

PARTICIPANT AGREEMENT

This Interventional Stroke Therapy Outcomes Registry (“**INSTOR III™**”) Participant Agreement (hereinafter the "Agreement") is made and entered into as of the ____ day of _____ 20__ (“Effective Date”), by and between the NeuroVascular Research Foundation (“NVRF”), with offices at 436 Inspiration Lane, Gaithersburg, MD 20878 and _____ (“Participant”), located at _____.

NVRF and Participant shall herein be referred to as a “Party” or collectively as the “Parties.”

RECITALS:

A. NVRF, a 501 (c) (3) non-profit foundation, established **INSTOR III** for the purpose of collecting observational data from licensed health care providers relating to treatment for acute stroke for hospital Quality Assurance purposes, and in order to improve treatment outcomes and benefit the public good. **INSTOR III** fulfills the requirements specified by all major medical associations involved in stroke care, including the American Academy of Neurology, the American Association of Neurological Surgeons, the Society of NeuroInterventional Surgery, the Society of Vascular and Interventional Neurology, the American Society of Neuroradiology, and the Society of Interventional Radiology, as well as the American Stroke Association.

B. Participant is a licensed healthcare provider administering treatments and providing care for patients suffering from acute stroke, and enrolled in **INSTOR III** through this binding Agreement.

C. NVRF wishes to collect observation data in **INSTOR III** from Participant according to the terms and conditions of this Agreement, and Participant wishes to provide observational data to NVRF for use in **INSTOR III**.

D. As explained in The NeuroVascular Research Foundation Overview (the “Overview”), a copy of which is attached as Exhibit A, **INSTOR III** is not, and is not intended to be, a clinical trial subject to any governmental or regulatory control or obligation. **INSTOR III**, and any results from **INSTOR III**, is not intended to support approval of any product claim or indication.

COVENANTS:

NOW, THEREFORE, for and in consideration of the mutual covenants and promises of the Parties, and for other good and valuable consideration the receipt and sufficiency of which are acknowledged, Participant and NVRF hereby agree as follows:

1. Commitments of Parties: NVRF shall make available a data collection document (the “Data Collection Form” or “DCF”) via the Internet at the **INSTOR III** website, the address of which shall be provided to the Participant by NVRF. Following all applicable Health Insurance Portability Accountability Act (HIPAA) requirements, NVRF shall restrict access to the **INSTOR III** section of the website to authorized Participants who have access to only their own data. NVRF shall control access to **INSTOR III** by assigning authorized Participants a unique identification code (“Participant Code”) and HIPAA-compliant password known only to NVRF and Participant. Participant shall use reasonable efforts, for each stroke patient treated, to enter

and submit the observational patient treatment and clinical outcome data (the “Data”) requested on the DCF, as soon as, and when possible, within fifteen (15) days, of patient's hospitalization, procedure or medical care treatment.

