CHARTER

SICKLE CELL DISEASE IN AFRICA NETWORK

(SCD IN SSA SICKLEINAFRICA CONSORTIUM)

JUNE 2021

REVISED 16 May, 2023

I. AUTHORITY

Under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Part 75.

II. PURPOSE

The purpose of the Consortium is to sustain, enhance and grow the Sickle Cell Disease (SCD) in Sub-Saharan Africa (SSA) research program and to promote and expand capacity building activities relevant to SCD in sub-Saharan Africa. Enhancement of network infrastructure and the addition of new participating sites will advance SCD-related epidemiologic, translational, and clinical research in the region while concurrently improving SCD care.

III. OBJECTIVES

The Sickle Cell Disease in Africa Network (SCD in SSA Network) referred to as Consortium, is funded by the NHLBI - NIH to realize the following objectives:

A. The program makes it possible to more accurately describe the current status of SCD as well as risk modifiers including access to care and clinical management in SSA countries, and provide comparative data to what is observed in the US and other countries.
B. This program supports the development and enrollment of SCD patients into a single patient-consented electronic registry.
C. This program supports cohort research studies that plan to follow SCD patients enrolled in the registry in the participating countries. These cohort research studies permit the evaluation of:
    i. the incidence of clinical events, such as pain crisis and acute chest syndrome (ACS);
    ii. the possible association with various factors including care and management, such as infection prophylaxis and hydroxyurea use, as well as socio-economic and environmental factors; and
    iii. the impact on health outcomes of improving the identification and care of patients with SCD that will have occurred during the follow-up period.
D. This program also anticipates supporting implementation science research studies to evaluate planned intervention(s), such as newborn screening, infection prevention or wider hydroxyurea use, to identify factors that impact uptake across multiple levels, including patient, provider, clinic, facility, organization, and often the broader community and policy environment.
E. This program also anticipates improving SCD standards of care.
F. This program will establish an SCD patient biorepository from the registry participants.

IV. DESCRIPTION OF CONSORTIUM

A. <u>Structure</u>

    i. Goal

The goals of this consortium will be achieved through a collaboration consisting of a Clinical Coordinating Center (CCC), a Data Coordinating Center (DCC), and up to six consortium sites in these countries: Ghana, Nigeria, Tanzania, Mali, Uganda and Zimbabwe with Zambia.

S/ No	Project Name/ Lead Affiliate	Country
1	Sickle Pan-African Research Consortium Clinical Coordinating Center (SPARCo CCC), Muhimbili University of Health and Allied Sciences (MUHAS)	Tanzania
2	University of Cape Town, Sickle Africa Data Coordinating Center (SADaCC)	South Africa
3imnnnnnnq2wq34eserdszdfgfdxnbvcf	Kwame Nkrumah University of Science and Technology	Ghana
4	SPARC-Net/ University of Abuja	Nigeria
5	SPARCo/ Muhimbili University of Health and Allied Sciences (MUHAS)	Tanzania
6	University of Mali	Mali
7	Makerere University	Uganda
8	SHAZ/ University of Zimbabwe and University Teaching Hospital of Zambia	Zimbabwe and Zambia

ii. Members and roles:

1. CCC;
    - Expanding a sickle hemoglobinopathy registry database to facilitate patient-tracking and follow-up and serve as a backbone for future SCD research.
    - Enhancing approaches to the development of regionally appropriate standards of SCD care, as well as the organization of research and clinical skill development activities.
    - Coordination of Consortium sites to allow for development, implementation, and conduct of SCD cohort studies, implementation research and the integration of SCD Management Guidelines into health-care system.

2. DCC;
    - To provide overall project coordination, administration, data management, and biostatistical support of the SCD in Sub-Saharan Africa Network.

3. Consortium Sites:
    - To implement and improve the sickle hemoglobinopathy registry/ database and updating the Consortium database elements, phenotype definitions, and ontologies
    - Engaging stakeholders for collaborative efforts and sustainability.
    - Instituting and successfully completing consortium research studies.

