National Institutes of Health (NIH) Biomarkers for Vascular Contributions to Cognitive Impairment and Dementia Consortium (MarkVCID)

1. Charter Rationale and Basic Principles

In response to a call from the National Institute of Neurological Disorders and Stroke (NINDS), in collaboration with the National Institute on Aging (NIA), for a multisite consortium dedicated to developing and validating biomarkers for small vessel disease (SVD)-related vascular contributions to cognitive impairment and dementia (VCID), the MarkVCID Consortium was established. MarkVCID consists of major medical research institutions and one Coordinating Center. The goal of MarkVCID is to generate a suite of validated biomarkers ready for application to clinical trials aimed at identifying disease-modifying therapies for VCID.

The guiding approach of MarkVCID is for its research to be **openly shared** both within and outside the MarkVCID consortium to the greatest extent practical. New initiatives and internal and external collaborations are encouraged. As such, MarkVCID investigators are broadly entitled access to share MarkVCID data, samples, analytic tools, and other resources.

Data and samples will also be shared with external collaborators, openly and without embargo, in compliance with consortium external data sharing policies to the greatest practical extent. Publications resulting from the use of MarkVCID data will acknowledge the MarkVCID consortium.

This charter describes the MarkVCID philosophy and rules of consortium interaction.

2. Leadership and Consortium Structure

MarkVCID is a federated consortium of research centers with a Coordinating Center that provides organizational expertise to the consortium. The Coordinating Center operates in conjunction with the Consortium Steering Committee and six subcommittees comprising representatives from each participating research site, an External Advisory Committee, and NINDS leadership. The primary decision-making bodies for MarkVCID are its committees.

2.1. Committees and Subcommittees

2.1.1 Steering Committee

The Consortium Steering Committee (CSC) is responsible for the overall scientific direction of MarkVCID. This committee serves as the chief policy and decision-making body for MarkVCID. The CSC's overarching goal is to inform data-driven selections by the NINDS of candidate biomarkers for consortium-wide validation studies and to determine the steps required to move these biomarkers into small- and large-scale interventional trials. The CSC has teleconferences at monthly to bi-monthly intervals in which subcommittee and Coordinating Center progress is presented and subcommittee recommendations reviewed and decided upon. Conference calls are chaired by the Coordinating Center PI and consist of the PI of each of the participating sites or designated substitute, NIH/NINDS representatives, and the Directors of the Administrative and Data Cores. Additional external members are invited to participate on an *ad hoc* basis at the request of committee members. Decisions are made through majority vote, with each research site having one vote (the Coordinating Center and NINDS leadership are nonvoting members), though in general the chair's goal is to achieve unanimous consensus.

2.1.2. Subcommittees

Consortium subcommittees are formed around six critical scientific and administrative areas: 1) Clinical & Cognitive Data; 2) Imaging-Based Biomarkers; 3) Fluid-Based Biomarkers; 4) Protocol, Recruitment, Diversity & Retention; 5) Postmortem Procedures & Analysis; and 6) Sharing. These subcommittees focus on developing standardized protocols and procedures in their domain (see details below) and make recommendations to the Steering Committee. Each subcommittee consists of an investigator from each of the research sites, the Coordinating Center PI, NIH/NINDS members, Directors of the Administrative and Data Cores, and additional members of the Coordinating Center as appropriate. For each subcommittee, there is a Coordinating Center and a research site member lead. Decisions are made by similar rules as the CSC, with one vote per research site, majority rule, and a goal of unanimous consensus. Subcommittees meet at a frequency determined by the subcommittee according to topics addressed and associated milestones. For specific issues not covered by the Consortium's subcommittees, the Steering Committee may establish additional working groups.

Clinical & Cognitive Data Subcommittee is responsible for identifying clinical measures to make biomarker data applicable to potential VCID trials enrolling diverse all-comer populations by refining phase I common core data elements, trainings, and data collection efforts.

Imaging-Based Biomarkers Subcommittee is responsible for refining imaging protocols and manuals to support four imaging biomarker kits, overseeing site certification through training and implementation of harmonized kit protocols, and reviewing incoming site data for acquisition, de-identification, transfer, and upload issues.

