APPLICABLE REGULATIONS

45 CFR 46.115	IRB Records
21 CFR 312.57	Recordkeeping and Record Retention
21 CFR 312.58	Inspection of Sponsor's Records and Reports
21 CFR 312.62	Investigator Recordkeeping and Record Retention
21 CFR 312.68	Inspection of Investigator's Records and Reports
21 CFR 812.140	Records
21 CFR 812.145	Inspections
ICH E6, 2.10, 2.11	The Principles of ICH GCP
ICH E6, 4.9	Records and Reports
ICH E6, 5.5	Trial Management, Data Handling, and Record Keeping
ICH E6, 5.15	Record Access
ICH E6, 8.0	Essential Documents for the Conduct of a Clinical Trial

8. REFERENCES TO OTHER APPLICABLE SOPs



STANDARD OPERATING POLICY AND PROCEDURE FOR FINANCIAL CONFLICT OF INTEREST

Initial Draft: August 2006 Secondary Review: Dec 13 Version No.: 2 Updated: December 2013 Reviewed October 2014 Effective Date: 30 Sept 2015	FINANCIAL CONFLICT OF INTEREST	Supercedes Document: December 2013 Exec Committee Approval 30 Sept 2015
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1. POLICY

- 1.1. There are a number of conflicts of interest which may arise during the course of a research study. Disclosure, certification and management of financial conflicts of interests will be addressed in this standard operating procedure.
- 1.2. Failure to comply with these fundamental ethical obligations jeopardizes the validity of the entire research program and puts the trustworthiness of the data derived in question.
- 1.3. Financial conflict of interest oversight is not required for all studies. For instance, a chart abstraction study may not require financial conflict of interest management.
- 1.4. When a sponsor outside PECARN implements a protocol at PECARN sites, the sponsor will manage the financial conflict of interest.
- 1.5. Those studies which require financial conflict of interest oversight by PECARN will be identified by the PECARN steering committee at the time of final protocol approval. If conflict of interest oversight is required, the steering committee will identify interested parties. Interested parties are individuals or groups which stand to gain or lose from the results of the research. An example of an interested party would be a drug manufacturer that stands to expand their market based on results of an investigator-initiated IND study.
- 1.6. The following may cause a financial conflict of interest:
 - 1.6.1. Any compensation that is affected by the outcome of clinical studies
 - 1.6.2. Any equity or ownership interest in an interested party that is not publicly traded or whose value cannot be readily determined, including, but not limited to stock options or royalty payments

- 1.6.3. Any equity or ownership interest in excess of \$50,000 in an interested party that is publicly traded
- 1.6.4. Any proprietary interest in the investigational product (e.g., patent, trademark, copyright or licensing agreement)
- 1.6.5. Any significant payments of a cumulative value of \$25,000 from the interested party to the Investigator or institution for a covered study, in excess of the actual costs of conducting the clinical study, and including but not limited to grants, equipment, consultation fees and honoraria.
- 1.7. FDA regulations and guidance provide detailed instructions about required financial disclosure. This policy is intended to meet the requirements of federal regulations that all research involving human subjects.
- 1.8. Any investigator participating in a PECARN study must also be aware of conflicts within the network. An Investigator who sits on a PECARN subcommittee and submits a proposal to that subcommittee must recuse themselves from voting on the proposal.

2. PURPOSE

- 2.1. It is the intent of PECARN to comply with federal regulations and guidelines and follow the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP).

3. SCOPE

- 3.1. This procedure applies to any PECARN Investigators (Principal Investigators, Co-investigators, Sub-investigators), who are participating in a PECARN clinical study. This also applies to the PECARN investigator's spouse and dependent children.

4. DEFINITIONS

- 4.1. PECARN Investigators-Investigators approved by PECARN steering committee to conduct PECARN related research activities.
- 4.2. The HEDA investigator-the investigator who is responsible overall for the site's participation in the PECARN.
- 4.3. The lead investigator-the investigator who received official Steering Committee approval to conduct the study and who provides leadership of the conduct of the study.
- 4.4. The site investigator-the investigator who is identified by the lead investigator as being responsible for conduct of the study at a designated PECARN or PECARN related site.
- 4.5. The HEDA investigator-is the investigator identified in the PECARN cooperative agreement as the individual providing leadership and oversight of all PECARN related research at the respective site.

5. RESPONSIBILITY

- 5.1. The Data Coordinating Center (DCC) is responsible for obtaining and storing the certifications and disclosures from PECARN Investigators.

- 5.2. All PECARN Investigators are responsible for complying with regulations and institutional requirements governing disclosure of financial interests in a clinical study that may impact upon its conduct, evaluation or outcome.

6. PROCEDURES

- 6.1. The following procedures are required for those studies identified by the steering committee to require financial conflict of interest oversight:
- 6.2. PECARN Investigators are required to submit either a certification (FDA form 3454) that a conflict does not exist, or a disclosure (FDA form 3455) of the financial conflict of interest.
- 6.3. Certifications and Disclosures will be submitted by the investigator on an annual basis.
- 6.4. Failure to provide certification or disclosure at required deadlines will result in a halt in study enrollment.
- 6.5. Financial conflicts of interest are to be disclosed to the appropriate local review bodies (e.g. Conflict of Interest Committees, IRB), and if specified, to potential research subjects.
- 6.6. In addition, disclosure or certification will be provided to the DCC to track and house. For disclosures, the management plan approved by the local review body will also be provided to DCC.
- 6.7. PECARN investigators will also maintain documentation on site.

7. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 54	Financial Disclosure by Clinical Investigators
21 CFR 312.53	Selecting Investigators and Monitors
21 CFR 812.43	Selecting Investigators and Monitors
ICH E6, 5.8	Compensation of Subjects and Investigators
ICH E6, 5.9	Financing
DHHS	Final Guidance Document: Financial Relationships and Interests in Research involving Human Subjects: Guidance for Human Subject Protection (May 5, 2004)

8. REFERENCES TO OTHER APPLICABLE SOPs

- 8.1. IRB SOP
- 8.2. Protocol development SOP

9. ATTACHMENTS

- A. **Form FDA 3454**, Certification: Financial Interests and Arrangements of Clinical Investigators

To retrieve Form FDA 3454 go to FDA Forms Distribution Page for CDER at the following URL:

<http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>

Follow directions on the web site page for downloading this form, or make a copy of the form provided as an attachment in the SOP printed document.

