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1 Cerebral Palsy Research Network Development

Network Development	Version Changes Approved by the Executive Committee 5/10/2017

1.1 Standard Operating Procedures

These standard operating procedures (SOPs) have been developed by the CPRN Executive Committee and will be reviewed and modified on an as needed basis to address the needs of network, its investigators, its committees, funders and other constituents as needed. Suggestions for changes to these SOPs can be made directly to the Executive Committee or by emailing suggestions to sops@cprn.net. Changes to the SOPs will be subject to a majority vote of the Executive Committee.

1.2 Background

Cerebral palsy (CP) refers to a group of disorders affecting movement and posture, attributable to non-progressive injuries to the developing brain (1). CP is the most common cause of physical disability in childhood with a reported prevalence in the United States of 3.5 per 1000 births (2) that is slightly higher in males (3.8:3.2/1000), and in non-Hispanic black children (1.5:1)(3). Lifetime costs of medical care for an individual with CP were estimated at $921,000 in 2003 dollars (4); however, estimated social costs of CP such as loss of independence and productivity, and the need for specialized care and education may significantly eclipse the medical costs (4).

Children with CP have wide variability in presentation and severity. The Gross Motor Functional Classification System (GMFCS) is the international standard for classifying CP by severity of functional mobility for clinical or research purposes (5). The GMFCS has been shown to be reliable, valid, stable (6), and has utility for making prognoses and treatment recommendations (7). Children in level I can perform most functional activities similar to their peers, albeit with some difficulties. Those in Level II can walk unaided, but require support when negotiating uneven surfaces or stairs. Children in level III require external aids to walk and may use wheelchairs for longer distances. Children in levels IV and V are non-ambulatory. In level IV they may be able to stand with support to transfer or for exercise purposes, while those in level V do not achieve any functional weight-bearing and are typically dependent for all of their mobility and care. Approximately 60 - 70% of children with CP are classified as GMFCS I–III, while 30-40 % are classified as GMFCS level IV-V (8,9). Children in GMFCS Level IV-V are also more likely to experience significant co-morbidities including seizures, cognitive, visual, hearing and communication difficulties, medical problems, progressive hip displacement and scoliosis.

No cure is available or imminent for CP. The primary lesion in the brain is not progressive, but the musculoskeletal consequences may worsen over time (10-12), leading to significant and lifelong impact on the lives of these children and their families. Common motor impairments in CP include abnormal muscle tone (spasticity and dystonia), muscle weakness and imbalance, and loss of selective muscle control, all of which can contribute to loss of functional mobility or issues with care and comfort, depending on the level of severity. With time, the resultant reduced physical activity and hypertonia lead to restricted motion at

affected joints (dynamic contracture) that may result in true muscle shortening (fixed contracture) and bony deformities due to the abnormal muscle stresses on developing bone (13). Many treatment options exist for these impairments, often used sequentially or in combination: physical therapy, bracing, serial casting, oral muscle relaxants, muscle injections to reduce imbalance in specific muscles (botulinum toxin-A, phenol), and neurological or orthopedic surgery. Neurosurgical options include selective dorsal rhizotomy (SDR) to reduce lower limb spasticity by sectioning a percentage of the dorsal rootlets in the spine, and the intrathecal baclofen (ITB) pump which delivers medication to the spine to reduce muscle tone. The most common orthopedic procedures for improving joint mobility and alignment are muscle-tendon lengthening of the contractures and rotational osteotomies. These operations are commonly performed, and although each intervention targets different impairments, decisions of which type of operation to pursue and when, are often difficult and complex.

In recognition of the gaps in our knowledge, and the benefits that could emerge from focused research, the National Institutes of Health (NIH) convened a workshop titled "The state of science and treatment in Cerebral Palsy" in Bethesda, Maryland, in November 2014. Among the 70 attendees was an international group of participants, including experts in pediatric and adult cerebral palsy as well as scientists working in related fields, developmental pediatricians, neurologists, physiatrists, physical therapists, laboratory-based neuroscientists, patient advocates, individuals with cerebral palsy, parents, and NIH program and intramural staff. The plenary discussions summarized the current knowledge, challenged existing dogma on neuroplasticity, and identified critical gaps in research and clinical treatment. Conclusions included: the need for a national registry, an increased focus on comparative effectiveness research, more basic and translational research, more research into the issues that face adults with CP and the need for more young investigators to join the field.

The NIH Workshop assigned leaders present at the meeting to lead a task force of volunteers to further the discussions for the key conclusions and to propose a plan. The national registry effort was headed by Deb Gaebler, M.D. from Rehabilitation Institute of Chicago and NINDS Advisory Council member Paul Gross. Gross and Gaebler quickly agreed to divide the registry discussion between epidemiological surveillance and a center-based approach to track patients and interventions. The center-based group determined that defining a set of registry elements to be collected as part of clinical practice, as exemplified by Nationwide Children's Hospital's "Learn from Every Patient" project, was feasible at a national level. Five months following the NIH Workshop, an effort to define a center-based national registry begun. Gross, having developed two prior clinical research networks, led the effort to wrap a research network around the effort to define the center-based CP registry. The registry definition was completed in the 2015 and 17 charter members were invited to join the Cerebral Palsy Research Network in February 2016.

1.3 Scope

1.4 Mission

The mission of the Cerebral Palsy Research Network (CPRN) is to improve outcomes that people with cerebral palsy value most through high quality clinical research and quality initiatives.

1.5 Vision

The Cerebral Palsy Research Network vision is to translate the knowledge from research such that every clinician treating persons with CP is offering the best, most current treatments available. Every center with a CP clinic will include its patients' treatment data in the CPRN registry. This registry, combined with a patient-powered registry and broad participation from people with cerebral palsy, will enable clinician-researchers to find practice variation and create quality initiatives to improve outcomes for all patients with CP, regardless of where they are treated.

1.6 Goals

1.6.1 Initiative 1: Stimulate and conduct high-quality, multi-center, multi-discipline quality initiatives and clinical research for cerebral palsy.

Rationale: Cerebral palsy, while the most common motor condition in children, is neither prevalent enough for single center research nor narrow enough in etiology or manifestation for single discipline research to yield field-changing results. Multi-center, multi-discipline research is necessary to derive meaningful outcomes that can be targeted for appropriate populations and etiologies. The synergy between quality improvement initiatives and comparative effectiveness research organizations has been demonstrated by recent efforts of organizations like Improve Care Now and the Hydrocephalus Clinical Research Network. And the integration of patient reported outcome registries has altered the landscape for how treatments and outcomes can rapidly improve in numerous diseases including Irritable Bowel Syndrome, Oncology and Hydrocephalus.

1.6.1.1 Goal 1: Attract ten institutions and researchers with a track record of excellence and commit to clinical research, quality improvement and collaboration.

- CPRN's goal is to attract the best and brightest clinicians and researchers committed to studying this condition and dedicated to making a dramatic impact on improving care and treatment for people living with cerebral palsy. We need clinicians and researchers want to devote time and energy into establishing a high quality evidence base for treatments that result in the best outcomes.
- Metrics for measuring success: *We'll know we've been successful if…*
    - we've established and documented criteria for individual and center inclusion in the network by June 2016. Preliminary criteria for inaugural participants will be a track record of research and collaboration within an institution treating a high-volume of CP cases and the availability of time and interest by a primary investigator for studying cerebral palsy. Commitment Information Technology administrators as well as alternate PI and practice partners of the PI to participate in the studies is also important.
    - we have signed on ten charter member institutions and primary investigators and related study support staff by April 2016.

1.6.1.2 Goal 2: Establish clinical and patient reported registries to enable not only high quality research but also provide a basis for Identifying practice variation that supports the creation of quality improvement initiatives.

- CPRN's clinical registry will characterize the patient population sufficiently to enable hypothesis generation and an accurate estimate of patient cohorts and study recruitment capability across the network. That same registry will capture practice variation that when combined with patient reported outcomes will support the establishment and tracking of quality improvement initiatives that will fundamentally improve outcomes and drive treatment standards for people with cerebral palsy.
- Metrics for measuring success: *We'll know we've been successful if…*
    - CPRN sites standardize the data collected on CP patients.
    - The CPRN registry provides significant quantities of preliminary data that is used to support multiple grant applications.
    - CPRN studies are able to predict and accrue eligible patients with a high rate of speed and accuracy.
    - CPRN develops multiple quality improvement protocols resulting in patient reported outcomes that reflect improvement.
    - Patient reported outcomes are collected and reviewed by clinicians for more than 50% of clinic visits at CPRN sites.
    - CPRN expands membership to include data only, quality improvement sites for its registry.
    - Most major CP centers, defined as sites with an annual caseload of 500 clinic visits and/or surgical events, having joined CPRN, will have implemented CPRN quality improvement protocols and other improvements as dictated by study findings.

1.6.1.3 Goal 3: Launch two to three clinical studies focused on the most pressing and widespread clinical research questions and one to two quality initiatives all based on input from clinicians and people with CP.

