NIH StrokeNET
Acute Stroke Working Group:

October 7, 2015

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Acute WG Members

Pooja Khatri (Chair – U-Cinci)
Jeff Saver (Co-Chair - UCLA)

RCC REPS

- Azam Syed Ahmed (UW-Madison)
- Ed Jauch (MUSC)
- Brett Meyer (UCSD)
- J Mocco (Mt Sinai)
- Kiva Schindler (Emory)
- Lee Schwamm (MGH)
- Phil Scott (U-Mich)
- Cathy Sila (Case Western)
- Wade Smith (UCSF)
- Michel Torbey (OSU)

OTHERS

- Bill Barsan (ex officio member from NETT)
- Joe Broderick (StrokeNET PI)
- Scott Janis (NINDS)
- Renee Martin (DCC)
- Max Wintermark (Imaging Advisory Group)

Working Group Role RECAP

1. To provide **scientific and design input** to the PPIs regarding trial concepts prior to submission to NINDS for concept approval when requested by NINDS or directly by PPIs

2. To provide **feasibility assessment** of NINDS-approved concepts when activated by NINDS
    1. Estimate how many subjects StrokeNET can enroll per year at how many sites?
        - Use survey data for hard numbers and then make further calculations based on epidemiology assessment, literature, and clinical judgment
    2. Provide those recs to the StrokeNET Executive Committee

3. To **assess gaps in the field and provide guidance** regarding Acute Stroke clinical trial issues (including potentially growing clinical trials to fill those gaps from within StrokeNET)

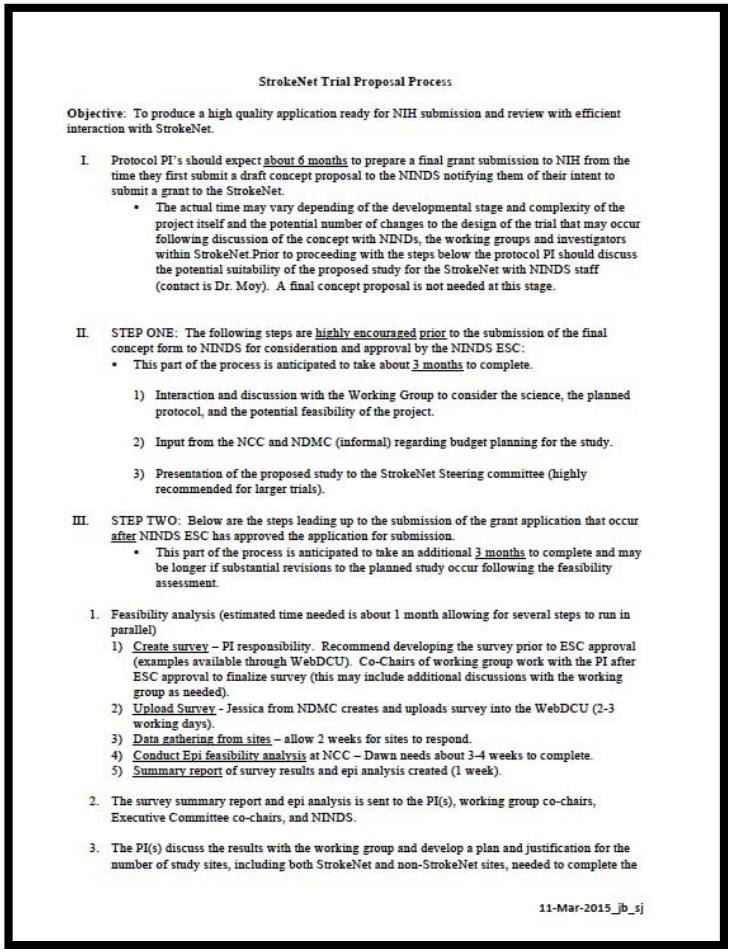
SPECIFIC ACTIVITIES

February, 2015 to October, 2015

Process Discussions

- Feedback/input to Joe/Scott about integrating WG feasibility process with PI and StrokeNET grant submission processes
  - March 2, 2015
  - May 4, 2015
- WG roles in funded trials
  - Aug 3, 2015

"StrokeNET Summary of Trial Proposal Process"



StrokeNet Trial Proposal Process

Objective: To produce a high quality application ready for NIH submission and review with efficient interaction with StrokeNet.