B. **Form FDA 3455**, Disclosure: Financial Interests and Arrangements of Clinical Investigators

To retrieve Form FDA 3455 go to FDA Forms Distribution Page for CDER at the following URL:

<http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>

Follow directions on the web site page for downloading this form, or make a copy of the form provided as an attachment in the SOP printed document.



STANDARD OPERATING POLICY AND PROCEDURE

Information Systems and Data Management

Initial Review: Zuspan, April 2004 Version No.:3 Effective Date: 30 Sept 2015	Information Systems and Data Management- ACCESS CONTROLS	Reviewed: October 23, 2013 Exec Committee Approval 30 Sept 2015
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1. Purpose

- 1.1. To ensure PECARN information systems have appropriate access controls in order to prevent unauthorized use or disclosure of confidential information.

2. POLICY

- 2.1. Security controls or methods that allow access to PECARN information systems must include, at a minimum:
 - 2.1.1. Unique user identifiers that enable persons to be uniquely identified.
 - 2.1.2. A secret identifier (at minimum, a password).
- 2.2. Appropriate access controls should be granted to ensure that study members can perform their necessary tasks without compromising the security of research data
- 2.3. Group logins must not be used to gain access to PECARN information systems containing confidential information. Group logins may be used when accessing systems that do not include confidential information.
- 2.4. PECARN staff must not share or reveal their login or password to others.
- 2.5. PECARN staff must adhere to local policies regarding access, storage and copying of data. All data, electronic or hard copy must be maintained in a secure location. Any computer or workstation utilized for data access or storage must be password protected and the data only accessible to authorized persons.
- 2.6. PECARN members and staff are entirely responsible for any and all activities that occur under their account.

- 2.7. PECARN staff must notify the DCC immediately of any unauthorized use or any other breach of network, computer, or study-related security.
- 2.8. Confidential data may not be downloaded to individual laptops or home computers.
- 2.9. Most e-mail systems are not secure and confidential data should only be shared using a secure manner of communication.

3. SCOPE

- 3.1. This policy applies to all information systems related to PECARN research activities.

4. DEFINITIONS

- 4.1. PECARN staff members: All personnel employed by PECARN-affiliated institutions who are involved in PECARN research activities.
- 4.2. PECARN information systems: Any computer related systems that are used to electronically transmit data or information related to PECARN research, for example but not limited to, eRoom™, email systems, and data entry systems.
- 4.3. Lead investigator: The investigator who received official Steering Committee approval to oversee and provide leadership of the conduct of the study.
- 4.4. The Site Investigator: The investigator who is identified by the lead investigator as being responsible for the conduct of the study at a designated PECARN or non PECARN site.
- 4.5. PECARN investigators: Investigators approved by the PECARN steering Committee to conduct PECARN-related research activities.
- 4.6. Principal Investigators: Investigators for the HRSA cooperative agreements at each PECARN node and the DCC.

5. RESPONSIBLE PARTIES: PECARN staff/members and the DCC.

6. PROCEDURE

- 6.1. User Access Roles and Responsibilities
 - 6.1.1. For each study, the lead investigator will identify a site investigator for each participating site.
 - 6.1.2. Each site investigator or nodal administrator will identify the names and roles of appropriate people who need access to data systems and will notify the DCC

when there are changes in roles or personnel at the site so that system access can be granted or rescinded.

6.1.3. DCC may terminate or deny access to any PECARN member if there is a violation in any existing PECARN policy related to study data, or if there is any question about data security.

6.1.4. The DCC will provide access to data systems, passwords and other appropriate information at the request of the PECARN investigators or nodal administrators.

6.1.5. The DCC will review account activity on a regular basis.

7. References

7.1. 45 CFR 164.312

7.2. UUHSC Policy Manual



STANDARD OPERATING POLICY AND PROCEDURE FOR Public Use Data Set

Initial Draft: March 2011 Version No.: 1.0 Effective Date: 10July 2012 Revision Date: September 2015	DEVELOPMENT OF A PUBLIC USE DATA SET	Original Nodal PI Approval-10July 2012 Exec Committee Approval date: 30 September 2015
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1. PURPOSE

Data from PECARN studies constitute an important scientific resource. To enhance the public health benefit of these studies, public use data sets will be made available to qualified researchers.

2. SCOPE

Data sets will be made available for all PECARN studies unless HRSA deems them to be unreliable or invalid.

Data sets distributed under this policy will be de-identified in accordance with the Health Insurance Portability and Accountability Act (HIPAA). PECARN data sets will be provided only to investigators who agree to adhere to the signed research data use agreement, defined outside of this policy. Execution of a research data use agreement will require approval by investigators' relevant Institutional Review Boards (IRB) or demonstration of exemption from the need for IRB approval by institutional policy. Data set creation and distribution will be performed by the Data Coordinating Center (DCC) in collaboration with the study PI and after final approval from HRSA.

3. DEFINITIONS

Public Use Data Set: De-identified data set derived from completed PECARN research protocols.

Research Data Use Agreement: Agreement between the recipient institution, investigator and the DCC, governing the use of the specific data set.

4. PROCEDURES

The DCC will provide the data set on a CD or DVD as SAS datasets or CSV text files. Electronic copies of the data worksheets, the final study protocol, and a data dictionary will be provided on the disks. No further support will be provided by the DCC, network investigators, or HRSA, to the recipient investigator.

The DCC will maintain a list and brief description of available datasets on the www.pecarn.org website. Investigators will request the use of a specific dataset by submitting a formal request that includes;

- a research plan describing the proposed research
- a signed data Research Data Use Agreement (RDUA)
- approval from the researcher's IRB for use of the dataset or documentation that the use of public data sets is exempt from IRB review by institutional policy

The DCC will disseminate the dataset after receipt of the aforementioned items.

5. TIMING RELEASE OF PUBLIC USE DATA

Notification of availability of the public use data sets will be made via the PECARN website **3 years** after the last subject has been enrolled and all follow-up procedures have been completed.

6. CONFIDENTIALITY

1. Data requests for the PUDS data, both external and internal to PECARN, are considered confidential; therefore, the DCC will not identify nor release names of investigators who submit public use data set requests except to the HRSA project officer as requested.
2. The DCC Principal Investigator and DCC Director will maintain the PUDS and will respond to investigator requests to the PUDS. The DCC will ensure that the proper documents are received prior to releasing the PUDS to an investigator.
3. The DCC PI and Director have access to PUDS requests and therefore, they will not act as primary investigators using the PUDS to avoid conflict of interest.