- CPRN's goal is attract funding and execute multiple clinical studies that address major issues facing families and patients with diagnoses of cerebral palsy. Examples of key issues are: comparative effectiveness of lower extremity surgical interventions…,
- Metrics for measuring success: *We'll know we've been successful if…*
    - we have created a method for identifying the major clinical research gaps that are pressing and widespread for those enduring cerebral palsy by 2016.
    - our charter members and patient advocates can, by June 2017 agree on a preliminary research agenda.
    - Institutional Review Boards/Research Ethics Boards approve our research methods for human subjects by July of 2016.
    - our research teams are quickly accruing appropriate study participants within protocol guidelines. (Note: each study will have a relevant data collection timeline against which to measure success –need to define when studies are set).
    - our findings are statistically sound and significant and indicate a path toward improvements in cerebral palsy patient care.

1.6.1.4 Goal 4: Publish 10 journal papers.

- CPRN's goal is to inform the medical, patient and stakeholder communities, and, through that channel, inform the broader public, about the importance of our findings. The current paradigm for doing this is to publish in peer-reviewed journals and to have those stories be covered by mainstream press outlets as well as coverage in the social media outlets of the leading patient advocacy organizations.
- Metrics for measuring success: *We'll know we've been successful if…*
    - our papers are selected for publication and highlighted in major journals.
    - our research attracts mainstream press and social media attention

1.6.2 Initiative 2: Create a world-class multi-center and patient-centered clinical research organization.

<u>Rationale:</u> The success of model multi-center clinical networks like Children's Oncology Group, Hydrocephalus Clinical Research Network and Improve Care Now rests on a sound foundation of organizational excellence and patient involvement. In order for researchers to focus on their work, administrators need to provide them the infrastructure to accomplish the complex tasks of coordinating multi-center clinical trials and quality improvement studies. This infrastructure is intended to allow the network to grow rapidly while accommodating more studies and participants and still being responsive to patient needs and outside parties. Making sure these details are attended to in a professional, timely, and prudent manner is the rationale behind this initiative.

1.6.2.1 Goal 5: Create the fiscal infrastructure to generate public and private funding for the registry and multiple quality improvement and research studies.

- CPRN's goal is support our investigators to competitively pursue funding for the studies that are so important to our mission. Having a nonprofit funding vehicle with minimal overhead, and mechanisms for properly managing tax deductible philanthropy, along with institutional and government income, will be imperative. CPRN values quality and transparency and our fiscal efforts should be both professional and open to scrutiny.
- Metrics for measuring success: We'll know we've been successful if…
    - we've secured the founding philanthropists' resources for launching the network by June 2015.
    - we've established an operating budget for income and expenses by June 2016, developed processes for annual budgeting, and monitored financial reports quarterly.
    - we've established a fiscal agency agreement with a host nonprofit by June 2015.
    - we've established a written financial controls policy by June 2016 and reviewed yearly.
    - we've established written methods for promptly processing personnel and vendor payments and for handling income.

1.6.2.2 Goal 6: Create the operational framework and establish relationships with key organizations to help direct and support the studies.

- CPRN's goal is to provide the most professional and responsive operational support to CPRN study groups with a staffing and support footprint that is prudent, efficient, and reflective of excellent stewardship of the resources entrusted to us. Where outsiders are more cost-efficient

and effective at delivering a service, CPRN will contract out the work, assuming it does not compromise study integrity or patient privacy. Where partnerships and collaborations could successfully deliver the necessary service, those will also be examined and considered before building out our own infrastructure.

- Metrics for measuring success: We'll know we've been successful if…
    - we have created group collaboration tools, resources, and events (Intranet, conference calling, meeting facilities, and working processes) that are well adopted, understood, and that help all participants feel connected, helpful, and productive measure by participation and follow-up as of June 2016.
    - we have provided clear project management direction and communication through the use of collaborative tools and communications demonstrated by the achievement of milestones and deliverables by December 2016.
    - we have provided IT infrastructure and support for study data collection and data management demonstrated by the launch of the registry at multiple sites and the successful transfer, transform and load of data into the CPRN registry by September 2016.
    - we have authored and provided written administrative materials to all relevant participants including: study manuals, IRB submission and renewal paperwork, and CPRN constitution and administrative manuals by December 2016.
    - we are rated as very responsive and professional by our medical researchers in half-annual surveys.

1.6.2.3 Goal 7: Create appropriate governance structures to oversee the work of CPRN participants and represent the needs of the CP community.

- CPRN's goal is to have the results of our work stand up to professional scrutiny and the needs of the cerebral palsy community. There can be no question about the ethics and integrity of our work. Appropriate governance oversight will ensure that all decisions are fair and that the work is conducted with utmost professionalism.
- Metrics for measuring success: *We'll know we've been successful if…*
    - we've defined the requirements, terms, responsibilities and process for selecting executive advisory board members by January 2018 and recruited the charter members by June 2018.
    - CPRN participants feel there are fair and just decisions being made concerning who does or doesn't participate in the CPRN and that the process for making these decisions is documented and transparent to all interested parties.
    - we have created the appropriate managerial oversight to make sure goals/metrics/milestones are being monitored and communicated effectively back to the group.
    - our studies are considered of high-quality by peers in the medical research profession.
    - patients, caregivers and other stakeholders are consistently involved in the planning and execution of our research.
    - our studies are considered pressing and important by the cerebral palsy community.

1.6.2.4 Goal 8: Attract sufficient public and private funding from institutional and government support to achieve our study goals described above.

- CPRN's goal is to have the necessary resources to do true collaborative, and field-changing, clinical research. An initial 5-year total outlay of approximately $500,000 to support the development and maintenance of our Data Coordinating Center and registry database has already been committed. CPRN investigators will need to seek public and private grant funding to support the studies informed by the CPRN registry.
- Metrics for measuring success: *We'll know we've been successful if…*
    - we've attracted additional grant funding for at least four studies and/or quality improvement protocols totaling for an annual research/QI investment of $1,000,000.
    - we've established a business model for our QI initiatives to sustain those efforts and the infrastructure and staffing to execute them.
    - our QI results and business model enable broad participation by centers that treat people with cerebral palsy by 2020.
    - our funding partners feel very satisfied with the progress and impact of our research and are properly thanked for their involvement and support.
    - the patients treated at our centers are experience improved outcomes as measured by our patient reported outcome metrics.

1.6.3 Initiative 3: Create a lasting impact through broad participation and adoption of key findings through a variety of knowledge translation mechanisms.

Rationale: Our work will have been in vain if it did not impact treatment improvements and outcomes for people with cerebral palsy. Because we can only directly influence the professionals in the CPRN, and the patients they touch, our goal is to scale our quality improvement efforts as broadly as is practical. This expansion and inclusion of centers will maximize the impact of our work. We will implement knowledge translation mechanisms that maximize the improvements in care as broadly as is possible.

1.6.3.1 Goal 9: Decrease practice variation among members of CPRN.

- CPRN's quality improvement methods will seek to improve outcomes meaningful to patients through reducing practice variation. Our registry will capture many of the degrees of variation across CPRN centers. Our QI methodologies should have the effect of reducing that variation in practice.
- Metrics for measuring success. *We'll know we've been successful if…*
    - we establish quantifiable differences across the treatment of patients at CPRN sites and target some of that variation for QI initiatives.
    - by 2020, the quantifiable differences in practice variation have reduced and patient centric outcomes have improved.

1.6.3.2 Goal 10: Make knowledge available to consumers and clinicians via flexible formats and accessible platforms

- One of CPRN's goals is to not only reach beyond CPRN centers but also inform patients and families about best practices in the treatment of CP. We will need to collaborate with the American Academy of Cerebral Palsy and Developmental Medicine and other professional societies to maximize the distribution and training of our findings. And we will need to establish

direct and indirect connections to patients and families to disseminate our findings. We will leverage different training methodologies and media to improve the uptake of our work.

- Metrics for measuring success. *We'll know we've been successful if…*
    - we have established collaborations with AACPDM, POSNA, APTA, AANS, AAP, AAPMR, AAN and other professional societies to leverage our work to improve the state of care and outcomes in CP.
    - we have formed partnerships with leading patient advocacy organizations and hospitals to disseminate our findings to their constituents and patient populations.
    - we have shared our results in a broad variety of formats (publications, video, CMEs, web, etc.) to enable the broadest adoption of our findings.

1.6.3.3 Goal 11: Increase the percentage patients receiving evidence based treatments with in our network.

- CPRN's goal is better treatment and better clinical and patient reported outcomes for people with cerebral palsy based on clinically proven treatments. We will only be successful if the mix of care for patients shifts toward treatments with the strongest evidence base.
- Metrics for measuring success. *We'll know we've been successful if…*
    - we've published evidence-based best-practice guidelines for all medical professionals that encounter patients with cerebral palsy in major journals by 2020.
    - treatments tracked in the registry will skew toward "green light" interventions.

2 CPRN Organizational Structure

Organizational Structure	Version Changes Approved by the Executive Committee 5/10/2017

2.1 Overview

2.1.1 Clinical Sites

Clinical sites were chosen to participate in the CPRN based on the expertise of the center, commitment and capability to execute multi-center research and quality improvement. Each site has established infrastructure that will support the collaborative responsibilities of the Network.

