Grant Number: 1U01NS086872-01 REVISED

Principal Investigator(s):
Joseph Paul Broderick, MD

Project Title: NSTN National Clinical Coordinating Center

Christine C. Jones
Sponsored Research Services
University of Cincinnati
51 Goodman Drive, Suite 530
Cincinnati, OH 452210222

Award e-mailed to: ospaward@uc.edu

Budget Period: 09/30/2013 – 07/31/2014
Project Period: 09/30/2013 – 07/31/2018

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF CINCINNATI in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number U01NS086872. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with 42 CFR Part 50 Subpart F. Subsequent to the compliance date of the 2011 revised FCOI regulation (i.e., on or before August 24, 2012), Awardees must be in compliance with all aspects of the 2011 revised regulation; until then, Awardees must comply with the 1995 regulation. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

James Washington
Grants Management Officer

Additional information follows

SECTION I – AWARD DATA – 1U01NS086872-01 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$754,509
Fringe Benefits	$260,798
Personnel Costs (Subtotal)	$1,015,307
Consultant Services	$82,839
Supplies	$10,000
Travel Costs	$133,546
Other Costs	$18,300
Consortium/Contractual Cost	$366,968
Federal Direct Costs	$1,626,960
Federal F&A Costs	$845,231
Approved Budget	$2,472,191
Federal Share	$2,472,191
TOTAL FEDERAL AWARD AMOUNT	$2,472,191

AMOUNT OF THIS ACTION (FEDERAL SHARE) $0

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$2,472,191	$2,472,191
2	$2,367,154	$2,367,154
3	$2,347,302	$2,347,302
4	$1	$1
5	$1	$1

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Number:	93.853
EIN:	1316000989A1
Document Number:	UNS086872A
Fiscal Year:	2013

IC	*CAN*	*2013*	*2014*	*2015*	*2016*	*2017*
NS	8472428	$2,472,191	$2,367,154	$2,347,302	$1	$1

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: VIVALJCT / **OC**: 414L / **Released**: WASHINGTOJ 09/27/2013
Award Processed: 09/27/2013 07:05:00 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1U01NS086872-01 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 1U01NS086872-01 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.

d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at 'http://grants.nih.gov/grants/policy/awardconditions.htm' for certain references cited above.)

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase V Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the Central Contractor Registration. Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Treatment of Program Income:
Additional Costs

SECTION IV – NS Special Terms and Conditions – 1U01NS086872-01 REVISED

This revision rescinds the restriction for consultant work in Canada. Funds awarded are now available for expenditure.

THE PREVIOUS TERMS AND CONDITIONS STATED BELOW REMAIN IN EFFECT EXCLUDING THE RESTRICTIVE TERM.

This award provides funding for the "NSTN National Clinical Coordinating Center."

RESTRICTION: Funds for this award are restricted pending certification of IRB approval. No funds may be drawn down from the payment system and no obligations may be made against federal funds for any research involving human subjects in this project pending NINDS acceptance of the certification of IRB approval.

RESTRICTION: This award is being made without foreign clearance for consultant work in Canada. Funds awarded for this activity are restricted and may not be used for any other purpose without foreign clearance approval and notification by NINDS staff.

This award includes funds for twelve months of support. The competing budget period is awarded for less than 12 months. Future year budget periods will start on AUGUST 1. Allowable preaward costs may be charged to this award, in accordance with the conditions outlined in the NIH Grants Policy Statement (revised October 2012) and with institutional requirements for prior approval. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/nihgps_2012/index.htm

The funds in this award shall not be used to pay the salary of an individual at a rate in excess of Executive Level II ($179,700 in Fiscal Year 2012) per year. See NIH Guide Notice: NOT-OD-12-035 http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-035.html

This award includes funds awarded for consortium activity. Funds awarded for consortium/contractual costs for participating clinical centers may be re-budgeted between sites in accordance with expanded authorities but may not be used for any other purpose without the written prior approval of NINDS staff. Consortia are to be established and administered as described in the NIH Grants Policy Statement (NIH GPS). The referenced section of the NIH Grants Policy Statement is available at: http://grants.nih.gov/grants/policy/nihgps_2012/index.htm

STROKE NETWORK NATIONAL CLINICAL COORDINATING CENTER (NCC) SPECIAL TERMS - 1 U01 NS086872-01 PI: Broderick, J.