2. Representations and Warranties of Parties: Parties further agree, represent and warrant that:
- a) The Parties have full power and authority to enter into this Agreement, to execute and deliver the documents and instruments required of the Parties herein, and to perform all obligations hereunder; and that such execution, delivery and performance by Parties does not (i) violate any provision of any law, governmental rule or regulation currently in effect, (ii) violate any judgment, decree, writ, injunction, award, determination or order currently in effect that names or is specifically directed at the Party or its property, and (iii) require the consent, approval, order or authorization of, or any filing with or notice to, any court or other governmental authority.
 - b) To the knowledge of the Parties, no pending or threatened litigation exists which if determined adversely would restrain the consummation of the transactions contemplated by this Agreement or would declare any of the Party’s obligations or covenants illegal, invalid or non-binding.
 - c) Participant and its employees, advisors, representatives and agents possess any and all licenses, permits, qualifications, skills, training and experience required to perform the treatments and to provide the care services required by patients, in accordance with any and all applicable laws and the highest standards expected of physicians or health care providers providing similar services.
 - d) Participant shall abide by good clinical practices (GCP'S) and shall use best efforts to ensure that all Data submitted shall be entered accurately and further, Participant shall not misrepresent, falsify, modify or otherwise intentionally misstate the Data.
 - e) Participant shall enter into this Agreement, perform its duties and obligations hereunder and otherwise participate in **INSTOR III** in accordance with any and all applicable local institutional review board ("IRB") or ethical committee ("EC") procedures. The treatments under discussion in this outcomes data registry are performed in recognition of the fact that “compassionate” or “emergency” therapy is carried out in accordance with “best clinical judgment” and in accordance with appropriate informed consent as required by local hospital regulations, and which are applicable under these emergency clinical circumstances.
 - f) Participant shall comply with all applicable federal, state and local laws, rules, regulations and guidelines, including, but not limited to, any such applicable laws, rules, regulations and guidelines concerning data submission of this nature.
 - g) NVRF shall comply with all applicable federal and state laws, rules, regulations and guidelines concerning data collection of this nature, which shall include the secure collection, storage, retrieval, and reporting of such data, including all appropriate provisions of the Health Insurance Portability Accountability Act (HIPAA).
 - h) All Data that Participant provides to **INSTOR III** shall be blinded, and to the extent possible, non-patient identifiable information. All patient Data shall be coded using a non-descript, non-meaningful code system prior to submission and known only by Participant. Participant shall be responsible for establishing and maintaining the non-descript codes that identify the patient only to the Participant. All Data entered to the

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DCF shall use these codes. Participant shall not provide NVRF or **INSTOR III** any “Personal” information, which includes but is not limited to such information as the patient’s name, social security number, hospital number, medical record number, chart number, or other personal information which identifies the individual, or from which an individual’s identity can be reasonably ascertained by NVRF or any party other than Participant.

- i) Participant shall obtain any and all consents, permissions or licenses required by law or otherwise from each patient with respect to whom Participant intends to submit Data. Participant agrees to retain all such consents, permissions or licenses for one year following the termination of this Agreement, and shall make such records available for inspection within a reasonable time of the receipt of notice from NVRF.
 - j) In the event that NVRF or any other party associated with NVRF or **INSTOR III** is exposed to or receives Protected Health Information, (i) NVRF shall use reasonable efforts to maintain the confidentiality of such Protected Health Information, except to the extent applicable law requires disclosure, and (ii) Participant hereby agrees to indemnify and hold NVRF harmless from and against any and all losses, costs, damages, fines or expenses (including without limitation, attorney’s fees) from any failure by Participant to have obtained all consents, permissions or licenses required by law from such patient.
 - k) Participant shall provide to NVRF and **INSTOR III** any and all Data pertaining to Adverse Events as specified in the DCF.
3. Data Collection Process and Training: Upon enrollment, NVRF will provide training via telephone or video conferencing using a training database. When Participant has completed the training program and is ready to begin entering Data, NVRF will assign Participant a Participant Code as described herein, and an initial password to access the DCF. Participant agrees to change the password immediately upon accessing the DCF and to comply with all NVRF and HIPAA requirements to protect Participant’s secure login and password information. All Data entered to **INSTOR III** shall be entered under the Participant Code. Participant shall use the DCF only for collecting the Data. All data entered by Participant is immediately available to Participant and retrievable at any time.
4. Registry Fees: Participant will pay NVRF an Annual Fee for each participating site according to the schedule attached hereto as Exhibit B. Fees will be billed upon enrollment and sixty (60) days prior to the expiration of the annual term. Payment of the annual fee entitles Participant to training and ongoing user support, to access **INSTOR III** and input Data, to view outcome data reports online in real time for Participant’s Data, to download Participant’s data in a spreadsheet format, and to view cumulative population outcome reports. For additional fees, Participant may receive assistance with special data reports or analysis of their data. The Annual Fee is non-refundable.
5. Adverse Event Reporting: Participant shall report all Adverse Events in strict accordance with local institutional requirements. Adverse Event reporting using the DCF shall not and is not intended to be, a substitute for reporting of Adverse Events to governmental agencies by the Participant as may be required by any federal statute or regulation, and NVRF shall not assume any such reporting responsibility on behalf of any party by including Adverse Event reporting in **INSTOR III** procedures. Information reported by Participant to **INSTOR III** solely in compliance with federal statute or regulation regarding Adverse Events shall not become part of **INSTOR III**.