Personnel at each Clinical site may include

- Site Principal Investigator
- Site Alternate Investigator
- Research Coordinator

Founding sites, including Children's Hospital of Alabama, Cincinnati Children's Hospital, Nationwide Children's Hospital, and SickKids may have an additional Site Principle Investigator.

2.1.2 Data Coordinating Center (DCC)

The Data Coordinating Center (DCC) serves as the data management and bio-statistical resource for the CPRN. Resources available at the DCC include: clinical trial management, statistics, database development, data form design, data analysis, manuscript preparation, meeting coordination and hosting.

Personnel at the DCC

- DCC Principal Investigator

The DCC has a multidisciplinary staff to manage multiple projects including:

- Biostatisticians
- Technical programming staff
- Data Management and support staff

2.1.3 Advisory Board

The Advisory Board is an external peer review group that advises the CPRN on strategic direction, structure and management. The CPRN Chair convenes and attends the meetings or seeks advice through individual calls. The Advisory Board meets as necessary either in person or by conference call. Members of the Advisory Board do not participate in CPRN research.

Responsibilities of CPRN Advisory Board members.

- Provide strategic guidance to the CPRN. Review and work on strategic documents and give advice to the CPRN administration and researchers on strategic choices.
- Read pre-meeting preparatory material or other material sent as part of CPRN business.
- Review the financial statements and budget documents for strategic suitability and sustainability as requested by the CPRN chair (board will not act in a "fiduciary-responsible" manner of a formal nonprofit board as the formal fiduciary agent is University of Utah).
- Help make connections useful for funding and promoting the organization's work, and driving the organization's scientific agenda.

Members of the Advisory Board

- CP expert outside the CPRN
- Expert in Network structure and organization
- Patient Advocate
- NIH Liaison

2.2 Responsibilities of CPRN Personnel

CPRN Chair:

- oversee and facilitate Network development and research
- consult with Advisory Board and Committees re: strategic direction of Network
- liaison between Advisory Board and Network participants
- liaison with DCC PI
- investigate and pursue Network funding opportunities
- may be a study PI
- attend CPRN meetings/calls
- lead Executive Committee meetings
- liaison with cerebral palsy advocacy community
- liaison with the American Academy of Cerebral Palsy and Developmental Medicine and other professional organizations that serve the CP community

Site Principal Investigator:

- act as a resource/mentor for site personnel
- ensure that local resources are available for site personnel (time, money)

- promote compliance with protocols
- cooperate on all network studies
- contribute to development of new protocols, monitor conduct of studies, ensure adherence to study protocols, participate in analysis and publications
- may be a study PI
- attend CPRN meetings
- voting
- ensure local site IRB approval of all studies
- oversight of Clinical site performance

Alternate Site Investigator

- cooperate on all network studies
- contribute to development of new protocols, monitor conduct of studies, ensure adherence to study protocols, participate in analysis and publications
- attend CPRN meetings/calls especially when Site PI is not available to attend.
- promote compliance with protocols
- cooperate on all network studies
- may be a study PI

Clinical Research Assistant:

The Clinical Research is primarily charged with the implementation of CPRN research projects at each Clinical site not supporting EMR data collection. Responsibilities include:

- ensuring the local conduct and coordination of CPRN protocols under the direct supervision of the senior site investigator and site investigator
- recruit study patients
- complete case report forms and study files
- enter data into database
- obtain informed consent (where applicable)
- prepare IRB applications
- ensure adherence to the protocols
- sets up training systems if required
- report on study progress
- assure the highest standards of data quality
- evaluate the feasibility of new protocols
- assist investigators with protocol development
- liaison with Site Investigator to ensure adequate local resources, equipment, and supplies to support studies
- may propose and conduct ancillary studies with a study PI
- may be a study PI
- attend Clinical Research Assistant Committee meetings
- invited to attend Investigator Committee meetings

Study Principal Investigator (PI):

- originates and takes primary responsibility for Network study
- may be a CPRN site researcher but not a site PI or alternate PI. Study PI must work directly with the site PI in this capacity.

DCC Principal Investigator (PI):

- supervision and management of DCC staff (who will be involved in data management, data monitoring, data security, reports to investigators, study documentation)
- collaborate with each Study PI and with the CPRN chair to ensure appropriate support of CPRN goals
- attend Investigator Committee meetings and participate in study development
- be a resource for study design and data analysis
- collaborate on manuscript preparation
- may be a study PI

Lead Statistician

- supervision of the biostatistical resources working on CPRN projects.
- oversee the statistical plans for CPRN
- collaborate with the Study PI and other DCC resources
- attend Investigator Committee meetings and participate in study development
- be a resource for study design and data analysis
- collaborate on manuscript preparation
- may be a study PI

Community Engagement Director:

- Lead the Community Advisory Committee (CAC)
- Manage the selection and engagement of the members of the CAC
- Liaison between:
    - Investigators and CAC members to appropriately engage in research
    - CAC and the Executive Committee
- may be a study PI.

2.3 Growth of CPRN

CPRN plans to grow the registry and network in order to accomplish its research, quality improvement and knowledge translation objectives. The executive committee establishes the criteria for network expansion and the opportunity to join CPRN is promoted through CPRN.NET and through the membership of AACPDM. Key criteria includes a demonstrable commitment to research, acknowledged support of CPRN technology infrastructure (forms, data elements, extraction) by the sites Chief Medical Information Officer, commitment to support the registry

data collection amongst the disciplines that treat CP at the site, and ethics approval as well as an executed business associates agreement with our DCC.

CPRN may include additional non-CPRN sites in studies to achieve enrollment targets.

2.3.1 Categories of Sites

In its initial phase of growth, CPRN envisions all sites as both registry sites and network participants. In the future, CPRN expects to differentiate between research sites and quality improvement sites. All sites will participate in the CPRN registry at a minimum.

2.3.1.1 Quality Improvement Sites

Quality Improvement (QI) sites will implement the CPRN registry and participate in the development of any protocols, additional data collection, and processes associated with CPRN QI initiatives. CPRN envisions a very broad base of institutions participating in its registry and QI initiatives as a key way to improve outcomes for people with CP and to accelerate knowledge translation of our evidence based findings. The ability to "turn on" the CPRN registry as part of the standard distribution of the electronic medical record system such as Epic will greatly lower the bar for participation in CPRN. Planned automated data extraction and transfer to the DCC and rapid reporting of results of quality indices should make participation as a CPRN QI site very desirable.

QI sites will be required to pay a participation fee (price to be determined) and commit sufficient clinical and data resources to support the CPRN QI initiatives. Quality improvement results are expected to dramatically outweigh the costs.

2.3.1.2 Research Site

Research sites will implement the CPRN registry and participate in the development and execution of CPRN protocols and studies. Members in good standing will engage in the research activities of the network and demonstrate an ongoing commitment to multi-center collaborative research by participating in network meetings, proposing studies and participating in grant applications and ensuing studies.

Research sites may be required to pay a participation fee (price to be determined) and commit sufficient clinical and data resources to support the CPRN research initiatives.

CPRN research sites may also participate in CPRN QI initiatives.

2.3.2 Adding Sites

When the executive committee deems that it is appropriate to add sites to CPRN, a public call for applicants will be made with clearly stated criteria for consideration. Sites that demonstrate commitment through execution of appropriate agreements and submission of the CPRN Registry IRB protocol will be admitted on a trial basis. Sites will exit the trial period when they have successfully begun enrolling patients in the registry and established a working extraction of records from their EMR and transfer of the data to the DCC for loading into the CPRN Registry.

2.3.3 Adding Investigators

Adding investigators initially goes hand in hand with the description of adding sites above. Once a site is invited to CPRN, it can name a site Principal Investigator and a site Alternate Investigator. Only the site Principal Investigator has voting rights in appropriate CPRN governance. Founding sites may have two PIs and two votes.

Study Principal Investigators are not necessarily CPRN Principal Investigators. In order to encourage the most impactful multi-center and multi-discipline research, any investigator at a CPRN site can propose a study concept to CPRN in conjunction with the CPRN Site Principal Investigator. Study Principal Investigators with approved studies may be added as a CPRN Principal Investigator.

2.3.3.1 Adding Investigators to existing sites

Periodically, CPRN sites may wish to add another clinician to the CPRN. Such requests will be considered as they may help with succession planning, network capacity and/or generation of new study ideas. These proposals would be brought forth by existing CPRN members and presented to the Executive Committee. There are three circumstances that would be considered:

1. The Site PI feels that the Site's participation in an existing study is dependent on or would be greatly enhanced by the new person.

2. The new person proposes a new study which is endorsed by their site PI, and that new study is accepted by the Research Steering Committee.

3. The site PI is leaving and the alternative PI is not able to become the Site PI.

If one of these criteria is met, the Executive Committee would vote to accept the new person as a Provisional member for one year. A Provisional member participates in CPRN conference calls and meetings, but:

a. does not vote
b. is not able to propose additional studies (except as approved under criterion 2 above)

c. is not able to access network data (except as required by an approved study under criterion 2 above).