- Integrating the Consortium SCD Management Guidelines into national systems

B. Governance

Program governance will be provided by a collection of committees with specific structures and responsibilities.

i. Steering Committee

1. Composition
    - Chair: Two Co-chairs will be appointed by NHLBI and will not be affiliated with any of the currently funded Network sites.
    - Members consist of:
        - Principal Investigator of the CCC
        - Principal Investigator of the DCC
        - Principal Investigator from each Consortium site
        - NHLBI staff: Program Officer (PO), Project Scientist (s) (PS) and Grants Management specialist

2. Responsibilities
    - Serve as the main governing board and monitor research progress;
    - Facilitate coordination and synergy for the entire Program;
    - Develop recommendations for uniform procedures and policies;
    - Identify issues that have broad applicability across the program;
    - Determine research collaborations such as methodology, data, and core measures and assessments available;
    - Review the protocols and manual of procedures developed by the Consortium Sites Teams for scientific validity;
    - Establish subcommittees as needed and additional ad hoc committees as needed.

3. Operation
    - Meet via intermittent conference calls, generally once a month or more frequently, as needed;
    - By voting consensus; each of the two co-chairs, the CCC, DCC and each of the Consortium Siteh Teams has one vote and NHLBI has one vote;
    - When possible, the Steering Committee (SC) and SickleInAfrica Consortium meetings (held simultaneously), two times a year, in an African location;
    - Coordinated by the DCC

ii. Executive Committee

1. Composition
    - Chair: The same two Co-chairs for the Steering Committee. Co-chairs will not be affiliated with any of the currently funded Consortium sites.
    - Members consist of:

- Principal Investigator of the CCC;
- Principal Investigator of the DCC;
- NHLBI staff: Program Officer (PO) and Project Scientist(s) as well as the grant management specialist.

2. Responsibilities

- Provide scientific management, leadership, and overall governance of the Consortium by providing direction and oversight of the Consortium's activities.

3. Operation

- Meet via intermittent conference calls, generally once a month or more frequently, as needed;
- By consensus; if voting is needed, each Co-chair has one vote, the CCC and DCC each has one vote and NHLBI has one vote;
- Coordinated by the DCC.

iii. Publication Committee

1. Composition
   - Chair: Two co-chairs for the Steering Committee;
   - A primary member and alternate member from the CCC, DCC and each of the Consortium sites.
   - The Program Officer and Project Scientist(s) of NHLBI.
   - Subject expert\s as required.
2. Responsibilities
   - Review concepts for manuscripts, presentations or abstracts;
   - Review manuscripts, presentations or abstracts before submission or presentation;
   - Approve manuscripts, presentations or abstracts prior to submission or presentation.
3. Operation
   - Meet via conference calls;
   - Decision by consensus; if voting is needed, each Co-chair has one vote, the CCC, DCC and each of the Consortiumsites has one vote and NHLBI has one vote;
   - Coordinated by the DCC.

iv. Data and Safety Monitoring Board (DSMB)

1. Membership
   - Board members are appointed by NHLBI;
   - Board members have expertise in sickle cell disease, hematology, epidemiology, statistics and ethics;
   - Board members are independent from the SickleInAfrica.
2. Responsibilities
   - Review project protocols and their amendments

- Advise NHLBI on study feasibility, participant safety and burden, data monitoring, and successful achievement of milestones for each project;
- Provide recommendations to NHLBI regarding study continuation or modification;
- Meet at least twice a year to review all open protocols.

3. Management:
    - Coordinated by NHLBI;
    - The executive secretary chosen by NHLBI will develop a charter for the board;
    - Meet via conference calls and web-based systems;
    - All communications with the board need to go through the executive secretary.
    - Attendance will be determined by the consortium projects being reviewed. Representatives of the CCC and DCC will attend to facilitate consortium activities. consortium site investigators will attend as needed.

C. Policies

1. Communication and Coordination

Teleconferencing will be the primary medium for communication for committees, protocol teams, and working groups. The DCC, in collaboration with the CCC and the Co-Chairs of the Steering Committee, will prepare and distribute agendas and associated materials for these meetings, summarize the meetings with distribution of action items within 5 working days and minutes for approval by PIs, chairpersons and NHLBI within 10 working days. Protocols and database materials will be distributed to the appropriate parties using the same communication strategy.

Central to coordination of activities is a study website. A public facing website for dissemination purposes and an internal website with tabs for each Consortium Site will be maintained by the DCC. The public facing website will post a description of the program, a list of participating Consortium Sites, contact information, information regarding meetings, Consortium organization, governance, news items, publications and presentations.