Fluid-Based Biomarkers Subcommittee is responsible for refining and overseeing implementation of current biosample collection, shipping, and storage best practices, validation efforts, and analyses to support fluid biomarker kit; and reviewing proposals requesting MarkVCID biosamples based on scientific priority and sample scarcity.

Protocol Recruitment, Diversity & Retention Subcommittee is responsible for harmonizing protocol operations (MOP), developing uniform informed consent guidelines, inclusion/exclusion criteria, facilitating site IRB submission, and strategizing the recruitment monitoring and evaluation process to ensure the consortium meets enrollment and diversity targets.

Postmortem Procedures Subcommittee is responsible for establishing procedures for obtaining brain donation consent, collection and storing tissue; and identifying related core data elements including post-mortem imaging and autopsy data.

Sharing Subcommittee is responsible for reviewing publications and internal and external proposals requesting the use of imaging, clinical, and biofluid data with the goal to ensure consortium data and samples continue to be openly shared to the greatest practical extent.

2.1.3. External Advisory Committee

NINDS has established an External Advisory Committee (EAC) comprising prominent investigators in fields relevant to vascular contributions to cognitive impairment and dementia. The Committee assists in determining the broad direction of the Consortium. Independently of the CSC, the External Advisory Committee also provides input to the NINDS regarding which candidate biomarkers to move forward in multi-site biomarker validation studies. EAC members may participate in the annual meetings as well as additional ad hoc teleconferences and provide feedback regarding progress and issues that arise.

2.2. Coordinating Center

Day-to-day business of the Consortium is overseen by the Coordinating Center PI, Administrative Core Director, and Data Core Director. The Administrative Core is responsible for organizing, coordinating, and administratively driving Consortium activities. The Data Core is responsible for creating and maintaining the consortium data platforms and for administration, correspondence, and dissemination of MarkVCID data and information; the Core also consists of a biostatistics team that will guide the statistical analyses plans of each proposed biomarker.

2.3. Research Site

Participating research sites agree to follow standardized protocols and procedures and contribute data to MarkVCID's shared database, and, by contributing data, agree to the sharing policy of the Consortium. Research site PIs attend annual Consortium-wide meetings, serve as members of the Steering Committee, and attend all Steering Committee calls. The Research Site PIs assign a site member to all subcommittee meetings and ensure site attendance by assigning a second delegate as necessary.

3. Membership, Agreements, and Duties

3.1. Membership: All investigators and collaborators working or contributing as part of a research site or the Coordinating Center are considered members of MarkVCID.

All subcommittee/committee members will agree to perform all duties of said committees including regular participation in scheduled meetings, participation in decision making processes, and voting.

3.2. Research Sites: Research sites may be added to the MarkVCID Consortium upon review and approval from the CSC and NINDS.

3.3.1 Data Sharing: All MarkVCID research sites will sign consortium research agreements governing the sharing of data and agree to adhere to the spirit and letter of these documents. Data deposited into MarkVCID data systems by the research sites will be collected, stored, and shared with all members of MarkVCID, in accordance with the rules and regulations outlined in the MarkVCID research agreement. Data will be shared with external investigators after review and approval according to the MarkVCID Data Sharing, Analysis, and Publications Policy. Data distributed by MarkVCID cannot be redistributed without formal MarkVCID review and approval.

3.3.2 Data Analysis and Publications: All MarkVCID members are subject to the MarkVCID Data Sharing, Analysis, and Publications Policy. Participation in the MarkVCID project is explicit acceptance of the authorship and publication policies.

3.4. Reporting: All MarkVCID investigators agree to provide all expected reports including transition reports in a timely fashion as required by NINDS, and contribute to joint reports due to NINDS and other oversight bodies when necessary.

3.5. Conflict Resolution: The Steering Committee, in consultation with the External Advisory Committee, will settle disputes arising from MarkVCID activities with direct dialogue and mediation when possible. When this is not possible, a dispute resolution panel composed of three members (one member each from the CSC, NINDS, and EAC) will settle the dispute by a majority vote. This decision can be appealed in accordance with PHS regulation 42 GFR Part 50, subpart D and DHHS regulation 45 CFR part 16.

3.6. Charter Amendment: This MarkVCID consortium charter can be amended by agreement of the CSC and NINDS.