After being a Provisional Member for one year they would be eligible for full membership. Full membership could be proposed by a motion from the Executive Committee. If the new full member is the only investigator from that site, they will be the site PI. A Provisional Member who joined for a specific study may not wish to become a full member, and in that case they would stay as a Provisional Member until completion of their study.

Sites with multiple members are required to declare a Site Principal Investigator and an Alternate PI.

2.3.3.2 Procedure when the Site Principal Investigator Leaves an CPRN Clinical Site or Leaves the Site PI Role

- For the CPRN clinical site
    - The CPRN Chair asks the CPRN site leadership if they want to continue in CPRN and if so, to propose a new site PI.
        - If the site has another CPRN investigator, that person would typically become the site PI.
        - If the site doesn't have another CPRN investigator, they would be asked to propose a new site PI subject to the process in Adding Investigators at Existing Sites above.
    - Site specific data stays at the site.
    - If the investigator's on-site presence was necessary to conduct a specific study, that study will terminate at that site.
    - If the investigator's on-site presence is not necessary to conduct a study, any current studies may continue.
    - No new studies may start until a new site PI is approved (as per Adding Investigators at Existing Sites above).
    - If a site does not have a suitable new site PI, the departed investigator may be asked to continue directing studies at the CPRN site until they are concluded. The CPRN Chair must be informed in writing of the investigator's intention to continue to direct studies at their former site.

- The departing investigator, who is a study PI
    - Will continue to be the PI for their specific study (if they wish).
    - Will be allowed to attend all meetings and conference calls for the duration of that study.
    - Will be listed as investigator/eligible for authorship on publications related to that study
        - The departing investigator will be listed as affiliated with their current site.

- If the departing investigator is unwilling or unable to continue to direct their study, the CPRN Chair must be informed, in writing, and a new study PI will be identified.

- The departing investigator
  - May undertake all necessary steps to create a new CPRN site at the new location.
  - At the time of an RFA for additional CPRN sites, a standard application may be submitted.
  - Previous experience with CPRN will be considered in the site approval process.
  - The Executive Committee may, at its discretion, allow the investigator to continue in the role of an investigator within CPRN.

2.3.4 Site Non Performance

Sites that do not perform or participate regularly in CPRN activities may be placed on probation by the Executive Committee. The site PI will be informed in advance of issues that concern to the EC such as infrequent attendance of CPRN investigator meetings, significant lag in data collection or transmission to the DCC, failure to secure IRB approval for CPRN studies, failure to enroll patients in established CPRN studies, or other actions not in keeping with the spirit of collaboration and quality of CPRN.

Probationary status will detail the issues that need to be addressed and with the Site PI set a plan and a timeline for those issues to be cured. If the issues are addressed within the agreed upon timeline, the site will be removed from probationary status. If the Site PI cannot address the outstanding issues or demonstrate significant progress, the site may be removed, at the discretion of the Executive Committee, from the network including access to the network activities and benefits that accrue to network sites. Registry data that has been submitted to the network will remain in the registry.

3 CPRN Committee Structure

Committee Structure	Version Changes Approved by the Executive Committee 5/10/2017

3.1 Overview

CPRN conducts most of its work through standing committees, subcommittees, study groups, and ad hoc task forces to manage short term tasks. The primary standing committees of CPRN include the:

- Executive Committee (EC)
- Investigator Committee (IC),
- and the Community Advisory Committee (CAC).

The primary standing subcommittees, drawn from members of the above committees, include:

- Research Steering Subcommittee (RSS)
- Scientific Review Subcommittee (SRS)
- Manuscript Review Subcommittee (MaRS)

Study groups form the basis for generation and curation of study concepts. Study groups are assembled from members of the Investigator Committee and the Community Advisory Committee to explore, recommend and execute study protocols in CPRN. Study groups, with the permission of the EC, may include members from outside of CPRN that are deemed to bring necessary expertise to the study area or provide leadership in pursuing grant opportunities. Subcommittees report to to the Executive Committee to manage aspects of CPRN operations (protocol development approval, publications, data access, etc.) Subcommittees chairs and membership are chosen by the executive committee. Study groups are self organizing. Existing study groups as of May 2017 include:

- Adult Study Group (led by Mary Gannotti and Debbie Thorpe)
- Quality Improvement (led by Amy Bailes)
- Pediatric Patient Reported Outcomes (led by Paul Gross)
- Clinical Registry (led by Garey Noritz)
- Surgical interventions [PCORI study] (led by Paul Gross and Rich Stevenson)

3.2 Committees

3.2.1 Executive Committee (EC)

3.2.1.1 Purpose

The CPRN Executive Committee (EC) is the primary governing body of the CPRN. 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. The Executive Committee may appoint Subcommittees and Working Groups as needed to carry out specific tasks identified by the Executive Committee. All participating CPRN investigators must agree to abide by the policies approved by the Executive Committee.

3.2.1.2 Members

- CPRN Chair- Paul Gross
- Amy Bailes, PT Ph.D. (Cincinnati)
- Mary Gannotti, PT Ph.D. (Hartford)
- Susan Horn, Ph.D. (Utah)
- Ed Hurvitz, M.D. (Michigan)
- Jacob Kean, Ph.D. (Utah)
- Unni Narayanan, M.D. (SickKids)
- Garey Noritz, M.D. (Nationwide Childrens)
- Neurosurgeon (TBD) to replace Jerry Oakes, M.D.
- Communtiy Engagement Director, Michele Shusterman (CP NOW)

Additional membership of the Executive Committee is at the discretion of the Executive Committee. The EC is comprised of senior clinicians representing each discipline, a patient advocate, a biostatistician and the DCC PI.

3.2.1.3 Terms and Membership

EC members are selected by the CPRN Chair based on the recommendations of the other EC members. There is not a fixed number of members in the EC but members are selected to help guide the strategy and operationalization of CPRN. Most disciplines are represented in addition to having a community engagement director and DCC PI.

EC member terms are three years from the start of the member's inclusion in the EC. Renewal will be determined at the end of the three-year period based on the mutual interests of the member and the chair.

3.2.1.4 Voting:

For EC decisions each member has one vote and decisions are made by majority.

3.2.1.5 Responsibilities

Standard Operation Procedures (SOPs) development and maintenance.

Financial oversight – Members are responsible for reviewing the annual CPRN budget.

Study Concepts – Study concepts for consideration by the network must first be submitted to the EC for approval before proceeding to the Investigator Committee for a vote.

Network Membership -- The Executive Committee is responsible for decisions regarding Network membership and network expansion. They will take into account input from the Investigator Committee, the Advisory Board, and funding agencies. The criteria for considering a site to join the Network are listed in Chapter 2 on adding sites.

Dispute adjudication – In the event that decisions cannot be reached by a Committee or a subcommittee, they will be referred to the Executive Committee. Such decisions might include disputes over study prioritization, authorship, resource allocation, CPRN membership or voting privileges. Other unanticipated difficult decisions or disputes will also be the responsibility of the Executive Committee.

Executive Committee members are also members of the Investigator Committee and as such have the same responsibilities and opportunities as listed under Investigator Committee.

3.2.1.6 Meetings

The EC will meet via teleconference or through electronic mail once a months or as needed to review CPRN business. Additional meetings may be required and could coincide with the IC Meeting if this is convenient for the members.

3.2.2 Investigator Committee (IC)

3.2.2.1 Purpose

The purpose of the IC is to establish a diverse pool of clinical researchers from multiple disciplines committed to collaboration in the development and execution of high quality clinical research and quality improvement initiatives to improve outcomes for people with CP through CPRN. This body will formulate study groups to advance new protocols which will leverage the network capacity and registry data to pursue external funding for approved research concepts.

3.2.2.2 Members:

- Site Principal Investigator
- Site Alternate Principal Investigators
- CPRN Chair
- DCC PI

- Community Engagement Director
- Study Principal Investigator

3.2.2.3 Voting

For IC decisions, the senior member of the IC from each site is eligible to have one vote. In addition, the DCC PI, biostatistician and Community Engagement Director have one vote each. A quorum for a vote consists of 50% of eligible voters (as of <date>, there are xyz eligible voters, therefore, a quorum is abc voters). The number of positive votes required to pass a motion is 70% of eligible voters (see table below) in attendance at the time of the vote. Members do not vote on their own projects or proposals.

Voters	**Votes in Favor Required to Pass**
9	7
10	7
11	8
12	9
13	10
14	10
15	11
16	12
17	12

Comment [PG1]: To be determined after discussion of voting by IC.

3.2.2.4 E-voting

Votes may be conducted by email (usually after discussion of the issues on a conference call or at an CPRN meeting). An email will be sent to everyone in CPRN with voting privileges describing the proposal. The deadline for receiving votes will be 72 hours unless otherwise specified. The number of voters will be equal to the number of votes received.

Eligible votes who do not respond in the 72 hour (or otherwise specified) time frame will be counted as “abstained”. Votes in favor required to pass an e-vote will be determine using the table above.

3.2.2.5 Responsibilities

The IC is responsible for the initial concept, design, conduct and analysis of research protocols. They are also responsible for scientific reports (presentations, publications) when appropriate.

3.2.2.6 Meetings

The IC meets 1-2 times a month depending on network needs. Standing meeting times are the 1st Monday at noon Eastern time and the third Tuesday at 2 pm Eastern time. Attendance at

the IC Meeting should be given high priority by the members. If a Site PI is unable to attend the IC Meeting, he/she can provide input via the alternate PI or the Chair. Bi-weekly IC conference calls will be conducted to discuss on-going CPRN projects and protocols.

The IC will be convened in person at once annually at mutually convenient times and places if there are sufficient funds to support an in person meeting. At a minimum, a face-to-face side meeting will be held in conjunction with the annual AACPDM meeting.

3.2.3 Community Advisory Committee (CAC)

CPRN was founded on the principles of patient-centered outcomes research. Not only was CPRN founded by the parent of a child with CP, the organization's mission, vision and strategic objectives all place people with CP at the center of our work. Toward that end, CPRN has a community engagement leader, who works to make sure that a representative CP community voice is included in our studies and our priorities.

3.2.3.1 Purpose

CPRN has created a Community Advisory Committee (CAC) to have members of the community engaged in our plans and directions and be willing to join members of our Investigator Committee to plan and conduct studies. Members of the CAC are given opportunities to participate in study panels and steering committees to help make sure our research is patient-centric with outcomes that matter to people with CP and their caregivers.

The CAC is involved in the work of CPRN at several levels including advising on the strategic direction of CPRN, help prioritize its research and participate at every level of study development including design, recruitment, analysis, and dissemination. Patient involvement not only empowers the community, but also increases the relevance of study results.

3.2.3.2 Members

Membership of the CAC is by invitation from the community engagement leader. CPRN seeks to engage members of the community that are diverse demographically and across the gross motor classification scale.

3.2.3.3 Meetings

The CAC meets telephonically on an as needed basis but at least quarterly to give feedback on the direction and progress of CPRN. CAC members engaged in study groups participate as full members of those groups.

3.3 Subcommittees

3.3.1 Scientific Review Subcommittee (SRS)

3.3.1.1 Purpose

The purpose of SRS is to:

a) Provide scientific review of research proposals after the research concepts have been approved by the Investigator 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 CPRN Research Steering Subcommittee of its findings regarding pending research proposals to assist deliberations regarding proposal approval.

SRS is established by the Executive Committee and its actions are advisory to the Executive Committee.

3.3.1.2 Members

SRS membership will be appointed by the Chair of the Executive Committee. Typically, membership will consist of two members from each discipline represented by CPRN Investigator Committee, and the DCC PI. The Chair of the Executive Committee will also appoint a Chair of SRS.

3.3.1.3 Responsibilities

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

The Chair of SRS 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 DCC 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 SRS meeting. Presentations are made by the primary, secondary and methods/statistics reviewers. The SRS Chair will prepare a

summary of the key points raised by the reviewers and the committee deliberations. These will be approved by the committee.

The investigator will receive the SRS summary and all three written reviews verbatim. Only the SRS summary will be posted in the CPRN library and be made available to the Research Steering Committee. The minutes of the committee will contain only the SRS summary. SRS reports should be submitted within two weeks of the Research Steering Subcommittee meetings. The prescribed method of review includes a virtual meeting of the Research Steering Subcommittee. Proposals are typically reviewed at the next Research Steering Subcommittee meeting scheduled after the meeting at which the research concept was approved by the Investigator Committee.

3.3.2 Research Steering Subcommittee (RSS)

3.3.2.1 Purpose

The purpose of the Research Steering Subcommittee (RSS) is approve CPRN research protocols and grant applications for execution or submission. RSS will review protocols/applications that have been reviewed and recommended by the Scientific Review Subcommittee.

3.3.2.2 Members

RSS will consist of the existing members of the Executive Committee, the chair of the Scientific Review Subcommittee, and a panel of six community members from the Community Advisory Committee. The CAC members will represent both caregivers and adults with CP from across the GMFCS spectrum. CAC members will be selected by the Community Engagement Director and serve in the role for two years.

3.3.2.3 Responsibilities

RSS members will review the summary statements provided by the Scientific Review Subcommittee in advance of the RSS meeting. Study PIs will present their proposed protocol/grant application to the RSS for consideration. At the conclusion of the RSS meeting, the members of the RSS will vote to proceed with the application/protocol or request that additional issues are addressed before proceeding to submission or execution. (Execution, or implementation of a study in the CPRN network, will depend on existing available resources to execute study analysis or add new data collection to existing data collection instruments. This consideration will mostly be applied to new analyses of existing registry data.)

SRS will have provided a review of the scientific validity of the proposed study as well as having considered the patient centricity and patient engagement in the research plan. CAC members

of the RSS will provide oversight for the community relevance of the proposed study. EC members will provide oversight of the scientific impact, community relevance, priority and feasibility of the study given CPRN existing studies in progress and resources.

3.3.2.4 Meeting

RSS will meet virtually at least twice a year or more often as needed to provide timely feedback to developed protocols.

3.3.2.5 Voting:

For RSS decisions, each member has one vote and decisions are made by positive votes by 70% of the available members.

3.3.3 Manuscript Review Subcommittee (MaRS)

3.3.3.1 Purpose

The Manuscript Review Subcommittee (MaRS) was created by the Executive Committee of the CPRN and serves as an advisory committee to the Executive Committee. This subcommittee assists Principal Investigators in developing research grant applications to be submitted for funding, reviewing presentations and publications, and making recommendation to the Research Steering Committee.

3.3.3.2 Members

MaRS will include at least one member of the Executive Committee. Its other members will be selected by the Executive Committee. As CPRN is a multi-disciplinary group of principal investigators, every attempt will be made to engage one member of each discipline to serve on the Manuscript Review Subcommittee. Terms for each committee member will be reviewed / renewed on a two-year basis by the Executive Committee.

3.3.3.3 Responsibilities

The responsibility of the MaRS will be to utilize the operating procedures for the internal peer review process to promote CPRN publications and presentations and to ensure their scientific quality. In addition, the MaRS will assist with timely dissemination of CPRN findings to the scientific and non-scientific communities. Finally, the MaRS members may be asked by the Scientific Review Subcommittee Chair to review, critique and help CPRN Principal Investigators to develop grant proposals to fund CPRN-related research proposals.

3.4 Ad hoc Task Forces and Study Groups

3.4.1 Non Surgical Ad hoc Task Force

The non surgical subcommittee consists of clinicians from developmental pediatrics, physical medicine and neurology. The non surgical subcommittee is responsible for defining the registry data elements for the non surgical encounters with patients. The committee is led by an appropriate member of the executive committee.

3.4.2 Orthopedic Surgery Ad hoc Task Force

The orthopedic surgery subcommittee consists of clinicians from orthopedic surgery. The orthopedic surgery subcommittee is responsible for defining the registry data elements for the orthopedic surgery encounters with patients including in clinic and peri-operative . The committee is led by an appropriate member of the executive committee.

3.4.3 Neurosurgery Ad hoc Task Force

The neurosurgery subcommittee consists of clinicians from neurosurgeons. The neurosurgery subcommittee is responsible for defining the registry data elements for the neurosurgery encounters with patients including in clinic and peri-operative . The committee is led by an appropriate member of the executive committee.

3.4.4 Physical / Occupational Therapy Ad hoc Task Force

The physical / occupational therapy subcommittee consists of physical and occupational therapists. The physical / occupational therapy subcommittee is responsible for defining the registry data elements for the physical / occupational therapy encounters with patients. The committee is led by an appropriate member of the executive committee.

3.4.5 Adult Study Group

The adult study group is a multi-discipline group of clinicians and therapists that treat adults with CP. The adult study group is responsible for defining additional registry data elements for longitudinal study of adults and adult outcomes. The adult study group engages adult members of the Community Advisory Committee to prioritize areas of research and to engage in study planning.

3.4.6 Quality Improvement

The Quality Improvement (QI) study group is a multi-discipline group of clinicians, therapists and community members that are responsible for defining CPRN's QI initiatives. The QI study group engages the Community Advisory Committee to determine which outcomes are most important to improve and to participate in the QI initiative development.

3.4.7 Pediatric Community Registry Study Group

The Pediatric Community Registry Study Group is a multi-discipline group of clinicians, therapists and community members that are responsible for planning CPRN patient reported outcomes registry.

3.4.8 Study Steering Committees

Grant funded studies will form a Study Steering Committee (SSC) to execute the planned study. The SSC will include at least one member of the EC as a liaison in addition to the DCC PI to assure that CPRN resources are appropriately balanced and applied to achieve the milestones set forth in the funded grant application without disrupting the other work of CPRN. The SSC will be chaired by the PI named on the grant. The SSC may function independently of other CPRN studies and will develop appropriate governance structures necessary to support the successful execution of study and grant requirements.

3.5 Advisory Board

The Advisory Board is an external peer review group that advises the CPRN, as needed, on strategic direction. Members of the Advisory Board do not participate in CPRN research. The Advisory Board is described further in 2.1.3.

3.6 Data Safety Monitoring Board

The DSMB will be developed and convened as necessary to monitor the progress of specific clinical trials within the CPRN.

4 CPRN Policy and Procedures for the Development and Approval of Research Concepts and Protocols

Research Concepts and Protocol Development	Version Changes Approved by the Executive Committee 5/24/2017

4.1 Overview

4.1.1 Purpose

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

A clinical protocol should:

- clearly define the study question (entry criteria, intervention, patient-centered outcome, analysis) research population;
- define procedures that must be followed to ensure the collection of valid and trustworthy data;
- outline the responsibilities of each member of the study team including members of the Community Advisory Committee (CAC).

4.1.2 Policy

This document describes the approved method of initiating a CPRN research project. Any changes to this process must be approved by the CPRN Executive Committee.

4.1.3 Scope

This policy applies to all CPRN Principal Investigators and Alternate Principal Investigators and other involved in CPRN related research and all participating sites.

4.1.4 Roles and Responsibilities

4.1.4.1 The Study Principal Investigator is a CPRN or an external investigator is responsible for drafting the concept or protocol, in conjunction with an existing CPRN study group or participating CPRN site investigators, subcommittees including the CAC, subject matter experts, the DCC, biostatisticians, information technology/database experts, and others, as appropriate. If the concept is approved, the study PI: develops the protocol with other committee members, presents the protocol for approval, assists the DCC with protocol operationalization, ensures that all participating CPRN sites comply with the approved clinical protocol, work with the DCC to analyze the data and writes the first draft of the ensuing manuscript.

4.1.4.2 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.

4.1.4.3 The Site Investigator (SI) is the investigator responsible for conduct of the study at a designated CPRN clinical site. The SI is responsible for: obtaining local IRB approval, ensuring that all staff at the clinical site comply with the approved protocol, as such, the SI will be asked to sign a protocol signature page certifying that s/he has read and will comply with the protocol.

4.1.4.4 The DCC is responsible for: protocol development in conjunction with Study PI, protocol operationalization in conjunction with Study PI, finalizing the protocol in a standard format ensuring that all participating CPRN clinical sites comply with the approved protocol.

4.2 Procedures

4.1.5 Research Concept

4.1.5.1 An investigator with a research concept, drafts an initial proposal and, through the Site Principal Investigator of the submitting site, requests review by Executive Committee prior to submission to the Investigator Committee in order to:

- *Assess the importance of the research question and its general appropriateness for CPRN*
- *Determine whether the research topic addresses an identified priority (e.g. CPRN research agenda [to be published in the Fall 2017])*

4.1.5.2 The investigator, in partnership with the site PI, and others in the network as appropriate will work to develop the science and feasibility of the proposal. The site PI's role is to oversee the Investigator Committee review of the concept and to:

- Determine, in consultation with the Scientific Review Subcommittee Chair, the general feasibility of conducting the proposed study within CPRN;
- Assist the investigator in refining the science of the concept proposal;
- Assist the investigator in navigating the CPRN protocol development process.

4.1.5.3 Investigators not affiliated with CPRN may request consideration for a proposal by the Executive Committee. The EC, at its discretion, may allow the investigator to present the research concept to the Investigator Committee for consideration. The investigator will be treated as a provisional CPRN Site Investigator through the protocol submission, presentation and review. If the protocol is approved, the investigator and site will be extended an invitation to join CPRN.

4.1.6 Concept Submission, Presentation and Review

4.1.6.1 The study PI and study group will refine the concept, and if approved by the study group, the investigator will submit a two-page concept paper to the CPRN IC. The deadline for concept submission will be 15 business days prior to the next scheduled IC meeting. It is recommended that the investigator attend the IC meeting and present the research concept. The concept is limited to two pages in order to encourage brevity, clarity, and focus. Appendices and references may extend the two-page limit. If the concept paper exceeds two pages, (excluding appendices and references) the SRS Chair will return the submission to the investigator for revision. The concept should be single-spaced using 11-12 point standard type and one-inch margins.

The concept paper should address the following:

- Why the proposed topic is important to cerebral palsy community and stakeholders?
- Why the study requires the CPRN?
- Background in brief
- Specific aims
- Methodology in brief
- Patient engagement and patient-centered outcomes
- Subject population
- Sample size requirements

The concept proposal submission should include a cover page that includes:

- Project Title
- Principal Investigator and affiliate institution
- Co-Investigators
- Funding plan - statement of preliminary funding plan and agency

See Attachment A

4.1.6.2 The concept paper should be submitted electronically to the CPRN Chair at least 15 business days prior to the Investigator Committee meeting at which it will be discussed. No budget is necessary at this step.

4.1.6.3 Investigator Committee Capacity - As a general rule, no more than one new concept can be reviewed at an IC meeting.

4.1.6.4 The Investigator will present the research concept during the CPRN Investigator Committee meeting. A PowerPoint presentation is recommended. The purpose of the presentation is to encourage scientific dialogue; to develop a broad understanding of the proposal among IC members; to understand the study impact on and importance to the patient population; to review and consider the scientific merit and to address questions not covered in the presentation. This presentation will be approximately 10-15 minutes in length, with approximately 30-45 minutes of subsequent discussion.

4.1.6.5 After the conclusion of the presentation and discussion, the IC will vote by secret ballot (subsequent to the meeting through eVoting) to determine whether or not the concept should be endorsed for further development into a CPRN protocol. A 70% majority of the IC 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 CPRN. IC approval by 70% or more will allow the Investigator to proceed with protocol development. Concepts that receive 50-69% approval may be revised and resubmitted to the IC 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 IC.

4.1.7 Protocol Development

4.1.7.1 Once the research concept is approved, the investigator will identify other co-investigators or collaborators if not already identified, 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 of a grant application. Irrespective of the format, the protocol/grant should contain sufficient detail about the proposed study such that the Scientific Review Subcommittee (SRS) members may assess scientific merit and feasibility. The essential elements of a protocol to be submitted to the SRS are described in Attachment B (Protocol Template: A Guideline for Writing a Clinical Protocol for CPRN). Investigators are required to have a teleconference meeting to work on the study design, protocol development and statistical methods with the DCC. The length of the protocol is not limited.

4.1.7.2 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.

4.1.7.3 The protocol should also contain a preliminary budget and budget narrative. The investigators must work with a CPRN DCC to develop a draft budget.

4.1.7.4 After the protocol is preliminarily developed by the study group, investigators are required to meet, in person when possible and feasible, with the DCC to further develop the protocol. While this should occur at least six weeks before submitting the protocol to the SRS, it is important that the scientific details of the protocol be sufficiently developed prior to the DCC visit to enable the group to meet the goals of refining study details. The DCC 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.

4.1.8 Protocol and Budget Review and Development

4.1.8.1 The protocol should be submitted to all members of the SRS for a scientific review within two months after concept approval. The protocol must be submitted to the SRS 25 days prior to the SRS meeting. The SRS chair will distribute the protocol to the SRS members who will conduct a detailed review of the protocol. An investigator from the study team will present the protocol by video conference at a SRS meeting.

4.1.8.2 After the SRS meeting at which the protocol is reviewed, the SRS chair will submit two documents to the CPRN Chair. The first document should be a confidential, detailed, written summary of the SRS's commentary on the protocol. The chair will submit this document to the SRS within two weeks of the date on which the protocol was reviewed. The document will be distributed by the SRS Chair to the investigator only. The investigator may share the summary with other members of his/her team at his/her own discretion. The SRS chair will also submit a shorter written summary of their committee's commentary on the protocol. This document will be made available to all Research Steering Subcommittee (RSS) members to aid in reviewing the subsequent revised protocol, and in determining if the investigator has been responsive to committee 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 RSS in determining whether or not to approve the protocol. These documents could be identical at the discretion of the SRS chair based on the sensitivity of the commentary. The SRS Chair will post the general summary of the comments of the Research Steering Subcommittee in the CPRN secure share and make it available for the RSS in time for the next protocol review.

4.1.9 Protocol and Budget Refinement

4.1.9.1 After the SRS review and presentation at the SRS, the investigator will continue to refine the work, including the option to return to meet in person with the DCC. One to three members from the SRS may be identified to work with the investigator as needed to address the SRS comments and further develop the protocol and/or budget.

After receiving the reviews, the investigator will make appropriate revisions to the protocol. While the SRS recommendations are not binding, the investigator should give strong consideration to the comments that were provided. The investigator must submit the revised protocol 20 business days prior to the RSS meeting at which it will be considered. The investigator should highlight substantive changes, particularly as they respond to summary comments from the reviewers. It is also required that the investigator(s) submit point-by-point responses to the major summary comments of the SRS, as one would do in resubmission of a manuscript. It is the responsibility of the SRS chair to review the committee's feedback as well as the investigator's response and be prepared to provide the RSS with an assessment of the responsiveness of the revised protocol, and/or any remaining issues from the perspective of the SRS. The RSS will have the opportunity to review the protocol and related documents and assess the investigator's response to the SRS's comments before the vote on the protocol.

4.1.10 Research Steering Subcommittee Approval

4.1.10.1 The revised protocol must be submitted to all members of the RSS for a scientific review within six months after the initial protocol submission. Investigators may not delay protocol submission later unless special circumstances apply.