The internal website will be used as repositories for study related materials. These will be password protected with different levels of access appropriate for a given user's role. For example, all sites in a multi-site study would be able to see case report forms (CRFs) and the protocol, but not see details about participants at other sites. DCC staff will be responsible for granting and maintaining appropriate access for users. Some content will be common across studies implemented by the network, such as information about inventories at shared sites, should such sites exist. Reports on enrollment and retention will be posted to the investigator website by site. The website for each study will be used for study documents (protocol, manual of procedures, CRFs), publications and presentations, meeting minutes, and a directory of collaborating investigators. The website will be automatically updated daily to reflect the current state of data collection and study documentation. There will also be a password protected portion of the website for materials that are relevant across projects. This will include action items, meeting minutes and other materials for executive and steering committee meetings.

Publications will be required to have a PubMed Central reference number to ensure they have been submitted to PubMed Central.

2. Protocol Review

Each NHLBI approved Consortium research project will be guided by a single protocol that governs study activities at all relevant Consortium sites. Protocols and amendments (i.e. modifications or any change beyond correction of typographical errors) will be reviewed by the following parties in the following order prior to the execution of any other study related activities:

1. Steering Committee
2. DSMB
3. Institutional review boards (IRB)/ethics committees

Protocols will be developed by a protocol team chaired by the project PI (or designee) with inclusion of appropriate members from the CCC and DCC. Following the protocol development by the protocol team, the protocol will be reviewed by the SC and EC members not on the protocol team, with the review focusing on the scientific merit and operational feasibility of the study design and approaches developed to answer the questions identified by projects. Reviews by the SC and EC will be coordinated by the DCC which will be responsible for compiling and summarizing comments received from the SC and EC in a written document that describes major issues that need to be addressed and minor issues. If major issues are identified, the protocol or amendments will need to be reviewed again by the SC and EC once the protocol team has revised the protocol to address comments. The "final" revised protocol (whether in response to minor and/or major comments) will need to be provided to the EC for a final review before being approved to be submitted to the DSMB and/or Ethics Boards.

When a protocol is submitted for initial review to the SC, the SC's review committees will have up to 1 month to review the protocol.

After a protocol or amendment has initial approval by the SC and EC to go forward, the members of the protocol team will present the protocol to the NHLBI DSMB in the open session of the meeting/call that will be set up by the NHLBI executive secretary for the DSMB The protocol (including the informed consent/assent forms) will need to be provided to the DSMB 3 weeks ahead of the DSMB meeting. The DSMB may have comments to be responded to ahead of or at the time of the meeting; ask for modifications to the protocol; and recommend whether the study should proceed or not. The DSMB will have open and closed sessions and may include executive sessions. Detailed responsibilities and review procedures will be explicitly described in the NHLBI DSMB charter which will be approved by the DSMB in its first meeting.

3. Creation of Additional Subcommittees

Additional subcommittees can be created to meet needs recognized by the SC as the program progresses. Any member of the SC can propose a subcommittee and the subcommittee will be established if there is consensus among the SC members. Specific rules regarding leadership, membership and responsibilities will be agreed to by the SC. This charter will be modified to include these descriptions of the subcommittee.

4. Data Management and Analysis

Reproducibility is one of the cornerstones of science. These policies aim to ensure analyses of data collected under the SCD in SSA initiative are reproducible. Two documents will need to be generated that help ensure this objective is met: a data management plan (DMP) and a statistical analysis plan (SAP). These policies largely apply to the activities of the DCC but if projects would like to conduct their own data analyses, these policies apply to those analyses. Any data

management and data analysis activities conducted by the projects will need review and approval from the DCC.

The DMP describes how data will be collected, what quality assurance procedures will be used to ensure high-quality data and how the data will be stored. This plan needs to include copies of data collection instruments (e.g. CRFs). The expectation is that data will be collected using systems at the research sites. The DCC will review this document and data collection can commence once approval is granted.

The SAP describes how the data described in the DMP will be analyzed with sufficient detail that an independent analyst can replicate the analysis. The DCC will generally draft SAPs for projects after completion of the protocol and the SAP will be finalized prior to database lock. DCC members will generally be responsible for carrying out the analyses described in the SAP. The DCC will review this document and data collection can commence once approval is granted.