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6. Confidentiality: All information, written, oral or electronic (including but not limited to any and all information on paper, electronic, magnetic or optical media) transmitted by either Party and its authorized representatives, agents, consultants, employees and/or its designees to the other Party and/or Party's representatives, agents, consultants, employees and/or its designees, shall be treated as strictly confidential and shall not be disclosed without the express prior written consent of the transmitting Party. This provision shall not apply to Data compiled in the database population, as documented in Section 7, below. This provision shall not apply to information which: (i) at the time of disclosure is in the public domain; (ii) after disclosure, becomes part of the public domain by publication or otherwise, not due to any unauthorized act by either Party; (iii) was in the Party's lawful possession prior to disclosure of the information to the other Party; (iv) is lawfully disclosed to the Party by a third party having a legal right to so disclose and such third party not being under any obligation to keep such information confidential. The Parties agree that any and all confidential information received under this Agreement shall only be used (1) in the conduct of **INSTOR III** business and the evaluation of its results, and (2) as may be required to comply with legal or regulatory requirements. The Parties shall be entitled to disclose confidential information where required by law or legal process, but in such event shall use reasonable efforts to give the other Party advance notice thereof and shall cooperate at their own expense with any efforts undertaken by the other Party to secure confidential treatment for same.
7. Data Ownership. Participant shall be the sole owner with respect to its individual Data, except that to the extent information regarding individual patients has been provided to NVRF under this Agreement, all rights, title and interest in and to the compilation of the Data in the **INSTOR III** database shall be the property solely of NVRF. Participant hereby irrevocably grants to NVRF a paid-up, perpetual license to incorporate Participant's Data into the **INSTOR III** database in aggregate form and into reports, publications, documentation and other media and materials created or derived from the **INSTOR III** database. The intent of use of this data is for hospital quality improvement as used by participant as well as eventual increased knowledge and improvement of patient clinical outcomes. **INSTOR III** will not identify the sources of the compiled data without the express written permission of Participant. The compilation of data generated during the course of **INSTOR III** and any new inventions, discoveries, or improvements developed or conceived by NVRF related to **INSTOR III**, shall belong solely and exclusively to NVRF and Participant shall execute and deliver, without further compensation, any documents required to effect, perfect, or record NVRF's ownership.
8. Connection to **INSTOR III**: NVRF makes no warranty, expressed or implied, regarding connection or access to the **INSTOR III** website and database. It shall be the responsibility of Participant to obtain and maintain appropriate equipment, hardware, software and service providers to access the **INSTOR III** website in a manner sufficient to support the input of data to the DCF. NVRF shall use reasonable efforts to maintain the **INSTOR III** website and the operation thereof, but Participant acknowledges that events beyond the control of NVRF or its agents may impact access to the site.
9. No Liability for Medical Care: It is understood that participation in **INSTOR III** is wholly (i) voluntary and (ii) limited to the provision of observational data. Participant agrees and acknowledges that its participation in **INSTOR III** is not intended to in any way influence or inform any patient's medical care. Accordingly, Participant agrees that NVRF shall have no responsibility or liability with respect to patient's medical care or treatment under any circumstances, including, without limitation, any claim or action for malpractice against Participant, and Participant agrees to indemnify and hold NVRF harmless and defend NVRF and NVRF's trustees, directors, officers, employees and agents from and against any and all demands, claims, losses, costs, damages, liabilities or expenses (including without limitation, attorney's fees) incurred or paid as a result of any such claim.

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10. Term and Termination. This Agreement shall continue until terminated or until **INSTOR III** is closed, whichever first occurs. The Parties each have the right to terminate this Agreement, with or without cause, upon thirty (30) days notice to the other Party (the "Effective Date of Termination"). NVRF has the right to discontinue data collection with respect to all or part of **INSTOR III** at anytime, and NVRF may thereafter terminate this Agreement by notice to Participant. Participant shall have no recourse against NVRF by virtue of NVRF's discontinuance of data collection related to all or part of **INSTOR III** and any termination of this Agreement by NVRF as a result thereof.
11. Acknowledgment of No Clinical Trial. Participant expressly acknowledges and agrees that **INSTOR III** is not, and is not intended to be, a clinical trial subject to any governmental or regulatory control or obligation. **INSTOR III** and any results from **INSTOR III** are not intended to support approval of any product claim or indication.
12. Advertising and Promotion: No press release, advertising, promotional written literature or oral statements in connection with or alluding to **INSTOR III** or this Agreement, or the relationship between the Parties, shall be made by either Party without the prior written approval of the other Party. Notwithstanding this clause, Participant grants NVRF the right to include Participant's facility in a list of **INSTOR III** references, which will be available on the **INSTOR III** website. Participant and NVRF may agree on general statements that could be included in written literature, presentations, or press releases regarding participation in **INSTOR III**, which may be used without further approval of the other Party. In the event the Parties do agree on such statements, the Party releasing such statement shall immediately notify the other party of such use.
13. Entire Agreement; Amendment. This Agreement embodies the entire agreement between the Parties and supersedes all prior agreements and understandings, if any, relating to **INSTOR III**, and may be amended or supplemented only in writing executed by the Party intending to amend the Agreement.
14. Assignment. This Agreement may not be assigned or otherwise transferred by either Party without the prior written consent of the other Party, which consent shall not be unreasonably withheld.
15. Relationship of Parties. The relationship of the Parties to this Agreement is that of independent contractors and not that of master and servant, principal and agent, employer and employee, or partners. Participant understands that NVRF shall not be responsible for any acts of Participant and that Participant shall not have authority to speak for, represent, or obligate NVRF in any way without the prior written consent of NVRF.
16. Waiver. A Party shall not, by any act, delay, omission or otherwise be deemed to have expressly or implicitly waived any of its rights, powers and/or remedies unless such waiver shall be express and in writing. A waiver by either Party of any of the terms or conditions of this Agreement in any one instance shall not be deemed or construed to be a general waiver of such term or condition or waiver in any other instance.
17. Severability. If any provision of this Agreement is held to be illegal, invalid, or unenforceable under present or future laws, such provision shall be fully severable. The Agreement shall be construed and enforced as if such illegal, invalid, or unenforceable provision had never comprised a part of this Agreement; and the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid, or unenforceable provision or by its severance from this Agreement. In lieu of such illegal, invalid, or unenforceable provision, there shall be added automatically as a part of this Agreement a provision as similar in terms to

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such illegal, invalid, or unenforceable provision as may be possible to make such provision legal, valid, and enforceable.

18. Survival. The provisions of Sections 5, 6, 7, 9, 11, 12, 16, and 17 shall survive any termination of this Agreement.
19. Notices. All notices and demands of any kind in connection with this Agreement shall be in writing delivered by hand, first class certified or registered mail, return receipt requested, or by recognized national overnight delivery service to the other Party at the address appearing at the end of this Agreement. Service of such notice or demand shall be deemed complete on the day of actual delivery. A Party may designate a different mailing address or different person to which all further notice or demands shall thereafter be addressed with written notice to the other Party.

IN WITNESS WHEREOF, intending to be legally bound, the Parties have executed this Agreement, effective as of the date first written above.