4.1.10.2 The investigator should present the revised protocol at the RSS meeting. 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, an RSS vote will be held by secret ballot at the meeting or later through eVoting. Protocols receiving 75% support are approved for further development of a grant application. Protocols receiving 50%-74% approval may be revised and resubmitted at the following RSS meeting. Protocols receiving less than 50% approval will not be considered further for CPRN implementation. Abstentions will not count in determining whether a majority has been reached.

4.1.10.3 If the protocol is approved, the SRS 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.

4.1.10.4 If the protocol receives less than 50% approval, the investigator may pursue the research through other means but the CPRN registry and research infrastructure will not be available for use for the study implementation. Other CPRN sites and site investigators may participate in the study at their own discretion.

4.1.11 Grant Application

4. 1. 11. 1 Following development and approval of a CPRN 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 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.

4.1.11.2 The SRS is available to help develop and rigorously review the grant application following protocol approval by the RSS.

4.1.12 Approval of Grant Application

4.1.12.1 Submission of the grant proposal to an external agency requires prior approval by a vote of the EC, with at least 75% approval. The grant application must be submitted electronically to the CPRN Chairman for posting to the EC Evoting system at least two weeks before the external grant application deadline. It must be sufficiently complete that changes made during the last two weeks (following EC approval) are not scientifically or fiscally substantive.

4.1.13 Protocol Development: Expedited Review Process

4. 1. 13. 1 Proposals that have not been endorsed previously by the RSS 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 site PI and the SRS Chair. This process cannot be used to meet routine grant cycle deadlines. The expedited process should be conducted as follows:

4.1.13.2 Investigators must submit a 2-page concept paper for the Site PI and SRS Chair to review. Upon approval of the concept by the SRS Chair and the Site PI, the concept can be submitted to the RSS for a vote as time allows. RSS members will vote on these concepts electronically if the timing does not coincide with a CPRN meeting.

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4. 1. 13. 3 Either 75% approval of the RSS membership or unanimous approval by the SRS is required for concept approval.

4.1.13.4 If the concept is approved, investigators should immediately schedule opportunities to work with DCC and SRS representatives, 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 the SRS and the RSS for consideration electronically or at a CPRN in-person or telephone meeting. The timing will be determined by the SRS chair.

4.1.13.5 The SRS will review the protocol/grant at the subsequent meeting if time allows, or electronically if necessary. A representative of SRS will provide confidential feedback to the investigator after the committee meets. This feedback will highlight concerns identified and suggestions for strengthening the scientific aspects of the protocol/grant application.

4.1.13.6 An RSS vote will be conducted, either in telephonically or electronically, to approve the protocol/ grant. Seventy-five percent approval by RSS members is required for the protocol/grant to be endorsed. Approval at this stage indicates that the investigator may continue to develop the proposal into a full grant submission.

4.1.13.7 Investigators will work with representatives of DCC and the SRS to complete the full grant application. The full grant application will be submitted for EC vote at least 2 weeks prior to the external grant submission deadline. The EC vote will be conducted, either in telephonically or electronically. A majority (> 75%) approval by EC members is required for the grant to be endorsed.

4.1.13.8 In exceptional circumstances, parts of this process may be obviated, as will be determined and resolved by the SRS chair and the CPRN chair.

4.1.14 Ancillary Studies

4.1.14.1 An ancillary study is an observational study proposed as a supplement to an CPRN study. Ancillary studies may be proposed by any member of the Investigator Committee.

4.1.14.2 The proposal should be done with the support and mentorship of the study PI. Ancillary studies:

- cannot be a randomized trial
- cannot involve an intervention that could interfere with the main study
- study population is either identical to, or a subset of, the patients that are enrolled in the main study

4.1.14.3 The ancillary Study PI should present a proposal to the SRS Chair and the original Study PI for preliminary approval and must receive favorable reviews from both. The reviews are primarily to ascertain that the primary study is not compromised. The ancillary study PI will then initiate the protocol process outlined above.

Attachment A – Concept Cover Page

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

Funding Plan: (*example*) If endorsed by CPRN, we anticipate developing extramural funding proposals to support the conduct of this study. We have preliminary interest from a …

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

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 Scientific Review Subcommittee (SRS), the CPRN Executive Committee and other committees to fully review and give constructive input into the science and implementation of the project.
Furthermore, we encourage investigators to be in communication with SRS reviewers and the DCC to answer any questions and clarify any areas necessary (and revise the document if necessary) prior to full Committee 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 Data Coordinating Center (DCC) can help complete (these sections are indicated in the guideline template). You can discuss these items when you meet with the DCC.

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 care of people with cerebral palsy. 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.

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. The patient-centeredness of the outcome should be discussed. 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 CPRN 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 SRS and other committees 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 the SRS 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 DCC 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 surgeries 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 Study Principal 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 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 DCC) 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.

12. Study Monitoring & Quality Assurance

The DCC will assist with 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.

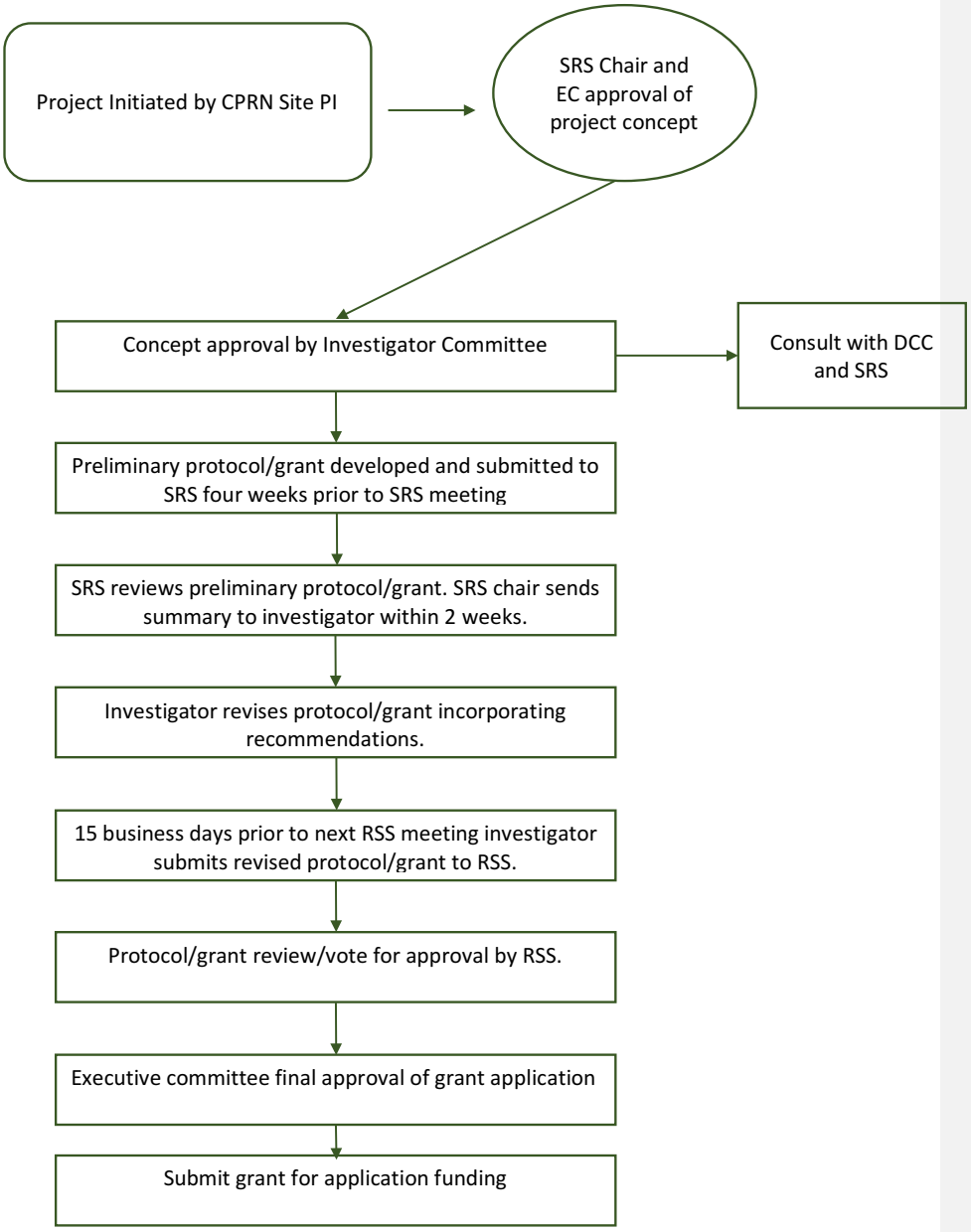
13. Organization of project and capabilities of the investigators.

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.

14. Dissemination and Implementation plan

Investigators should prepare an initial dissemination and implementation plan for how their evidence will be expected to be incorporated into practice both within CPRN sites and to the broader practicing public.

CPRN Research Concept and Protocol Development Process



5 CPRN Policy and Procedures for Manuscripts, Authorship and Publication

Manuscript, Authorship and Publication	Version Changes Approved by the Executive Committee 5/24/17

5.1 Overview

5.1.1 Policy

This document describes the approved method of initiating a CPRN manuscript. Any changes to this process must be approved by the CPRN Executive Committee.

5.1.2 Scope

This policy applies to all CPRN Principal Investigators and Alternate Principal Investigators and other involved in CPRN related research and all participating sites.

5.2 Procedures

5.2.1 Manuscripts, Authorship and Publication

CPRN studies use several different methodologies. Some have very specific study questions and timelines and others are prospective databases accumulating information in an open-ended fashion. The implications for writing manuscripts are as follows:

a. For study protocols with a specific study question and timeline, it is assumed that the PI will lead the writing of the manuscript and have the option of being the first author.
b. The CPRN Clinical Registry lends itself to several potential analyses and/or publications over time. The PIs of the CPRN Clinical Registry will lead writing of the initial manuscripts.
c. For any of the above study designs, once initial manuscripts have been written, other CPRN members may propose manuscripts on these datasets. Secondary manuscript and analysis proposals will be approved by the Investigator Committee.
d. For the CPRN Community Registry, CPRN will give first preference to proposals from the CPRN investigators. But non CPRN investigators may propose manuscripts and analyses based on the generalized collection of data in the CPRN Community Registry. Manuscript and analysis proposals for the CPRN

Community Registry will be approved by the Adult and Pediatric Patient Reported Outcomes Study Groups.

5.2.2 Manuscript presentation/preparation

5.2.2.1 Proposing new manuscripts

Principal Investigators or alternate PIs may propose publications or presentations related to CPRN. Participants are required to submit topics for publications and presentations in advance (see attachments C and D). These proposals would be subject to a vote of the Investigator Committee.

5.2.2.2 Manuscript development

In general, the PI of the study is assumed to be the Principal Author (PA) of the primary paper presenting the primary study results. The PA drafts the initial manuscript. Data analysis and writing of the statistical section is done with the DCC. The PA then sends the manuscript to the other members of the study steering committee and to the DCC statistician (one author). In addition, it is the discretion of the PA to send the manuscript to others whose direct input he or she would like. The PA adjudicates authorship (and all authors must meet the criteria under Authorship Guidelines). If CPRN members are not listed as authors and feel it is justified, they should discuss this with the PA. Similarly, the PA will determine author order and anyone unhappy with author order should talk to the PA. Situations that cannot be resolved by discussions with the PA would be referred to the MaRS. The journal selected is the PA's decision, but opinions from the rest of the authors should be sought.

A timeline for writing manuscripts is required. The clock starts for this timeline when the dataset is locked. It is then expected that the manuscript is submitted to the journal within six months. In general, this would be three months of analysis and three months of writing/revising. For manuscripts that are not submitted in the six-month time window, the PA would be expected to report to the Investigator Committee. The committee would consider whether additional resources and/or time are required, or whether a change in authorship should be considered.

5.2.2.3 Manuscript Review

All presentations and publications based upon data collected as part of the CPRN, shall be submitted to MaRS for review and approval 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 the entire MaRS membership prior to submission. Review and approval

of abstracts will follow an expedited process. This will be accomplished by the MaRS Chair with assistance from the Subcommittee member from the respective specialty. In the absence of specialty representation, the MaRS Chair will identify a PI from the network and the respective specialty to assist.

Manuscripts submitted to MaRS for review should 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 chair. The chair will assign a primary reviewer from the subcommittee and will be responsible for communication with the primary author to schedule the review and timely completion of the manuscript. This review will take no longer than 6 weeks.

A methodology/statistics reviewer from the Data 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 the committee will also be asked to vote for approval, approval with minor revisions (subject to re-review by the chair or designee), or approval with major revisions (subject to re-review by the full subcommittee). The PA will be asked to respond to the critique, with manuscript revisions as appropriate. Once the author and chair agree the revisions are complete, the chair will forward a recommendation for approval to MaRS for a vote, along with the original critique and responses. Manuscript approval is by majority vote of MaRS. The MaRS Chair will only vote in the case that a tie needs to be broken. Members of MaRS submitting manuscripts will recuse themselves from any voting related to that manuscript. The final decision of the MaRS will be communicated to the lead author and writing team.

5.2.3 Authorship Guidelines

5.2.3.1 Authorship shall adhere to the International Committee of Medical Journal Editors (ICMIE) authorship standards spelled out in the following link: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html.

5.2.3.2 Authorship shall be spelled out in the request for data/ publication proposal. This requires approval of the Investigator Committee. The CPRN will be referenced after the authorship list. To promote participation in the CPRN, select manuscripts determined by the Manuscript Review Subcommittee as having required the participation of the complete network beyond routine collection and submission of data will include all PIs in the authorship list. An example of this would be the following publication from the Hydrocephalus Clinical Research Network:

Journal of Neurosurgery: Pediatrics
Dec 2013 / Vol. 12 / No. 6 / Pages 565-574
ARTICLE
No significant improvement in the rate of accurate ventricular catheter location using ultrasound-guided CSF shunt insertion: a prospective, controlled study by the Hydrocephalus Clinical Research Network

Clinical article

- William E. Whitehead, M.D., M.P.H.1,
- Jay Riva-Cambrin, M.D., M.Sc.2,
- John C. Wellons III, M.D., M.S.P.H.3,
- Abhaya V. Kulkarni, M.D., Ph.D.4,
- Richard Holubkov, Ph.D.2,
- Anna Illner, M.D.5,
- W. Jerry Oakes, M.D.6,
- Thomas G. Luerssen, M.D.1,
- Marion L. Walker, M.D.2,
- James M. Drake, M.B.B.Ch., M.Sc.4, and

John R. W.Kestle, M.D.2 for the Hydrocephalus Clinical Research Network.

Where more inclusive author listings are not appropriate, the participants in CPRN will be acknowledged in the Appendix of the manuscript.

a. If a PI disagrees with the decision of MaRS to designate or not designate a paper as a network-wide effort, as described above, they may appeal to the Executive Committee.
b. Timelines will be spelled out in the manuscript proposal and reviewed periodically by MaRS. The Chair will contact the PI to assure adherence to the agreed upon guidelines.

5.3 Attachment C: Manuscript Proposal

Study Group Name:
Proposed Manuscript Title:

Principal Investigator/Principal Author:

PI Contact Information:

Proposed/Target Journal(s):

Proposed date of submission of first draft for review by MaRS: _____

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	Site	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.

5.4 Attachment D: Abstract Analysis Proposal

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 DCC statistician if needed.

Aims/Hypotheses:

Design:

Analysis Plan:

5 CPRN Data Access Procedures

Data Access	Version Changes Approved by the Executive Committee 5/31/2017

5.1 Overview

The purpose of this policy is to describe how CPRN data are accessed.

5.2 Data Access

5.2.1 General Principles

The CPRN members own all research data that originates from any CPRN protocol. Non-CPRN members may not access data produced from a CPRN study. A Public-Use Dataset (PUD) will be created when required by a granting agency or when the CPRN Executive Committee deems that a PUD would serve the best interests of the network and the CP community.

5.2.2 Individual Site Clinical Data Access

5.2.2.1 Each participating CPRN clinical site can access its institution's Registry data at any time with a request to the Data Coordinating Center (DCC) who will provide the requested data set. Data should be requested at least 2 weeks prior to the date that is needed.

5.2.2.2 Each participating CPRN clinical site cannot access and/or publish their own site specific data that are part of a multi-center investigation unless the analyses of the primary outcome(s) of the investigation have been completed and a proposal for the use of the data has been approved (see Chapter 4 Protocol Development).

5.2.3 Multi-center Data Access

5.2.3.1 Study Principal Investigator (PI) can collaborate with the DCC to analyze multi-center data at the time(s) specified in the statistical analysis plan of the protocol. This may include phone calls, email, dedicated sessions via remote meeting software, and/or PI visits to the DCC.

5.2.3.2 CPRN members can propose analyses of multi-center data after the primary analysis is complete. An approved proposal is required (Chapter 4 Protocol Development).

5.2.3.3 If a non-CPRN member who is working at a CPRN clinical site with the CPRN site PI would like to conduct research within the CPRN or access CPRN data, permission must be obtained by a vote of the CPRN Investigator Committee. The site PI is responsible for submitting this protocol and supervising the research. See Chapter 4 Protocol Development for details.

5.3 Analysis Procedures

5.3.1 Analysis Plan

The analysis plan is stated in the protocol submitted by the Study PI. The protocol will specify the timing, frequency, and types of analyses to be conducted. The DCC will collaborate with the Study PI as required to complete the analyses.

5.3.2 Data Locking

After enrollment of the study has been completed, or at the time specified in the statistical analysis section of the protocol, the data set will be locked. To ensure data integrity for main CPRN studies, the data can only be accessed at the time points outlined in the statistical analysis plan of the protocol. The data lock ensures that the required queries have been completed and the data have been verified and are correct.

5.3.3 Data Analysis location

After completion of the data lock, the Study PI can collaborate with the DCC for data analysis. Raw, multi-center data will not be exported from the DCC. Rare exceptions to this could be submitted for consideration by the Executive Committee in situations where special expertise is required that is not available at the DCC.