Data sharing among SCD in SSA investigators needs to adhere to proper data security standards to protect the confidentiality of research subjects and otherwise follow best practices for electronic transmission of data. The format of the data file that will be shared and the manner in which it is shared needs to be specified prior to sharing of the data and data files that fail to meet this prearranged format will be returned to the sender with an indication of how the data has failed to meet the prearranged format. Exceptions can be made, but this will require negotiation with the DCC. The file specification will frequently involve de-identification of datasets but the exact definition of this needs to be prearranged.

5. Data Sharing

   The SCD in SSA project is committed to quickly sharing results and data. Papers will be submitted summarizing the primary results of the SCD in SSA studies once the analysis is complete. These results will be published in major scientific journals and presented at scientific meetings. Subsequent analyses will also be presented at national and international professional meetings. Intellectual property and data generated under this project will be administered in accordance with individual policies of the funded Institutions and NIH policies, including the NIH Data Sharing Policy and the NIH Public Access Policy. Publication of data shall proceed as scientifically appropriate and in accordance with procedures outlined in the International Committee of Medical Journal Editors' Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Upon acceptance for publication in a peer-reviewed academic journal, manuscripts will be submitted to PubMed Central.

   Should any genomic data be generated as a consequence of these studies, the PIs and collaborating investigators will abide by the principles of the NIH Genomic Data Sharing Policy. Furthermore, research resources will be shared as described by NIH in "Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Programs." Posters and oral abstracts presented at conferences, as well as published reviews and manuscripts, will be posted by the DCC or through support from the DCC with a link to the PubMed library on the public facing website that will be developed for this initiative.

6. Data Security

   All study data and summaries of unpublished study must be stored on secure electronic media abiding by the standards enforced at the DCC. Other institutions likely have comparable security, but this needs to be assessed at the time of creation of the DMP.

7. Human Subjects Protection

All study activities are expected to conform to the expectations laid out in the latest version of the World Medical Association Declaration of Helsinki (i.e. the version adopted in October of 2013 as of this writing). All research sites, CCC, and DCC staff are required to follow Good Clinical Practice (GCP) and Human Subjects Protection (HSP) principles. Prior to the launch of any protocol, consortium sites must be in compliance with all regulatory and administrative policies, such as having the necessary IRBs/Ethic approvals.

D. Signatures

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National Heart, Lung and Blood Institutes (NHLBI), United States of America.

Signing Official:
Name:
Position:
Signature:
Date:

Program Officer
Name:
Position:
Signature:
Date:

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Muhimbili University, Tanzania

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Julie Makani
Position: Principal Investigator
Site: SPARCo Clinical Coordinating Center
Country: Tanzania

Signature:
Date:

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University of Cape Town

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Ambroise Wonkam
Position: Principal Investigator
Site: Sickle Africa Data Coordinating Center (SADaCC)
University of Cape Town
South Africa
Signature:
Date:

_____
Institute: Kwame Nkrumah University of Science and Technology

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Fred Sarfo
Position: Principal Investigator
Site: SPARCo
Country: Ghana
Signature:
Date:

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Institute: University of Abuja

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Obiageli Nnodu
Position: Principal Investigator
Institute: SPARC-Net
Country: Nigeria
Signature:

Date:

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Muhimbili University

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Emmanuel Balandya
Position: Principal Investigator
Site: SPARCo Tanzania
Signature:
Date

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University of Mali

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Aldioma Guindo
Position: Principal Investigator
Site: SPARCo Mali
Signature:
Date

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Makerere University

Signing Official
Name:
Position:
Signature:
Date:

Name: Prof Sara Kiguli
Position: Principal Investigator
Site: SPARCo Makere University
Signature:
Date:

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University of Zimbabwe

Signing Official
Name:
Position:
Signature:
Date:

Name: Dr Patience Kuona
Position: Principal Investigator
Site: SHAZ
Signature:
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University of Zambia Teaching Hospital

Signing Official
Name:
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Signature:
Date:

Name: Dr Catherine Chunda
Position: Principal Investigator
Site: SHAZ
Signature:
Date: