ISARIC Governance Framework v.4.2

Reviewed and ratified at ISARIC's 2nd Council Meeting in Annecy 3 July 2014

1. Governing principles

1.1 Vision

The vision of the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) is to foster global collaborative patient-oriented research between and during epidemics of severe acute respiratory infections and other rapidly emerging public health threats in order to generate new knowledge, maximise the availability of clinical information, and thereby save lives.

1.2 Mission

ISARIC is a global collaboration of research networks with a focus on investigator-led clinical studies in adults and children. ISARIC's mission is both to conduct world-class clinical research in the inter-pandemic influenza period and to provide a collaborative platform through which clinical studies could will be undertaken rapidly in response to the (re)emergence of a novel respiratory pathogens or other new infectious disease outbreak.

1.3 Objectives

The aim of the Consortium is to establish a sustainable federation of research networks with global geographic coverage that facilitates and coordinates international studies by its members on severe acute respiratory and emerging infections across a range of resource and clinical care settings and liaises with national and supra-national public health authorities.

The Consortium aims to conduct studies designed to elucidate understanding of disease pathogenesis and advance therapeutic interventions in patients with severe acute respiratory and other infections of all ages during inter-epidemic/pandemic periods, and with the flexibility and capacity to respond quickly to the range of plausible rapidly emergent threats. The scope of the anticipated studies includes surveys, registries, retrospective and prospective observational studies, and randomized controlled trials examining existing and novel therapies.

While it is anticipated that most participating networks will be hospital and/or community based, other networks that can quickly access patients are also eligible for membership.

The key objectives of the Consortium are:

- To understand human and pathogen factors contributing to severe acute respiratory infections and disease severity across all ages;
- To define optimal clinical management approaches adapted to the range of resource and clinical care settings globally;

- To develop operational readiness to conduct clinical research in response to new epidemic or pandemic infectious disease threats and to inform and guide evidence-based optimal clinical management;
- To develop capacity to undertake research in under-resourced areas and during humanitarian crises;
- To undertake global collaborative clinical research for severe acute infections and other threats in a timely, efficient, targeted and coordinated manner in order to maximise the information from studies and thereby save lives.

The Consortium will facilitate the work of investigators and networks, conduct cross-Consortium studies and assist with the solicitation of funding. Ownership of data, samples and publications resulting from Consortium-endorsed activities remains with the individual investigators and networks.

ISARIC will seek not to duplicate the activities of other agencies, but aims to work synergistically with other agencies, networks, and institutions.

1.4 Funding

1.4.1 Funding sources

It is expected that funding for the day-to-day operation of ISARIC and any activities carried out on behalf of the Consortium will come from a variety of public and private sources (not-for-profit and potentially for-profit). Funding applications for financial or in-kind support for specific research projects to both not-for-profit and for-profit organisations in the name of ISARIC and for ISARIC's core operation have to be endorsed by the Consortium's Executive Committee. Funding applications for specific ISARIC research projects should include in their budget an appropriate contribution to the operational costs of the Coordinating Centre, the Regional Hubs, and/or Working Groups as appropriate.

1.4.2 Collaboration with for-profit organisations

ISARIC encourages active collaboration of its members with for-profit organisations (e.g. with the pharmaceutical industry), on scientifically meritorious studies. However, any such collaborations, when ISARIC-labelled, need to be approved by the Executive Committee.

Funding obtained from for-profit organisations for ISARIC-endorsed activities should be governed in accordance with the guiding principles detailed in the Consortium's policy for industrial relations (see separate document). The guiding principles will be endorsed by the Council and revised by the Executive Committee as appropriate.

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2. Governance structure

The Consortium is formed of a governance arm and an operational structure (or arm) that interact very closely. The governance arm includes the Council of ISARIC and the Executive Committee, the Nominations Committee, and the Proposal Review Committee. The Governance arm also includes the Independent External Advisory Board and the Stakeholder Advisory Board. The operational structure or arm includes Regional representatives/hubs, Working Groups and their project teams, an Independent Data Access Committee, and the Coordinating Centre.