Of the $2,472,191, awarded in year -01, a total of $1,854,143 is currently available for expenditures necessary for establishing and maintaining the infrastructure for a Stroke Network Regional Coordinating Center. The balance of funds for year -01 ($618,048) is restricted from expenditure until the following milestone progress has been approved by the NINDS program official:

1. Execution of a Master Trial Agreement with each of the Stroke Network Regional Coordinating Centers (RCC) and their identified performance sites.
2. Executed Reliance Agreements with RCCs and their identified performance sites for a central IRB.
3. Implementation of an Operations Committee and a Steering Committee with representation from the National Data Management Center, RCCs and NINDS
4. Development of Standard Operating Procedure (SOPs) with the RCCs.
5. Development of SOPs with the Clinical Coordinating Center of the Neurological Treatment Trials Network (NETT) for the conduct of shared trials between the Stroke Network and NETT.

The initial award will be committed for three years in order to demonstrate Network feasibility. The amount of the award in future years may be prorated depending on the number of active protocols and unexpended funds available.

Future funding will require the annual submission of the Non-Competing Continuation Progress Report form (PHS 2590, revised 11/2007). The current form with instructions may be found at http://grants2.nih.gov/grants/funding/2590/2590.htm. This progress report is required three months prior to the end of each budget period and should be submitted to the centralized receipt center at the address below:

Division of Extramural Activities Support, OER National Institutes of Health
6705 Rockledge Drive, Room 2207, MSC 7987
Bethesda, MD 20892-7987 (for regular or US Postal Service Express mail) Bethesda, MD 20817 (for other courier/express mail delivery only)

During the third year of the award, the Principal Investigator will submit an application for an Administrative Continuation for the remainder of the original total budget. A draft of this application (items 2-5 below) should be sent to the NINDS program official by November 1, 2015.

Two months prior to the end of the third year budget period, the following should be submitted to the Grants Manager listed below:

1. A letter co-signed by the Business Official and Principal Investigator requesting an additional two years of support;
2. PHS 2590 Application Face Page;
3. A progress report summary for the current budget period;
4. A one-page research plan for the additional five years; and
5. A budget and justification using Page EE of the PHS 398 (budget for entire proposed period of support including F&A costs.)

NINDS staff will review these documents administratively. Approval will be contingent upon a demonstrated ability to provide clinical research resources and participation in Stroke Network research projects. While a decision to continue funding will be based on the overall success of the Network, the decision to continue with funding of this specific grant will be based on performance including, but not limited to:

1. Central IRB review within 2 months following NINDS Council approval of each protocol.
2. Start-up time on average for first three stroke trials less than 6 months from trial award/NGA to first patient, first visit.
3. For the first 3 trials, at least 50% of RCCs initiated the study within 4 months following issuance of trial award/NGA.

In future years, awards under the Streamlined Non-competing Award Process (SNAP) must submit a non-competing application via the eRA Commons by the 15th of the month preceding the month in which the budget period ends. The non-competing application can be submitted using the Research performance Progress Report (RPPR) format via the RPPR link in eRA Commons. NIH expects to require use of the RPPR for most SNAP awards in the Spring of 2013. See Guide Notice: NOT-OD-12-142 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-142.html)

To register to use the Commons go to https://commons.era.nih.gov/commons/. Questions regarding the Commons should be addressed to Commons Support at 1-866-504-9552 or commons@od.nih.gov.