I. Protocol PI's should expect about 6 months to prepare a final grant submission to NIH from the time they first submit a draft concept proposal to the NINDS notifying them of their intent to submit a grant to the StrokeNet.
- The actual time may vary depending of the developmental stage and complexity of the project itself and the potential number of changes to the design of the trial that may occur following discussion of the concept with NINDs, the working groups and investigators within StrokeNet.Prior to proceeding with the steps below the protocol PI should discuss the potential suitability of the proposed study for the StrokeNet with NINDS staff (contact is Dr. Moy). A final concept proposal is not needed at this stage.

II. STEP ONE: The following steps are highly encouraged prior to the submission of the final concept form to NINDS for consideration and approval by the NINDS ESC:
- This part of the process is anticipated to take about 3 months to complete.

1) Interaction and discussion with the Working Group to consider the science, the planned protocol, and the potential feasibility of the project.

2) Input from the NCC and NDMC (informal) regarding budget planning for the study.

3) Presentation of the proposed study to the StrokeNet Steering committee (highly recommended for larger trials).

III. STEP TWO: Below are the steps leading up to the submission of the grant application that occur after NINDS ESC has approved the application for submission.
- This part of the process is anticipated to take an additional 3 months to complete and may be longer if substantial revisions to the planned study occur following the feasibility assessment.

1. Feasibility analysis (estimated time needed is about 1 month allowing for several steps to run in parallel)
   1) Create survey – PI responsibility. Recommend developing the survey prior to ESC approval (examples available through WebDCU). Co-Chairs of working group work with the PI after ESC approval to finalize survey (this may include additional discussions with the working group as needed).
   2) Upload Survey - Jessica from NDMC creates and uploads survey into the WebDCU (2-3 working days).
   3) Data gathering from sites – allow 2 weeks for sites to respond.
   4) Conduct Epi feasibility analysis at NCC – Dawn needs about 3-4 weeks to complete.
   5) Summary report of survey results and epi analysis created (1 week).
2. The survey summary report and epi analysis is sent to the PI(s), working group co-chairs, Executive Committee co-chairs, and NINDS.
3. The PI(s) discuss the results with the working group and develop a plan and justification for the number of study sites, including both StrokeNet and non-StrokeNet sites, needed to complete the

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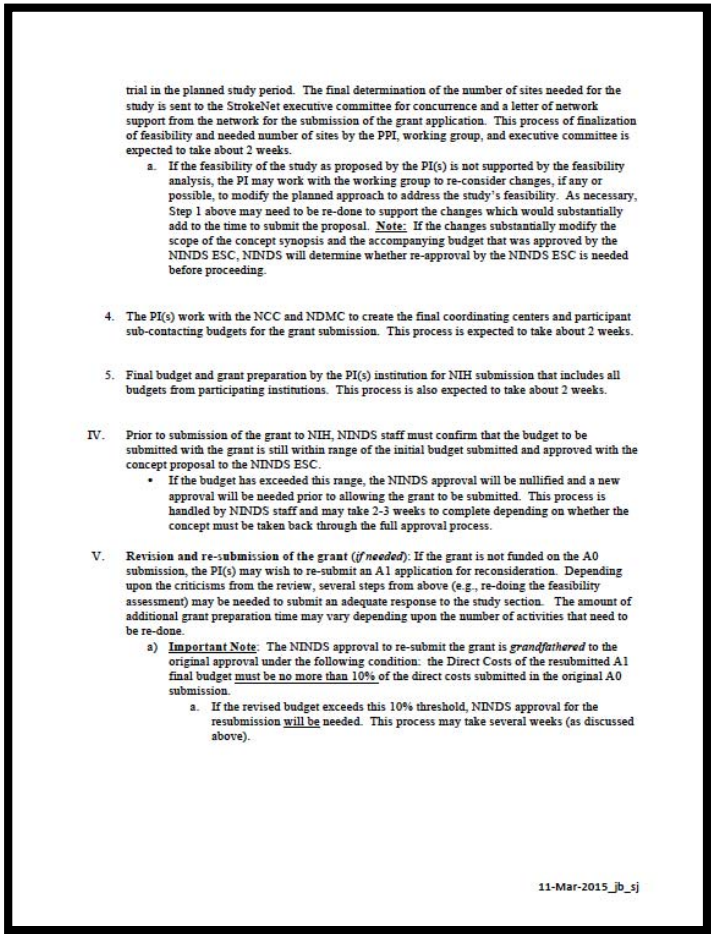

trial in the planned study period. The final determination of the number of sites needed for the study is sent to the StrokeNet executive committee for concurrence and a letter of network support from the network for the submission of the grant application. This process of finalization of feasibility and needed number of sites by the PPI, working group, and executive committee is expected to take about 2 weeks.
   a. If the feasibility of the study as proposed by the PI(s) is not supported by the feasibility analysis, the PI may work with the working group to re-consider changes, if any or possible, to modify the planned approach to address the study's feasibility. As necessary, Step 1 above may need to be re-done to support the changes which would substantially add to the time to submit the proposal. Note: If the changes substantially modify the scope of the concept synopsis and the accompanying budget that was approved by the NINDS ESC, NINDS will determine whether re-approval by the NINDS ESC is needed before proceeding.

4. The PI(s) work with the NCC and NDMC to create the final coordinating centers and participant sub-contacting budgets for the grant submission. This process is expected to take about 2 weeks.

5. Final budget and grant preparation by the PI(s) institution for NIH submission that includes all budgets from participating institutions. This process is also expected to take about 2 weeks.

IV. Prior to submission of the grant to NIH, NINDS staff must confirm that the budget to be submitted with the grant is still within range of the initial budget submitted and approved with the concept proposal to the NINDS ESC.
- If the budget has exceeded this range, the NINDS approval will be nullified and a new approval will be needed prior to allowing the grant to be submitted. This process is handled by NINDS staff and may take 2-3 weeks to complete depending on whether the concept must be taken back through the full approval process.

V. **Revision and re-submission of the grant** (*if needed*): If the grant is not funded on the A0 submission, the PI(s) may wish to re-submit an A1 application for reconsideration. Depending upon the criticisms from the review, several steps from above (e.g., re-doing the feasibility assessment) may be needed to submit an adequate response to the study section. The amount of additional grant preparation time may vary depending upon the number of activities that need to be re-done.
   a) **Important Note**: The NINDS approval to re-submit the grant is *grandfathered* to the original approval under the following condition: the Direct Costs of the resubmitted A1 final budget must be no more than 10% of the direct costs submitted in the original A0 submission.
      a. If the revised budget exceeds this 10% threshold, NINDS approval for the resubmission will be needed. This process may take several weeks (as discussed above).

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WG Role in Funded Trials

- Email (below) went out about WG role in funded trials and is listed below for reference
  - The appropriate working group (acute/prevention/recovery) and other relevant committees (such as endovascular, imaging, etc) will provide their input regarding protocols to study teams to help make them as feasible as possible as quickly as possible.
  - Design/implementation planning/decisions (i.e., governance) will be led by the individual trial's Steering Committee with related discussions on the StrokeNET Operations Committee.
  - Joe Broderick will sit on the steering committees of all funded trials as the point person from the StrokeNET/NCC side (and will designate others if we eventually have too many trials).
  - Implementation or strategic issues for which the steering committee of the trial would like input will be brought to the StrokeNET Executive Committee.
    - Specific questions during initiation or conduct of the trial that could use further input will be brought to individual committees, (such as the appropriate working group, minority recruitment committee, imaging committee, endovascular committee, etc) as appropriate.

Trial Reviews

- Pre-Concept-Approved Phase
  - **I WITNESS**: Lee Schwamm, Shlee Song, Steve Warach, Ona Wu and Larry Latour (5/4/2015)
- Feasibility Assessment Phase
  - **DEFUSE 3**: 2nd round for March resubmission (2/6/2015)
  - **IMPACT**: October Submission (7/20/2015)
  - **PreLIMBS**: October Submission (9/2/2015)
- Funded Trial Phase
  - **DEFUSE 3:** Protocol Input (8/3/2015)

SAH Trials Landscape

- Subcommittee: Wade Smith, Lee Schwamm, J Mocco
- Reviewed completed and ongoing SAH trials, and proposed areas of interest for further investigation
- Presentation – 8/17/2015

ACTION PLAN:
--Next call, feasibility of preLIMBS. Take that as Launchpad and then doing a SAH survey.
--Consider getting a StrokeNET fellow to drive this to further the educational value.
--Pooja will touch base with Scott Janis and Joe Broderick to fill them in on this discussion

Other Updates

- Acute Working Group minutes are posted on StrokeNET website.
- Please feel free to contact us with any questions or suggestions.
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  - JSaver@mednet.ucla.edu