"Participant"

"NeuroVascular Research Foundation"

By: _____
(Signature)

By: _____
(Signature)

Printed: _____

Printed: _____

Title: _____

Title: _____

Date: _____

Date: _____

Address: _____

Address: 436 Inspiration Lane

Gaithersburg, MD 20878

Telephone: _____

Telephone: 1 (877) 4INSTOR
1 (877) 446-7867

Fax: _____

Fax: 1 (301) 869-5225

Exhibit A

The NeuroVascular Research Foundation

The NeuroVascular Research Foundation (NVRF), a 501 (c) 3 non-profit, was formed in 2001 by J. J. Connors M.D. NVRF was created specifically to demonstrate that endovascular therapies for stroke treatment and stroke prevention could produce dramatic patient benefits. In order to document clinical outcomes, as well as procedural details, this data is captured in on-line databases (registries). **INSTOR III™** (*the **IN**terventional **ST**roke **Therapy **OUT**comes **REG**istry***) is the first interventional/endovascular stroke therapy registry in the world. **INTRASTOR™** (*the **IN**TRcranial **A**ngioplasty and/or **ST**enting **OUT**comes **R**egistry*) was created to evaluate intracranial angioplasty for the prevention of stroke.

Registries, now mandated by most medical societies involved in emergency stroke care (eg. the American Academy of Neurology, the American Association of Neurological Surgeons, the Society of NeuroInterventional Surgery, the Society of Vascular and Interventional Neurology, the American Society of Neuroradiology, and the Society of Interventional Radiology) as well as by the American Stroke Association, are used for Quality Assurance and Quality Improvement purposes by participating hospitals. **INSTOR III™** and **INTRASTOR™** are HIPAA compliant, secure, password-protected, encrypted registries that allow tracking of clinical outcomes and procedural details as well as anonymous benchmarking with other sites performing similar therapies. This not only allows confidential internal quality assessment and quality improvement operations within participating hospitals, but also allows aggregate evaluation of trends in overall stroke care and clinical outcomes, something that has never before been possible in the United States.

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Overview

Medical and interventional therapy of acute ischemic stroke is undergoing rapid change. In addition to the medical necessity of treating stroke effectively and efficiently, newly trained physicians are enthusiastic to treat acute stroke. However, medical knowledge cannot keep pace with new abilities, devices, techniques, or pharmaceutical agents. At present there is inadequate knowledge concerning the optimal appropriate device, technique, drug, dose, patient population or timing for emergency interventional stroke therapy even though there is increasing acknowledgment of the profound patient benefits achievable with this therapy.

PROACT II (Prolyse for Acute Thromboembolism) was the first blinded randomized endovascular trial for treatment of acute ischemic stroke and the outstanding clinical benefits were reported in 1998. The FDA has now approved the Merci retriever and the Penumbra aspiration system specifically for use in acute ischemic stroke, thus revolutionizing the treatment of stroke. While further trials are now underway, there are far more patients being treated in the United States that have no data collected at all on the specific treatment or the clinical outcomes.

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INSTOR III™ (the **IN**terventional **S**troke **T**herapy **O**utcomes **R**egistry) is a HIPAA compliant, encrypted, online database intended for internal hospital Quality Assurance and performance benchmarking against a national aggregate. It is not possible for an internal hospital database alone to perform this function. The following medical or industry associations specifically recommend or require a registry such as **INSTOR III™**

A. The American Academy of Neurology, the American Association of Neurological Surgeons, the Society of NeuroInterventional Surgery, and the Society of Vascular and Interventional Neurology state: *"All centers should participate in and enroll all stroke patients in available national stroke registries or multicenter stroke trials."* (Performance and Training Standards for Endovascular Ischemic Stroke Treatment. Meyers PM, Schumacher HC, Alexander MJ, et al. Journal of Stroke and Cerebrovascular Diseases, Vol. 18, No. 6 (November-December), 2009: pp 411-415.)

B. The American Society of Neuroradiology and the Society of Interventional Radiology state: *"Outcomes must be tracked and recorded. Submission of outcomes to a registry with national participation (e.g., INterventional Stroke Therapy Outcomes Registry (INSTOR III) is required."* (Training Guidelines for Intra-arterial Catheter-directed Treatment of Acute Ischemic Stroke: A Statement from a Special Writing Group of the Society of Interventional Radiology. Connors JJ, Sacks DS, Black CM, et al. J Vasc Interv Radiol 2009; 20:1507–1522.)

C. The American Stroke Association states: *"To facilitate data collection in a standardized way and to avoid the redundant efforts that would occur if CSCs designed their own databases, we expect that CSCs will make use of national databases or registries to collect data required for metrics and to collect additional detailed data that will assist in quality improvement, some of which we have noted in the additional data elements discussed above."* (Leifer DL, Bravata DM, Connors JJ, et al. Metrics for Measuring Quality of Care in Comprehensive Stroke Centers: Detailed Follow-Up to Brain Attack Coalition Comprehensive Stroke Center Recommendations. Stroke. 2011;42:849-877)

INSTOR III™ fulfills the requirements published by these organizations. **INSTOR III™** is not, nor is intended to be, a clinical trial and is not subject to any regulatory control or obligation, similar to "Get With The Guidelines" for either heart or stroke. Results from **INSTOR III™** are not intended to support approval of any product claim or indication.

Registry Objectives

The primary objective is to acquire data concerning the safety and efficacy of evolving stroke therapies and allow hospitals to track and improve their own healthcare delivery and quality of care. The "coin-of-the-realm" in acute stroke care is the 3-month clinical neurological outcome and is the primary clinical outcome for this registry.

Some of the specific objectives of **INSTOR III™** are:

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- Record the demographics, risk factors, clinical presentation, and methods used to diagnose patients with stroke and allow for risk-adjustment analysis
- Document treatment strategies, with particular emphasis on pharmacological and mechanical or technique-based interventions
- Evaluate the frequency of specific clinical events in relation to risk factors, diagnosis, and treatments provided
- Collect outcomes data on stroke patients both during initial hospitalization for stroke and at 3-months
- Provide the ability for participating health care providers to understand and visualize their own temporal trends in practice patterns and their relation to patient outcomes
- Facilitate quality assurance and continuing quality improvement efforts for stroke patients for hospitals
- Provide treatment and outcomes data to facilitate development and monitoring of standard procedures and treatment guidelines
- Provide data to allow institutions to determine the impact of differing evaluation, treatment, and management paradigms.

Methods

INSTOR III™ acquires HIPAA-compliant, anonymous, encrypted online data submitted by individual hospitals concerning acute stroke patients and their treatments (both intravenous and endovascular) for the purpose of internal hospital Quality Assurance and Quality Improvement. **INSTOR III™** allows confidential comparison by the hospital to pre-selected data points for QA benchmarking. **INSTOR III™** performs statistical analysis of the data immediately upon entry and the processes and clinical outcomes data is accumulated over time for the institution. Anonymous comparative data is available instantly to the participating hospitals on a continuing basis.

Purpose

The purpose of **INSTOR III™** is to assist in Quality Assessment, Quality Improvement, and Performance benchmarking for hospitals treating stroke, and in particular, for Comprehensive Stroke Centers. The eventual goal of this database is to improve patient care by providing a tool for hospital Quality Assurance and improving clinical outcomes by: 1) assessing the impact of clinical decisions on patient outcomes, 2) evaluating the care delivery process, both individually and collectively, and 3) provide feedback for optimal critical pathways for treating stroke patients. The purpose of **INSTOR III™** is to help physicians and hospitals provide the most appropriate and cost-effective care for optimal outcomes in patients with stroke. Secondly, **INSTOR III™** fulfills the requirements of the American Stroke Association as well as numerous medical societies including the American Academy of Neurology, the American Association of Neuroradiology, the Society of NeuroInterventional Surgery, the Society of Interventional Radiology, and the Society of Vascular and Interventional Neurology.

Exhibit B

Enrollment

| | |
|---------------------|---------------|
| Annual Fee: | \$2,500.00 |
| Implementation Fee: | <u>500.00</u> |
| First Year Total: | \$3,000.00 |

Renewal

| | |
|-------------|------------|
| Annual Fee: | \$2,500.00 |
|-------------|------------|

Please make checks payable to: [NeuroVascular Research Foundation](#)

Discounts

NVRF offers discounts for hospitals enrolling for multiple years or hospitals or health systems enrolling multiple facilities. Contact NVRF for additional details.