Non-SNAP applications should be submitted via RPPR if available, or to the centralized receipt center:

Division of Extramural Activities Support, OER
National Institutes of Health
6705 Rockledge Drive, Suite 5016 Room 5218C , MSC 7987
Bethesda, MD 20892-7987 (for regular or US Postal Service Express mail)
Bethesda, MD 20817 (for other courier/express mail delivery only)

Other documents applicable to this grant should be faxed to (301) 451-5635 or mailed to:

Grants Management Branch
National Institutes of Neurological Disorders and Stroke
6001 Executive Boulevard, Suite 3290, MSC 9537
Rockville, MD 20852 (Express Mail)
Bethesda, MD 20892-9537 (Regular Mail)

For additional information, you may access the NIH home page at http://www.nih.gov/ and the NINDS Home Page at http://www.ninds.nih.gov

NINDS Stroke Trials Network – National Clinical Coordinating Center (NCC)
Cooperative Agreement Terms of Award 1U01 NS086872-01 PI: Broderick, J.

The administrative and funding instrument used for this project is a cooperative agreement U01, an "assistance" mechanism (rather than an "acquisition" mechanism) in which substantial NIH scientific and/or programmatic involvement with the recipient of the U01 (Awardee) is anticipated during performance of the activity.

The NINDS purpose is to support and/or stimulate the Awardee(s)'s activity by involvement in and otherwise facilitating the activity in a "partner" role, but avoiding a dominant role, direction, or prime responsibility. Consistent with this concept, the dominant role and prime responsibility for the activity resides with the Awardee for the project as a whole, although specific tasks and activities in carrying out the studies will be shared among the Awardee and the NINDS Program Directors.

The terms and conditions below elaborate on required actions and responsibilities, and specific to these Terms of Award, Awardee agrees to these collaborative actions with the NINDS Program Directors toward achieving the project objectives. It is anticipated that these terms and conditions will enhance the relationship between the NINDS and the Awardee, and will facilitate the successful conduct and completion of all studies conducted within the network.

These special Terms of Award are in addition to and not in lieu of otherwise applicable OMB administrative guidelines, DHHS Grant Administration Regulations at 45 CFR Parts 74, and other DHHS, PHS, and NIH Grant Administration policy statements.

A. Awardee Rights and Responsibilities

The Awardee, through the NCC Program Director/Principal Investigator (PD/PI) has primary authority and responsibility for providing overall scientific and administrative leadership for the Stroke Network, including implementation of studies, coordinating a central Institutional Review Board (IRB) , establishing Master Trial

Agreements with the Regional Coordinating Centers (RCC) and all satellite sites, monitoring site performance and quality control, preparing publications and presentations, and collaborating with Stroke Network
investigators and interacting with other Investigators, unless otherwise provided for in these terms or by action of the Steering Committee.

The Master Trial Agreements must include the conditions and obligations from these Terms of Award and must be applicable to any site participating in a Stroke Network study including, but not limited to, conditions related to data sharing and access, publication, and intellectual property (NINDS may request review of a Master Trial Agreement prior to its execution). Exceptions or additions to such activities can be made by the Network Steering Committee (SC).

The Awardee will manage and conduct the NINDS funded Network clinical trials (or "studies") in compliance with all established DHHS, NIH, NINDS policies and procedures. The Awardee will be responsible for protecting patient safety and obtaining adequate patient recruitment to complete the study. It is the Awardee's responsibility

1) to ensure that all sites engaged in research involving human subjects have an appropriate OHRP-approved Assurance and an IRB approval of the research consistent with 45 CFR Part 46 and (2) to retain documentation of
compliance with the requirements of 45 CFR Part 46. It is the responsibility of the Awardee to comply with any FDA policy and regulations as relevant to all clinical trials and as published at 21 CFR Parts 50 and 312.

1. Data Rights

Data collected from all sites participating in any Stroke Network clinical trial will be submitted to the Stroke Network Data Management Coordinating Center (DCC). In general, sites own the data generated at their site. Except as provided in these Terms of Award, the Awardee is free to copyright without NINDS approval when publications, data, or other copyrightable works are developed under this grant. If research findings result in inventions, Awardee has the right to retain title to these inventions, pursuant to the Bayh-Dole Act of 1980 as implemented in 37 CFR 401, for their utilization, commercialization, and public availability and Executive Order 12591.