STANDARD OPERATING POLICY AND PROCEDURE FOR Development and Approval of PECARN Projects involving Secondary Analyses of Existing PECARN Data

Initial Draft: March 2011 Version No.: 1 Effective Date: 10July2012	DEVELOPMENT OF A PUBLIC USE DATA SET	Original Nodal PI Approval- 10July2012
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1. PURPOSE

- 1.1 The purpose of this policy is to provide guidance for PECARN and other investigators involved in PECARN research regarding the development, submission and approval process for secondary analysis of pre-existing PECARN research study data prior to public release of the dataset. This policy applies to post hoc analyses that are not part of the initial study or grant.

2. POLICY

- 2.1 Any changes to this process must be approved by the PECARN Executive committee and HRSA Project Officer (PO).
- 2.2 For ex: Proposals for secondary data analyses must be reviewed and approved by the PECARN Steering Committee, the Executive committee and the HRSA PO before being implemented.

3. SCOPE

- 3.1 This document applies to all sites, PECARN or otherwise, and all investigators, involved in PECARN-related research.

4. DEFINITIONS

- 4.1 Secondary analysis involves the analysis of pre-existing PECARN data.
- 4.2 Executive Committee: Investigators named on the HRSA cooperative agreements at each PECARN node, the Data Coordinating Center (DCC) and HRSA Project Officer (PO).

5. RESPONSIBLE PARTIES

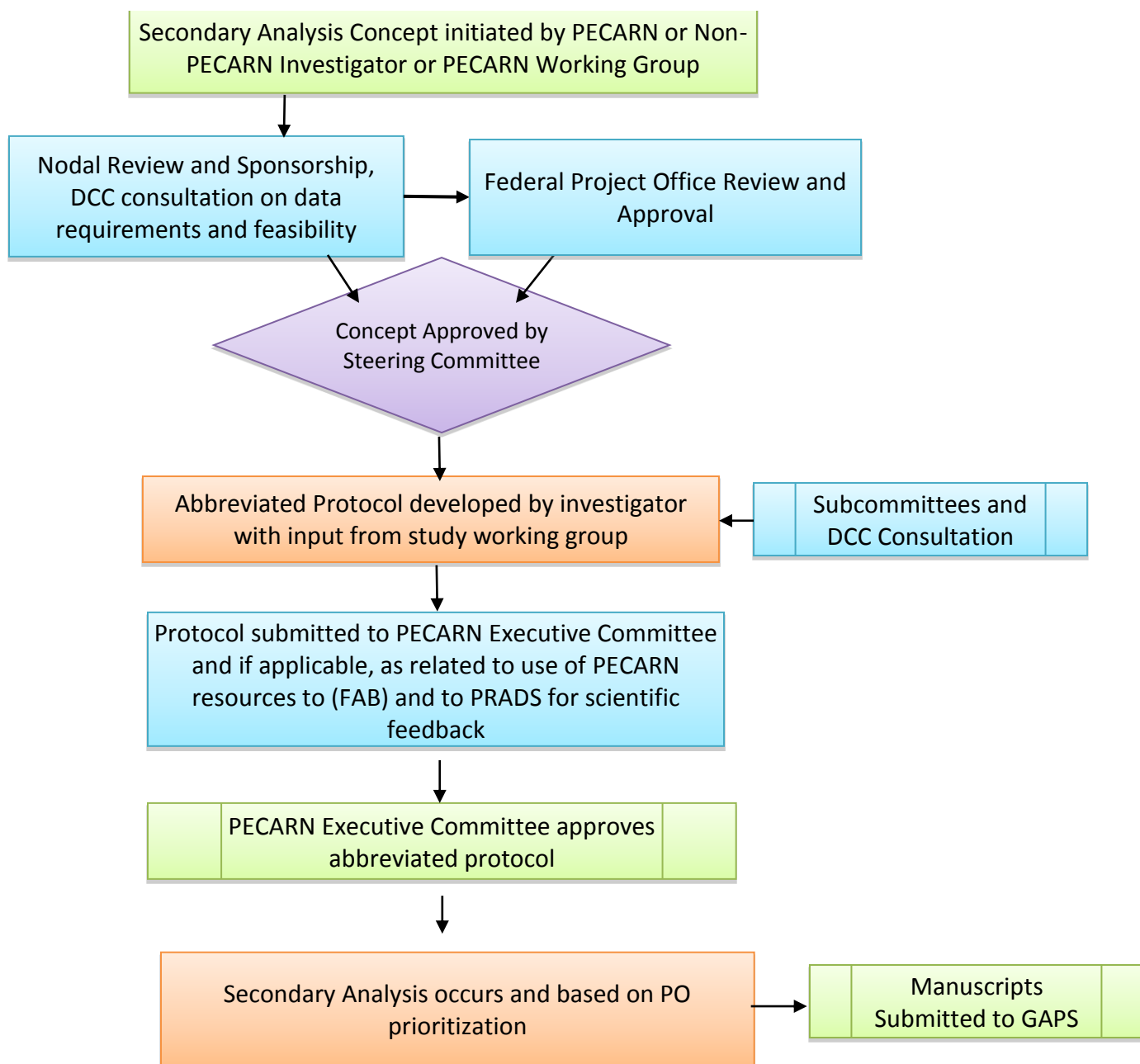
- 5.1 A PECARN or external investigator is responsible for preparing the initial draft of the secondary analysis concept or protocol in consultation with parent study PI.
- 5.2 The HRSA PO must approve all secondary analyses.

- 5.3 The investigator is also encouraged to consult with the parent study PI as well as participating PECARN nodal investigators, subcommittees, subject matter experts, the CDMCC, biostatisticians, information technology/database experts, and others, as appropriate.
- 5.4 The investigator who initiates the secondary analysis concept or protocol is responsible for assuring that the concept or protocol meets all regulatory requirements and is ethically and scientifically sound.

6. PROCEDURES

- 6.1 The development of research studies based on previously unplanned secondary analysis of PECARN data will follow the procedures as outlined in the PECARN *Standard Operating Policy and Procedure for Development and Approval of Research Concepts and Protocols* with the following amendments. After nodal review, the DCC should be consulted regarding feasibility of the project. The Project Officer must also review and approve the concept. Then the concept must be approved by the Steering Committee. (see diagram at end of this policy)
- 6.2 During concept and protocol development, the investigator must, in coordination with the study PI, consult with the DCC on issues related to data requirements, data availability, funding, feasibility and analysis. In addition, the investigator should consult with the Principal Investigator of the parent study.
- 6.3 The DCC will be responsible for the secondary analysis however the HRSA PO will prioritize the timing of the analysis.
- 6.4 After concept approval an abbreviated protocol will be developed by the investigator with input from the study working group and DCC. The investigator has the option of seeking input from the PECARN subcommittees as needed. The final protocol will be approved by the PECARN Executive Committee and does not need to go back to the PECARN Steering Committee for vote.