Rights to data, including software developed under the terms of this cooperative agreement, shall remain with the Awardee except that any such copyrighted material shall be subject to a royalty-free, nonexclusive and irrevocable license to the Government to reproduce, publish or otherwise use the material, and to authorize others to do so for Federal purposes.

If any non-academic, commercial, advocacy, or philanthropic entity ("Third Party") is involved in any Stroke Network protocol, the Third Party will be provided a copy of the study data and such access will be through NINDS or its agent. The Third Party will be free to utilize data internally for its own purposes, including internal research and business and regulatory purposes. A Third Party's ability to transfer data to others, publish, or otherwise use study data, will be established under an agreement between the Third Party and NINDS.

2. Intellectual Property Rights

Support or other involvement of a Third Party in any study may be advantageous and appropriate.

Under the Bayh-Dole Act (see 35 USC 201 *et. seq.*) and 37 Code of Federal Regulations Part 401, Awardee has the right to elect full title to any invention they discover in the performance of a study under NINDS funding, provided that neither NINDS nor the Third Party(if involved) shares ownership of the invention by virtue of co-inventorship.

B. NINDS Staff Responsibilities

An NINDS Program Director, Scott Janis, PhD, will be the Project Scientist for the Stroke Network. He will have substantial scientific-programmatic involvement during implementation of the Stroke Network and the conduct of all trials performed using the network, including technical assistance, advice, and/or other coordination above and beyond normal program stewardship for grants. The Project Scientist will function as one of the co-investigators, collaborating and interacting as necessary with the Principal Investigator in accomplishing the overall goals of the Stroke Network. The Project Scientist, on behalf of the NINDS, will serve on the Steering Committee for the Stroke Network, and will have the same access, privileges and responsibilities regarding the collaborative data as the other members of the Steering Committee.

In addition, the Project Scientist or other NINDS Program Directors may serve on other study committees regarding recruitment, intervention, follow-up, quality control, adherence to protocol, assessment of problems affecting a study and potential changes in the protocol, interim data and safety monitoring, final data analysis and interpretation, preparation of publications, and development of solutions to major problems such as insufficient participant enrollment.

A second NINDS Program Director, Joanna Vivalda, will be the Program Official for the Stroke Network. She will provide normal program stewardship as carried out for grants and will serve on the Stroke Network committees as deemed appropriate.

A change in the PD/PI key personnel at the Awardee institution requires the prior approval of the Program Official. NINDS must be sent the biographical sketch of the new investigator or key personnel 30 days prior to the changes along with confirmation that he/she has completed the NIH-required training in human subjects' protection.

The NINDS G**rants Management Specialist** is responsible for the negotiation, award and administration of this project and for interpretation of grants administration policies and provisions. Members of the grants management staff and the NINDS Office of Clinical Research will assure prudent stewardship of funds in compliance with relevant policy and regulation. These individuals work together in overall project administration. For up-to-date information, you may access the NIH home page at http://www.nih.gov/ and the NINDS home page at http://www.ninds.nih.gov.

C. NINDS Stroke Trial Network Committee Structure

1. An **Operations Committee** will consist of the Program Director/Principal Investigator (PD/PI) of the NCC who will serve as the chair, a co-PD/PI, if designated, the PD/PI of the DCC, the NINDS Project Scientist and selected RCC PD/PI's or their designees. The Operations Committee will oversee all the Stroke Network's activities and monitor performance. It is anticipated the Operations Committee will meet via weekly telephone conference calls.

2. A **Steering Committee (SC)** will consist of the PD/PI of the NCC and DCC, the NINDS Project Scientist, and a representative group of RCC PD/PI or their designees. The Steering Committee will be the main governing body of the Stroke Network's scientific operation and conduct. Working groups will be established on an as-needed basis to develop and oversee the implementation of specific protocols, and to provide in-depth evaluation and recommendations on such issues and publications/presentations, quality control, conflict of interest, and per -patient budgets.