PECARN Secondary Analysis Concept and Protocol Development Process





STANDARD OPERATING POLICY AND PROCEDURE FOR PERSONNEL TRAINING

Document History

Version Date	Purpose (Created, Original, Reviewed or Revised) and Date	Steering Committee Approval Date (N/A for review without revision)
Draft	Created 23 Aug 2006	
Version 2	Reviewed July 2015	
Version 3	Approved 30 September 2015	Exec Committee approval 30 Sept 2015

1. POLICY

1.1 PECARN personnel who are working in or overseeing research with human subjects will receive training regarding the ethically and scientifically sound conduct of human subject research. Proper documentation provides evidence that personnel are qualified by training and experience to conduct their duties. This standard operating policy and procedure provides a guideline for the procedures and documentation of training of personnel who design, manage and monitor clinical studies within PECARN.

1.2 PECARN sites are required to maintain a record of all training documentation pertaining to the performance of clinical trials and protection of human subjects will be maintained at the site. This includes training required by the local institution, PECARN trainings, external trainings and clinical licensure/certifications.

1.3 Documentation of training will be maintained and organized by the site in a logical fashion, and in a manner easily available for inspection.

2. PURPOSE

It is the intent of PECARN to comply with federal regulations and guidelines and follow the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP).

3. DEFINITIONS

3.1. The HEDA investigator is the investigator who is responsible overall for the site's participation in the PECARN.

3.2. The EMS Affiliate investigator (EMSA) who is responsible for overall for the EMS site participation in PECARN

3.3. The Lead Investigator-the investigator who received official Steering Committee approval to conduct the study and who provides leadership of the conduct of the study.

3.4. The Site Investigator-the investigator who is identified by the lead investigator as being responsible for conduct of the study at a designated PECARN or PECARN related site.

3.5. The HEDA Investigator-is the investigator identified in the PECARN cooperative agreement as the individual providing leadership and oversight of all PECARN related research at the respective site.

4. SCOPE

These procedures apply to all key personnel. Key personnel include all individuals that are responsible for developing, managing conducting, and monitoring clinical studies within PECARN.

4. RESPONSIBILITY

- 4.1 The Site Investigator is responsible for ensuring that all employees are qualified by training and experience to conduct their designated research-related duties. In cases where site personnel begin work after initial protocol trainings, the site investigator is responsible for ensuring completion of proper training and documentation.
- 4.2 The Site Investigator is responsible for overseeing fulfillment and documentation of local site-specific training requirements. Documentation of external trainings, medical licensure, and certifications of site personnel will also be overseen and maintained by the site investigator.
- 4.3 The Lead Investigator will develop a protocol specific training plan and curriculum.
- 4.4 The Lead Investigator will be responsible for ensuring that the proper training is completed and documented, in cases where a site investigator begins working on a study after the protocol specific trainings.
- 4.5 The Data Coordinating Center (DCC) will assist in the development of protocol specific curriculum, implementation of the training plan and documentation of PECARN protocol training attendance.
- 4.6 The Nodal PI will provide oversight and assistance in fulfilling the training requirements. Non-compliance with training requirements will be referred to the Nodal PI for remediation.

- 4.7 The Nodal PIs will determine the general research and GCP training needs for the PECARN Steering Committee (SC) and other investigators.
- 4.8 The DCC will assist in providing GCP and general research training at the request of the SC chair. Options for providing training include the PECARN SC meetings, study specific training, nodal training, on line education, and local training provided by the specific hospital.
- 4.9 Nodes will assess training needs within their HEDAs/Node and make arrangements for training as needed using local or PECARN resources.

5. PROCEDURES

- 5.1 The site will maintain documentation of training in the essential documents binder (EDB) or in another specified location listed in the EDB.
- 5.2 DCC will track required PECARN protocol specific training in eRoom or other designated location as requested by the Lead Investigator of the study.
- 5.3 The site will provide documentation of training for inspection by the PECARN site monitor or other appropriate personnel.
- 5.4 Following protocol approval by the PECARN steering committee, the DCC will provide assistance to the Lead Investigator to develop a timeline for training RA, PI and other appropriate individuals involved in the study.
- 5.5 The DCC will assist the Lead Investigator in fulfilling PECARN committee recommendations regarding training programs needed for the protocol. The DCC will assist the SC, as requested, in preparing general research lecture topics and recruiting presenters.
- 5.6 GCP and research training will be integrated into the PECARN SC meetings at the discretion of the Nodal PIs. GCP training and pertinent research information will be incorporated in study training sessions, regular protocol teleconferences, and site monitoring visits.
- 5.7 The DCC will provide a sign-in sheet or other method for documenting training in PECARN sponsored trainings. For other trainings held nodally or locally, the Nodal Administrator or site investigator will maintain training documentation listing the date, name and signature of attendees, and course topic. Attachment A provides a sample training sign-in sheet.
- 5.8 The sites are responsible for maintaining documentation of training materials, (i.e. power point presentations, documents supplied to the trainees).

6. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	General Responsibilities of Sponsors
21 CFR 312.53	Selecting Investigators and Monitors

21 CFR 812.40	General Responsibilities of Sponsors
21 CFR 812.43	Selecting Investigators and Monitors
ICH E6, 2.8	The Principles of ICH GCP
ICH E6, 5.5	Trial Management, Data Handling, and Record Keeping
ICH E6, 5.18.2	Selection and Qualification of Monitors
NIH Notice OD-00-029	Required Education in the Protection of Human Research Participants (June 5, 2000)
NIH Notice OD-00-039	Clarification on June 5, 2000 Notice (Sept 12, 2000)

7. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOP.

8. DEFINITIONS

- 8.1 Data Management is the management of data elements collected during the conduct of the study to ensure the quality and accuracy of data, compliance with Federal regulations and Good Clinical Practice guidelines.
- 8.2 The Lead Investigator-the investigator who received official Steering Committee approval to conduct the study and who provides leadership of the conduct of the study.
- 8.3 The Site Investigator-the investigator who is identified by the lead investigator as being responsible for conduct of the study at a designated PECARN or PECARN related site.
- 8.4 The HEDA Investigator-is the investigator identified in the PECARN cooperative agreement as the individual providing leadership and oversight of all PECARN related research at the respective site.
- 8.5 PECARN Investigators-Investigators approved by PECARN steering committee to conduct PECARN related research activities.

9. ATTACHMENTS

Attachment A: Training Program Sign-in, Sample

Attachment A

Section 1.01 TRAINING PROGRAM SIGN-IN, SAMPLE

Training Program Title_____

Date (s):_____Presenter:_____

Date(s)	Participant Job Title	Participant Name	Participant Signature

Date(s)	Participant Job Title	Participant Name	Participant Signature



STANDARD OPERATING POLICY AND PROCEDURE FOR PECARN Manuscript and Abstract Timelines

Initial Draft: 26 Jul 2012 Version No: 1.0	PECARN Manuscript and Abstract Timelines	Original Nodal PI approval: 7 Jan 2013
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1. PURPOSE

1.1 The Pediatric Emergency Care Applied Research Network (PECARN) infrastructure is funded by HRSA and the continuation of this funding is dependent on the ongoing publication of primary findings in biomedical journals. Secondary manuscripts provide important information in the understanding, diagnosis and treatment of pediatric emergencies. This policy is intended to address network manuscript timelines to support prompt publication of important research findings.

2. POLICY

2.1 Study abstracts and manuscripts will be planned, written and submitted following an established timeline.

3. SCOPE

3.1 This policy defines the responsibilities of PECARN members with regard to planning, writing and submitting abstracts and manuscripts for studies completed in the Network.

4. DEFINITIONS

4.1 Last Patient Completed (LPC): The date when all study and follow-up procedures have been completed on all subjects enrolled in a research study.

4.2 Public Use Data Set (PUD): The public use dataset release timeline is 3 years after the last patient has completed all study procedures.

4.3 Primary Manuscripts: Primary manuscripts are defined as including the primary outcome data of the study as described in the grant application.

4.4 Secondary Manuscripts: Secondary manuscripts are defined as those assessing outcomes and aims not included in the primary manuscript.

5. RESPONSIBLE PARTIES

5.1 Study Principal Investigator, Study Site Investigators, PECARN Data Coordinating Center (DCC), PECARN Grant Writing and Publications Subcommittee (GAPS) and the HRSA/EMSC/PECARN project officer (PO).

6. PROCEDURES

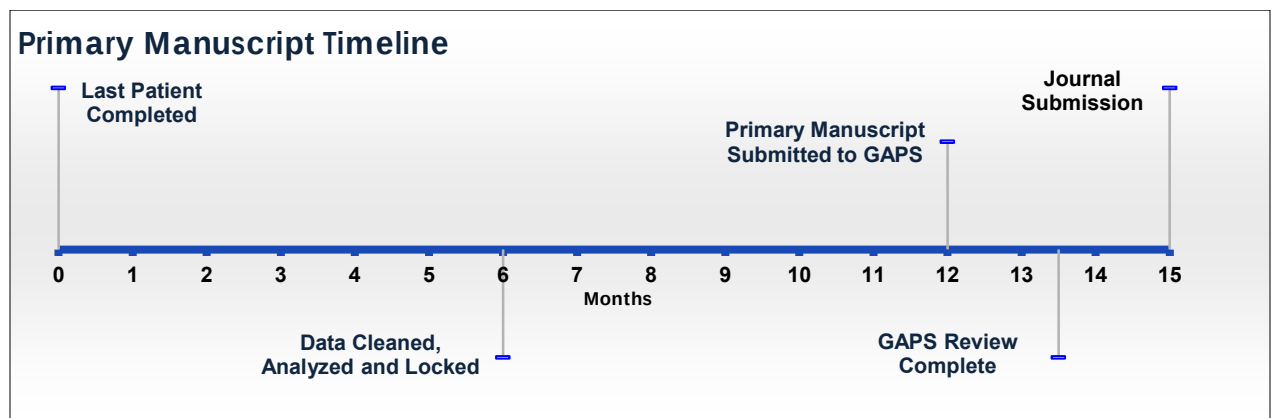
6.1 Manuscript List

- 6.1.1** At the onset of each funded research study, the principal investigator, along with the study team, will begin development of a list of all planned primary and secondary manuscripts.
- 6.1.2** The manuscript list will be developed in the beginning stages of all studies and can be revised during the study if findings change or additional study concepts are developed through the project working group (led by the study PI)
- 6.1.3** This manuscript list and any revisions will be submitted through the study PI to the PECARN Grant Writing and Publications Subcommittee (GAPS) and the PECARN Data Coordinating Center (DCC).

6.2 Publication Plan and Manuscript Analysis Request Form (Attachment 1)

- 6.2.1** A publication plan and manuscript analysis request form will be submitted for each planned primary or secondary manuscript as early as possible in the study planning process. This form can be found in Attachment 1 and in the *Publication Resources eRoom, Authorship Files, PECARN Publication Plan and Manuscript Request form*. Authors are encouraged to complete this as early as possible to help set priorities on importance of data elements being high quality, reviewed and monitored early and maximizing the output from the project.

6.3 Primary Manuscript Procedures and Timelines



6.3.1 Data Cleaning, Data Lock and Data Analysis

Responsible Parties: The Data Coordinating Center (DCC) and the Primary Author

Timeline: The data set for the planned primary analysis will be cleaned, locked and analyzed within **6 months** after the last patient has completed all study procedures (LPC).

6.3.2 Primary Manuscript – Submission to PECARN Grant Writing and Publications Subcommittee

Responsible Party: Primary Author

Timeline: The primary manuscript will be submitted to the PECARN Grant Writing and Publications Subcommittee (GAPS) within **12 months** of LPC.

Procedures: Within 2 months after study completion, the author should submit an updated *Publication Plan and Manuscript Analysis Request* form (attachment 1) to the DCC and to GAPS. This will guide the DCC in preparing the data and in providing clarity between the authors, the Study PI and the DCC team in the writing plan.

6.3.3 GAPS Review

Responsible Parties: GAPS

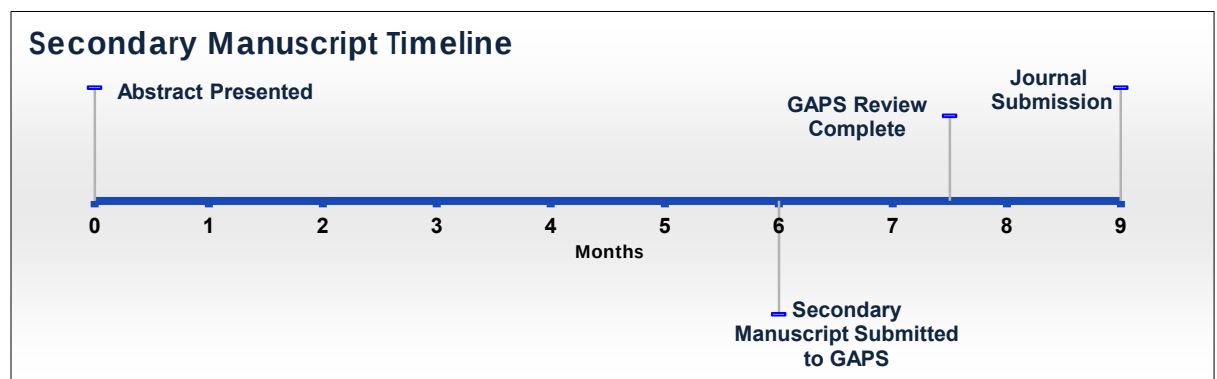
Timeline: The GAPS review requires 6 weeks for completion. The initial GAPS review should be completed within three weeks of submission with three additional weeks allowed for author revisions and collaboration with GAPS.

6.3.4 Journal Submission

Responsible Parties: Primary Author

Timeline: The manuscript should be submitted to a journal within 6 weeks of the completion of the GAPS review.

6.4 Secondary Manuscript Timelines and Procedures



6.4.1 Aim

Secondary manuscripts should be completed as soon as possible after the primary manuscripts and prior to release of the public use data set. This will aid in early dissemination of important knowledge and minimize the competition investigators will have with conflicting and future work. The network will strive towards the time lines as written but will also try to ensure support and resources to complete secondary manuscripts and avoid a punitive atmosphere.

6.4.2 Data Cleaning and Data Lock

Responsible Parties: The Data Coordinating Center (DCC) and the Primary Author

Timeline: The data set for the planned secondary analysis will be cleaned and locked within 6 months after the last patient has completed all study procedures (LPC).

6.4.3 Data analysis

Data analysis and publication of secondary papers will be based on a priority list as developed by the PI/first author with the study team in consultation with the DCC. This list will establish a priority order and timeline for each secondary manuscript. Once this timeline is established, deadlines will be tracked as outlined in section 6.6 of this policy. When there is conflict in the work to be done due to lack of synchronization of analysis, the nodal PIs, DCC PI and PO establish priorities for the work to be done at the DCC.

6.4.4 Secondary Manuscript – Submission to PECARN Grant Writing and Publications Subcommittee

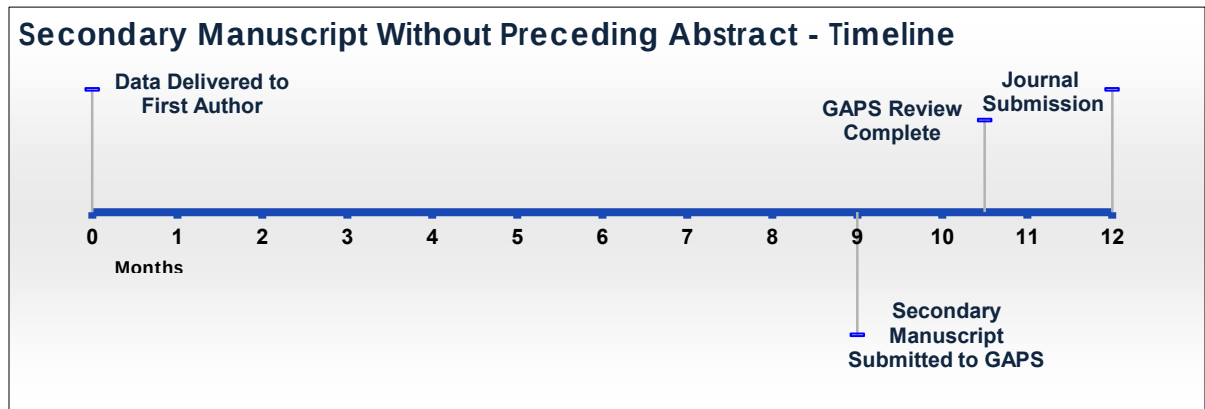
Responsible Party: Primary author

Timeline: Secondary Manuscript after Abstract Presentation

If an abstract is presented, the secondary manuscript from the abstract should be submitted to the PECARN Grant Writing and Publications Subcommittee (GAPS) within six months of abstract presentation.

Timeline - Secondary Manuscript without preceding Abstract

If a PECARN research study goes directly to manuscript without abstract presentation, then the manuscript should be submitted to GAPS within **nine months** of delivery of data to the first author, as outlined in the manuscript analysis request form.



Procedures: When the author is ready to begin writing a manuscript, he/she should revise the previously submitted *Publication Plan and Manuscript Analysis Request* form (attachment 1) and submit it to the DCC and GAPS. This will guide the DCC in preparing the data and in providing clarity between the authors, the Study PI and the DCC team in the writing plan. The timing of data analysis is determined based on the priority list as outlined in section 6.4.2.

6.4.4 GAPS Review:

Responsible Parties: GAPS

Timeline: The GAPS review should be completed within 6 weeks of manuscript submission.

6.4.5 Journal Submission:

Responsible Parties: Primary Author

Timeline: The manuscript should be submitted to a journal within 6 weeks of the completion of the GAPS review.

6.5 Abstract Timelines and Procedures

Responsible Party: Primary author

Procedure: Complete and submit an abstract request form to the DCC (attachment 2)

Data Analysis Timeline: Data analysis for abstracts will be based on a priority list as developed by the PI/first author with the study team in consultation with the DCC as outlined in section 6.4.2.

Deadlines: As noted in section 6.4, a manuscript should be submitted to GAPS within six months of abstract presentation. Therefore, abstracts should not be submitted for presentation until the investigator is ready to prepare the manuscript.

6.6 Tracking and Reminders

6.6.1 Tracking System: A manuscript tracking system will be maintained in the PECARN GAPS eRoom. This list will be viewable by the authors and the PECARN steering committee members.

Responsible Party: Representatives from the National Resource Center (NRC), with input by the DCC and GAPS, will maintain the tracking data base.

Procedure: On receipt of a manuscript analysis request form, the manuscript title, study and author will be entered into the tracking system. Upon study completion, the date of the last patient completed will be entered. This will start the timeline.

6.6.2 Reminders: Manuscript deadline reminders will be sent to the primary author, study PI, appropriate Nodal PI and the GAPS Chair at the following Intervals:

- ✓ On date of last patient completed (LPC) for *primary manuscripts*
- ✓ On date of abstract presentation for *secondary manuscripts*
- ✓ On receipt of the data from the DCC as outlined in the manuscript/abstract request form for *secondary manuscripts without a preceding abstract*
- ✓ Six months prior to manuscript due date
- ✓ Three months prior to manuscript due date
- ✓ One month prior to manuscript due date

Responsible Party: The National Resource Center (NRC) will send out the initial deadline reminders. Requests for extensions will be referred to the GAPS chair, see section 6.6.4.

Procedures:

Primary Manuscripts: The DCC will notify the primary author and the NRC of the last patient completed date for the study which will start the primary manuscript timeline.

Secondary Manuscripts with Abstract: The DCC will notify the primary author, study PI, NRC and the GAPS chair of the abstract presentation date which will start the timeline.

Secondary Manuscripts without preceding Abstract: The DCC will notify the primary author, study PI, GAPS chair and the NRC of the date that the data, as outlined in the manuscript analysis request form, has been delivered to the authors which will start the timeline.

Reminder format: Reminders will include a suggested timeline template for completion of the manuscript, and suggested ideas for inclusion of other authors to complete sections of the manuscripts. Reminders will also include suggestions for resources to review, mentor at the local and nodal level.

6.6.3 Late Reminders

Responsible Party: The National Resource Center (NRC) will send out the initial late reminder notices.

Late reminders to: The primary author, study PI, appropriate Nodal PI, GAPS Chair, HRSA Project Officer and the Steering Committee Chair.

Intervals: Reminders will be sent beginning on manuscript due date to GAPS; late reminders will be sent every two weeks after the initial deadline.

Management: In the situation where the deadline has not been met, the GAPS chair will contact the primary author and attempt to resolve the situation. In the absence of a satisfactory resolution, replacement of the first author will be discussed between the study PI, the Nodal PI, the HRSA Program Officer (PO) and the GAPS chair. The PO will serve as the primary enforcement liaison for questions and adjudication of any disputes not able to be resolved by the study team and nodal PIs.

6.6.4 Manuscript Deadline Extensions

Responsible Party: The primary author is responsible for requesting a deadline extension from the GAPS Chair.

Procedures: The GAPS chair may grant a deadline extension at his/her discretion. The chair will enter the extension date into the tracking database. No more than one extension can be granted. In general, the extension will be for a period of two weeks, however, a longer extension may be granted at the discretion of the GAPS chair.

Additional Deadline Extensions: Any request for an additional deadline extension must be submitted to the HRSA project officer who will consult with the study PI and GAPS chair prior to making a decision.

6.7 Additional Notes

6.7.1 Support: GAPS will be available to help set a project plan for the analysis and writing timeline should the writing team request it.

6.7.2 Authorship Changes: In studies with multiple funding sources, the study PI, nodal PIs and PO will be as inclusive as possible to complete the process of replacing or updating authorship. Authors will be sought from the original writing team on the specific paper, the study writing team and, if necessary, other PECARN investigators.

6.7.3 Exceptions: Any request for exceptions to this policy must be submitted to the project officer.

6.7.4 Secondary manuscript concepts post Data Lock: All new secondary manuscripts post data lock must obtain Executive Committee approval.

Attachment 1



PEDIATRIC EMERGENCY CARE APPLIED RESEARCH NETWORK Publication Plan and Manuscript Analysis Request Revised July 26, 2012

The purpose of this document is to define authorship, define analysis plan, and to outline the specific data that will be needed in the analysis of any PECARN primary or secondary manuscript. This document should be submitted to the DCC Program Director or Project Manager and to the GAPS Chair as early in the study period as possible. It can be updated and re-submitted when the manuscript writing has begun.

Please refer to the PECARN Authorship Guidelines and PECARN Manuscript Timelines Policy for detailed guidance.

Study Group Name:

Proposed Manuscript Title:

Principal Investigator/Lead Author:

PI Contact Information:

Proposed/Target Journal(s):

Proposed date of submission of first draft for review by GAPS review: _____
(This date will go into the master manuscript tracking spreadsheet. Authors should refer to the PECARN manuscript timeline if there are questions)

Authorship: Proposed writing team:

Please indicate individuals who are expected to contribute directly to the preparation of the manuscript. Contributors should be listed in the order in which it is anticipated they will be placed in the manuscript byline.

Name	Node	Contribution to Manuscript

Outline of Manuscript:

The information in this section will be used to assist the DCC in the analysis. Please be specific and contact the DCC if you have questions about any of the items below.

Population:

Which records should be used in the analysis? Detail any specific inclusion and exclusion criteria (beyond general study entry criteria) here.

Aims/Outcomes and other variables of interest:

Indicate outcome variable(s) and key predictors. Please review data collection forms to include specifics and detailed definitions. *Note: Use the data forms to be sure the data you intend to analyze are currently being/have been collected.*

Other variables to be included:

General characteristics, predictors, supportive outcomes

Design Overview:

Outline and describe the major components of the study design and analysis plan. If needed, consult with a DCC statistician on the design and analysis plan.

Brief background/relevance-

Aims/Hypotheses-

Primary, Secondary-

Design-

Analysis plan-

If this is a clinical trial please indicate where trial is registered.

Attachment 2

PEDIATRIC EMERGENCY CARE APPLIED RESEARCH NETWORK

Abstract Analysis Request Form

General Information:

Study / working group:

Abstract title / topic:

Author name and e-mail:

Submitting to:

Submission due by:

Abstract Outline:

Population. Which records should be included in the analysis? Detail any specific inclusion and exclusion criteria (beyond general study entry criteria) here.

Outcome(s) and key predictors. Indicate outcome variable(s) and key predictors. Please review data collection forms to include specifics and detailed definitions as needed.

Outcome(s):

Key predictors:

Study Overview. Outline the major components of the study design and analysis plan. Consult with a CDMCC statistician if needed.

Aims/Hypotheses:

Design:

Analysis Plan:



STANDARD OPERATING POLICY AND PROCEDURE FOR Development and Approval of PECARN Nodal Pilot Studies

Initial Draft: June 2012 Version No: 02 Dec 2013 Reviewed: Jan 2015	Development and Approval of PECARN Nodal Pilot Studies	Original Steering Committee Approval: February 2015 Exec Committee approval: 30 Sept 2015
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1. PURPOSE

- 1.1. The purpose of this policy is provide guidance for PECARN investigators and others involved in PECARN research regarding the development, submission of, and approval process for nodal pilot studies. If PECARN infrastructure resources are used for the pilot, PECARN funding should be acknowledged. See the publications eRoom for the most current acknowledgement statement.

2. POLICY

- 2.1. This document describes the method of initiating and obtaining approval for nodal pilot studies.

3. SCOPE

- 3.1. This document applies to all participating sites, as well as investigators, nodal administrators and others involved in PECARN-related research.

4. DEFINITIONS

- 4.1. A PECARN nodal pilot study is a project designed to gather information and data that will inform the planning of a larger study or trial; alternatively this project could be a discrete project which advances the PECARN research agenda. These studies may involve more than one node or include non-PECARN sites. These studies may use PECARN resources; however these studies should not interfere with, or use resources necessary for complete ongoing network wide studies in which the sites are participating

5. DEVELOPMENT AND APPROVAL PROCESS

- 5.1. This process is node specific.

6. COMMUNICATION WITH OTHER NODES

- 6.1. While there is no formal PECARN approval process for nodal pilot studies, all nodal PIs and the PECARN HRSA Program Officer should be aware of and approve these studies.

7. DATA MANAGEMENT PLAN

- 7.1. The data management will be left to the discretion of the Principal Investigator and Nodal PI.

8. DATA ANALYSIS

8.1. The data analysis will be the responsibility of the Principal Investigator and Nodal PI.

9. PECARN ACKNOWLEDGEMENT

9.1. If PECARN infrastructure resources are used for the nodal pilot study, PECARN funding should be acknowledged. See the publications eRoom for the most current acknowledgement statement.

10. PRESENTATION, ABSTRACT AND MANUSCRIPT SUBMISSION

10.1. All presentations (oral and poster), abstracts, manuscripts and other publications shall be submitted to the PECARN Program Officer for review and approval prior to submission. This review is intended to ensure that HRSA and the network are appropriately acknowledged and to enhance the quality of the work. Abstract, presentation and manuscript review will be the responsibility of the study PI and participating nodal PI(s), with no requirement for submission to GAPS.



STANDARD OPERATING POLICY AND PROCEDURE FOR Development and Approval of Ancillary Studies

Initial Draft: March 2012 Version No: 1.0 Version No: 3 -30 Sept 2015	Development and Approval of Ancillary Studies	Original Nodal PI approval- 10July2012: Exec Committee Approval 30 Sept 2015
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1. PURPOSE

- 1.1. The purpose of this policy is provide guidance for PECARN investigators and others involved in PECARN research regarding the development and submission of, and approval process for ancillary studies to be performed in conjunction with PECARN studies.

2. POLICY

- 2.1. This document describes the method of initiating and obtaining approval for ancillary studies to be performed in conjunction with active PECARN research studies. Any changes to this process must be approved by the PECARN Executive committee and the HRSA Program Officer.

3. SCOPE

- 3.1. This document applies to all participating sites, PECARN or otherwise, as well as investigators, nodal administrators and others involved in PECARN-related research.

4. DEFINITIONS

- 4.1. Ancillary Study: An ancillary study is one that addresses a research question to which the parent study can provide biological samples, participants, infrastructure, or data. The ancillary study will typically use the patient cohorts, data, and biological materials of the parent study to address new research aims. This policy addresses ancillary studies that will be completed in conjunction with ongoing PECARN policies.
- 4.2. Nodal Principal Investigators: Investigators named on the HRSA cooperative agreements at each PECARN and EMSA node and the DCC.

5. RESPONSIBLE PARTIES

- 5.1. A PECARN or external investigator is responsible for developing the ancillary concept or protocol, after communication with the parent study principal investigator (PI). The ancillary PI is strongly encouraged to collaborate with the PI of the parent study, participating PECARN site investigators, a PECARN nodal PI, subcommittees, subject matter experts,

the DCC, biostatisticians, information technology/database experts, and others, as appropriate in the development of the ancillary concept/protocol.

- 5.2.** The investigator who initiates the ancillary study concept or protocol is responsible for assuring that the concept or protocol meets all regulatory requirements, and is ethically and scientifically sound.

6. PROCEDURES – Review Process

- 6.1.** Proposals for ancillary studies are often time-sensitive and, therefore, may be expedited by the network based on agreement among the nodal PIs.

- 6.2.** The concept proposal submission should include the standard PECARN concept face sheet with the following additional information:

- Title of the Ancillary Study
- Title of the Parent Study
- Approval by the Parent Study PI

- 6.3.** In addition to the standard concept paper requirements, the concept paper should include the following:

- A statement of the temporal relationship between the ancillary and parent study, illustrating any time sensitivity or other pressing constraints
- The investigators should state how the study leverages or builds upon the work of the funded parent PECARN study.

6.4 Approval process (See diagram next page)

1. An ancillary study PI may proceed with concept development after approval by the parent study PI, the sponsoring nodal PI and agreement to participate by potential site PIs.
2. Once developed, the concept must be submitted to the parent study PI, nodal PI and to the HRSA Program Officer for review/approval.
3. With approval of the parent study PI, nodal PI and HRSA Program Officer, the ancillary study PI must then submit the concept to the PECARN Steering Committee for a vote. A 75% majority of the PECARN voting membership is required for concept endorsement.
4. If approved, the project can be developed by the investigator with input from parent study PI and the study working group and/or the investigative group which should include the PIs of the sites planning to participate in the ancillary study.
5. At this juncture, the investigators may also consult with the data coordinating center (DCC) and the feasibility and budget subcommittee (FAB) as desired.
6. The preliminary protocol/grant will be submitted to all PECARN subcommittees for review.
7. The investigator must respond to the subcommittee recommendations and then may finalize the protocol/grant.
8. The final protocol/grant requires review and approval by the PECARN Executive Committee and the PIs of the sites participating in the ancillary study.
9. Upon approval, the grant may be submitted for funding.
10. If significant budgetary or programmatic changes occur in the process of project development, the PIs of the sites planning to participate in the ancillary study must review and approve changes.

11. If the initial grant application is not funded, revised applications must be reviewed/approved by the parent study PI, the Executive Committee and the PIs of the sites planning to participate in the ancillary study.

PECARN Ancillary Study Concept and Protocol Development and Approval Process

4