- All major decisions will be determined by majority vote of the SC;
- It is anticipated that the SC will meet at least monthly by telephone conference call (potentially more frequently during the start-up phase of the Stroke Network) and 1-2 times per year by in-person meetings;
- SC working groups will be established by the SC to perform specific functions, such as:

Developing network stroke trial applications for grant submission;

Developing protocol concepts;

Finalizing protocols for funded studies;

Reviewing the feasibility of trial applications submitted to NINDS from both inside and outside the network;

Facilitating the execution of newly-funded or on-going NINDS-funded stroke trials;

Producing and submitting publications;

Developing per-patient budgets;

Assuring quality control;

Monitoring conflicts of interest;

Developing data sharing policies.

- Awardees will be required to accept and implement policies approved by the SC.
- Independent of the governance above, the NINDS Director retains responsibility for all NINDS funded research. The Director's authority overrides SC decisions made on behalf of the Stroke Network.

As noted under Section B, above, the NINDS Project Scientist, on behalf of the NINDS, will have the same access, privileges and responsibilities regarding the collaborative data as the other members of the Steering Committee. Subcommittees will be established as it deems appropriate; the NINDS Project Scientist and other Program Directors may serve on subcommittees, as appropriate.

3. Prior to submission of an application for a study to be performed in the Stroke Network, a **Protocol Working Group (PWG)** will be convened to collaborate with the PI of the proposed study (Protocol PI) to develop the Clinical Protocol and associated budget. PWG membership will consist of the Protocol PI and appropriate representatives from the DCC, NCC, and NINDS.

4. A **Scientific Advisory Board (SAB)** is an external group of experts appointed by NINDS who will review the network program and provide feedback to the NINDS Meetings will be held at least annually but can be convened as needed to address specific issues. RCC investigators and NCC staff may be asked to provide information about NINDS Stroke Network progress and participate in these meetings.

D. Collaborative Responsibilities

1. Protocol Selection

Over the next 5-year project period, the Stroke Network is expected to initiate approximately 4-5 NINDS-funded exploratory phase 1 and 2 stroke clinical trials and 2-4 phase 3 trials. The exact number of protocols supported will depend on the nature and extent of the investigations proposed and the availability of funds. Projects proposed to be conducted through the Stroke Network may come from the collaboration of investigators within the network, from investigators outside of the network, or from a n agreement between the NINDS and an industry partner. The Stroke Network may also be used to conduct NINDS-funded projects that were initiated before it was established.

The SC will develop and maintain Protocol Submission Standard Operating Procedures that will be publicly available to assist investigators interested in collaborating with the Stroke Network.

All protocol documents, including Investigator's Brochures, are confidential and must not be shared or distributed without the permission of NINDS. Investigators may conduct non-clinical studies such as analytical assays and ancillary correlative studies in conjunction with the protocol, if such non-clinical studies are approved by NINDS and company (if involved) prior to commencement.

2. Agent Selection

A clinical trial may utilize an agent **(drug, biologic, device, or other technology)** which is proprietary to a Third Party (defined above under A (1)). In this circumstance, NINDS will negotiate and execute an agreement with the Third Party for the clinical co-development of the agent. This agreement may be a Cooperative Research and

Development Agreement (CRADA) but other agreement types may be utilized. In such cases, the NCC will transfer the agent attained by NINDS under the partnership agreement to the RCC and the satellite sites. The Third Party involved may have a representative on the Protocol Working Group created to develop the agent- specific study.

3. **Master Agreement and Budget Planning**

Funding for this award covers clinical coordinating costs for all activities related to coordinating at least 6-8 clinical trials for the Stroke Network. These activities include: start-up activities; regulatory approvals; Stroke Network meetings, SC and other leadership committee functions; communication, documentation and reporting required to operate a central IRB of record; study drug management; collecting regulatory documents; working with potential network investigators in the protocol conception development and implementation phases; administrative tasks related to subcontracting with the RCC and satellite sites, monitoring recruitment and protocol adherence, and tracking and reporting performance; travel costs for at least two NCC team members to attend SC meetings in Bethesda, MD three times each year, plus other travel related to network operations, including at least one visit to each RCC throughout the funding period, for training purposes, plus up to two annual trips to DSMB meetings.

The NCC will be responsible for fiscal oversight for overall project finances and protocol-specific funding. The actual per-patient compensation to the sites (for enrolling patients and for collecting data) for each trial to be conducted within the network will be provided by separate sources of funding. Additional costs of performing trials within the Stroke Network may be supported by payments to the NCC) from individual trial budgets. The NCC will develop a Financial Policy for NINDS approval that specifies budgeting guidelines for Stroke Network studies (industry and non-industry trials) including monitoring, reconciliation and reporting plans that incorporates the following guidelines:

The NCC will enter a Master Trial Agreement with each RCC and satellite site so that the per-patient cost associated with specific Stroke Network protocols can be efficiently administered.

- Direct costs for approved Stroke Network trials are supported by grants from NINDS or other funding sources,

- The NCC will receive no Indirect Costs (facilities and administrative costs) on funds distributed to Stroke Network sites for protocol-specific patient costs. If non-Network sites are added to a trial, the NCC will receive indirect cost on the first $25,000 of the total non-Network sites consortium cost only (not per subcontract).

- The NCC will distribute the per-patient cost to the Stroke Network sites as total fixed unit basis. To take into account differences in indirect rates across clinical centers, the NCC will determine a low, moderate and high indirect tier for sites and include a fixed percentage of indirect costs (uniform within that tier) in the total cost.

- Protocol-specific funds will be designated by the NCC using unique sub-project grant numbers. RCC and satellite l sites will be assigned distinctive purchase order numbers and program codes.

4. **Site Selection**

The NCC will disseminate Stroke Network protocols to all clinical sites to allow sites the option to participate in each Stroke Network-supported study. The NCC will report site participation in Stroke Network-supported studies on a Stroke Network website.

The NCC is responsible for ensuring the clinical sites follow approved protocols and maintain quality control of data and ensure participant safety. Any problems concerning the compliance of clinical sites in the protocol or quality control of data should be reported immediately to the Administrative Program Official.

For those clinical trials supported by a Third Party, the NCC must obtain the written documentation or agreement from all participating sites that they will abide by the terms of the agreement between a Third Party and NINDS, including but not limited to special publication procedures and data sharing as well as the intellectual property options found above in C (2). **Collaborations with a Third Party may have unique conditions, so the RCC, as well as the satellite sites, should confirm the details of each collaboration with NINDS.**

5. **Central IRB**

In collaboration with the NINDS, the NCC will implement all procedures required to establish and implement a Central IRB for all Stroke Network trials. This includes coordinating a central IRB of Record and managing all required IRB communication and documentation including, but not limited to, tracking approval, maintaining regulatory documents, communicating with RCC and satellite site IRBs, and handling adverse event reporting and notifications. The RCC PI is responsible for complying with Central IRB requests (through the NCC) and implementing the approved protocol, including obtaining informed consent for all study participants at the satellite sites

6. **Data and Safety Monitoring**

NIH requires oversight and monitoring of all human intervention studies to ensure the safety of participants and the validity and integrity of the data. This policy is in addition to any monitoring requirements imposed by 45 CFR Part 46, the FDA, or the NIH Guidelines for Research Involving Recombinant DNA Activities.

As needed, an independent Data and Safety Monitoring Board (DSMB) will be appointed according to NINDS policy and procedures. The DSMB, established by the NINDS, will meet at least twice annually for the purpose of monitoring the conduct of Stroke Network clinical trials. The Protocol Principal Investigator, in conjunction with staff of the DCC, will provide any data requested by the DSMB for review.

The DSMB will meet via teleconference and in person as necessary to review the research protocols and plans for data and safety monitoring; to assist in the development of monitoring guidelines; to evaluate the progress of the trial, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, and participant risk/benefit changes; to oversee adherence to the protocol and maintenance of data confidentiality; to review safety data, including adverse events and reportable events; and to make recommendations regarding the continuation, modification, or conclusion of the study. Proposed protocol changes and manuscripts/abstracts must be approved by the DSMB.

The DSMB monitoring function is above and beyond that traditionally provided by IRBs; however, the Central IRB must be cognizant of the procedures used by DSMBs. The DSMBs will provide periodic reports to investigators for transmittal to the local IRBs. (Refer to ttp://grants.nih.gov/grants/guide/notice-files/not98-084.html and http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

7. **Publication**

Publication guidelines will be established by the Steering Committee. Investigators are encouraged to publish and to publicly release and disseminate results, data and other products of the Stroke Network clinical trials as

determined in collaboration with the SC. All publications must acknowledge the contributions of NINDS, the Stroke Network and, if applicable, a Third Party.

In studies where a Third Party is in partnership with NINDS for a proprietary agent, all manuscripts, whether individual or cumulative, should be provided to NINDS prior to submission for immediate delivery to the involved Third Party for its advisory review and comment. A Third Party will have a pre-determined period of time from the date of receipt for review. The Third Party may request a delay in the submission in order to ensure that its confidential and proprietary data, in addition to any intellectual property rights, are protected. All abstracts and posters will be provided to NINDS two weeks prior to submission to facilitate a short review period by the Third Party.

Specific data sharing policies will be developed in accordance with NINDS policy and NIH Guidelines. At the conclusion of each trial, the data will be put in a form suitably formatted for deposit in a national archive. The data will be made publicly available as determined by the SC with NINDS approval.

8. **Third Party Access**

Without prior authorization from NINDS, a Third Party is not permitted to contact any Stroke Network site directly to obtain protocol information, to arrange on-site data audits, or to discuss any other protocol or amendment matters. NINDS will contact the NCC and RCC to discuss the nature of a request by a Third Party for direct contact prior to authorizing the Third Party to make such contact. Awardee will reasonably cooperate with NINDS to accommodate a Third Party's need to audit raw data and source documents to the extent necessary to verify compliance with FDA Good Clinical Practices and the protocol.

E. Dispute Resolution

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between Awardee and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel composed of three members will be convened: a designee of the Executive Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two.

This special dispute resolution procedure does not alter the Awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.

F. Survival of Terms

The terms in this agreement about data, company access, publication and confidentiality issues will survive beyond the terms of this award until notification otherwise from NINDS.

It is the responsibility of the Awardee to comply with any FDA policy and regulations as relevant to this project and as published at 21 CFR Parts 50 and 312.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project

administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Elizabeth E Conklin
Email: conklinee@ninds.nih.gov **Phone**: 301-496-7480

Program Official: Joanna Vivalda
Email: joanna.vivalda@nih.gov **Phone**: 301-496-9135

SPREADSHEET SUMMARY
GRANT NUMBER: 1U01NS086872-01 REVISED

INSTITUTION: UNIVERSITY OF CINCINNATI

Budget	***Year 1***	***Year 2***	***Year 3***	***Year 4***	***Year 5***
Salaries and Wages	$754,509	$772,183	$770,436		
Fringe Benefits	$260,798	$268,179	$266,179		
Personnel Costs (Subtotal)	$1,015,307	$1,040,362	$1,036,615		
Consultant Services	$82,839	$64,445	$64,445		
Supplies	$10,000	$14,124	$14,124		
Travel Costs	$133,546	$119,324	$127,058		
Other Costs	$18,300	$18,300	$11,000	$1	$1
Consortium/Contractual Cost	$366,968	$367,180	$367,180		
TOTAL FEDERAL DC	$1,626,960	$1,623,735	$1,620,422	$1	$1
TOTAL FEDERAL F&A	$845,231	$743,419	$726,880		
TOTAL COST	$2,472,191	$2,367,154	$2,347,302	$1	$1

Facilities and Administrative Costs	***Year 1***	***Year 2***	***Year 3***	***Year 4***	***Year 5***
F&A Cost Rate 1	58.5%	58.5%	58%		
F&A Cost Base 1	$1,444,840	$1,165,732	$1,253,242		
F&A Costs 1	$845,231	$681,953	$726,880		
F&A Cost Rate 2		58%			
F&A Cost Base 2		$105,976			
F&A Costs 2		$61,466			