A schematic outline of the Consortium structure is depicted in Figure 1 below (Appendix I). Current membership of the committees are available on the ISARIC website (www.isaric.org)

2.1 The Council of ISAIRC

2.1.1 Role of the Council

The overall scientific direction and governance of ISARIC is provided through the Council. Responsibilities of the Council include approval of Executive Committee members, nominating members of the Nominations Committee, the endorsement of documents such as public postings approved by the Executive Committee, and the endorsement of suggested modifications to the ISARIC Governing Framework, Policy on Relations with For-Profit Entities, ISARIC Data-Sharing and other core ISARIC policy documents. The Council is responsible to and representative of the member organisations of ISARIC, and holds the Executive Committee responsible for the operation of the Consortium

2.1.2 Composition of the Council and voting rights

Voting members of the Council are:

- One representative for each member network (one vote each)
- The following Executive Committee members: Chair, Vice-Chairs, and Coordinating Centre representative (one vote each unless they are also voting on behalf of member networks)
- Regional representatives/hubs (one vote each)
- One representative for each Working Group (one vote each)
- Independent External Advisors (one vote each)

Individual members, external networks, and observers may participate in Council meetings upon invitation by the Council, but do not have voting rights

The composition of the Council is under annual review by the Executive and the Coordinating Centre.

2.1.3 Meetings of the Council

The Council meets in person on an annual or bi-annual basis and via teleconference when possible and resources permitting. The members of the Council may also correspond through an email list when required. Additional meetings (in person or via teleconference) will be scheduled as required. Meetings of the Council are presided over by the Chair of ISARIC. Minutes of each meeting of the Council are distributed to all member organisations and are submitted to the Stakeholder Advisory Board, if requested.

2.1.4 Nominations Committee

The membership of the Nominations Committee is drawn from within the Council and the Executive Committee. All nominations to ISARIC Chair, Vice-Chairs, other Executive Committee positions, Council membership beyond network member representatives, and other elected positions created at discretion of the Executive Committee should be addressed to the Nominations Committee.

The responsibilities of the Nominations Committee include:

- Preparing calls for nominations and drafting nomination and election criteria and procedures, for the approval of the Executive Committee
- Gathering all nominations and preparing recommendations with regards to their suitability as decided through published calls for nominations with the assistance of the Coordinating Centre
- Sending recommendations to the Council for consideration

The Committee is chaired by one of ISARIC's Vice-Chairs. Members of the Nominations Committee are chosen by the Council.

2.2 ISARIC Membership

ISARIC offers different pathways for interaction: network membership, individual membership, and observer status.

2.2.1 Membership for networks (also called Full Membership)

The Consortium aims to be inclusive and welcomes existing research networks to apply for 'full' membership in ISARIC, as long as they are:

- Independent and founded, led and run by academic investigators (i.e., not led by industry)
- Scientifically active, with scholarly contributions that are attributable to the network and in research areas relevant to the Consortium
- Multicentre (involving more than one department, hospital, agency etc.)
- Have ready access to patients with severe acute respiratory and emerging infections for enrolment into studies.

- Accept the ISARIC terms of reference for the management of ISARIC (as defined in this document, including the publication strategy, communication strategy, and the data-sharing policy).
- Supportive of and governed by practices consistent with the mission and vision of ISARIC.

A network is broadly defined, but essentially consists of more than two institutes or institutions (hospitals, academic departments, agencies etc.) that are separate but that have an overarching interest in common. Networks may be international, regional, national or local in terms of scope and activities.

When being included into the ISARIC Council, prospective members are asked to declare in writing that they agree to abide by the principles and operating procedures set out in the ISARIC Governing Framework in relation to all ISARIC related activities in which they choose to take part, including a specific agreement on data sharing (to be drafted), before participating.

No membership fees are levied.

Member networks are expected to nominate a new representative to the Council if their current representative is elected to sit on the Executive Committee as a voting member. It is the responsibility of member networks and individuals to keep the Coordinating Centre informed with regards to the change of contact points and representatives

2.2.2 Individual Membership

All applicants are encouraged to submit applications for Full Memberships when possible. The Individual Membership in ISARIC is open to any academic investigator who shares the ISARIC vision (1.1), but who is not eligible to be currently represented by one of the member networks of ISARIC or join through a network that does not already hold a membership.

Individual members will be eligible to contribute to Working Groups and Project Teams, as well as to be Chair of a Working Group or Project Team. Individual members will also be eligible to be elected to sit on the ISARIC Executive Committee an on the Council, but will only have voting rights in their capacity as elected Chair, Vice-chair, Working Group Chair, or Regional representatives/hubs. (For nominations procedure, see 2.1.4)

2.2.3 Partners with observer status

Non-members of ISARIC, such as representatives from external research networks, public health institutions, regulatory agencies, funding organizations, or pharmaceutical industry experts may be invited as observers on Working Groups, and project teams, but cannot be elected to Chair Working Groups or become

members of the Council or the Executive Committee. The participation of observers in ISARIC activities is at the discretion of the Executive Committee or Council.

2.3 Independent External Advisors

Independent External Advisors gather in the External Advisory Board, and offer advice to both the Council and Executive.

Independent External Advisors should be senior individuals with international standing in the field of public health, clinical investigation or another scientific field related to the Consortium. They should also provide representation for the different regions contributing to the Consortium. Their term of office is for two years in the first instance and begins at the start of the next calendar year following their endorsement by the Council. Independent External Advisors may be nominated by any member of the Consortium and are endorsed through a majority vote (i.e. > 50% of all members) of the Executive Committee.

Independent External Advisors may resign from office at any time by giving notice in writing to the Executive Committee. If it serves the best interest of the Consortium, they may be removed by a two-thirds majority vote of the Council. External advisors are required to give a declaration of Conflict of Interest to the Executive.

2.4 Executive Committee

2.4.1 Role of the Executive Committee

Executive responsibilities and day-to-day governance decisions for ISARIC activities lie with the Executive Committee. The Executive Committee steers the Consortium and provides general supervision of its activities, reports to the Council, and is advised by the External Advisory Board (see 2.3) and the Stakeholder Advisory Board (see 2.6).

2.4.2 Composition of the Executive Committee and voting rights

Drawn from the wider ISARIC membership, the voting members of the Executive Committee include:

- An elected Chair and up to four elected Vice-Chairs (one vote each)
- The Coordinating Centre (one vote)
- One representative per Working Group (one vote each)
- Two regional representatives/hubs each for Africa, Americas, Asia, and Europe (one vote each)

Members of the Executive Committee who do not have voting rights include:

- Observers (e.g., WHO, InFACT) and Individual members, included at the discretion of the Council (see 2.2.2 & 2.2.3)

At any given time, each research network should have no more than one voting member on the Executive Committee.

InFACT should nominate a representative as a non-voting observer to the Executive Committee, except if an InFACT investigator already holds the position of Chair, Vice Chair, or Working Group Chair.

2.4.3 Electing a Chair or Vice-Chairs to the Executive Committee

The Chair and Vice-Chairs are elected for a two-year term by a majority vote (i.e. > 50% of all voting members) of the Council. If not specified otherwise, the election will be held at the annual meeting of the Council. Terms of office begin at the start of the calendar year following the election. If it serves the best interest of the Consortium, the Chair and Vice-Chairs may be removed by a two-thirds majority vote of the Council.

It is possible for the Executive Committee to suggest changes in the terms of reference of the Chair (such as appointing an interim Chair), Vice-Chairs and other Executive Committee members, but any nominations or changes will be provisional until approved by the Council.

The Chair and Vice-Chairs may resign from office at any time by giving notice in writing to the Chair or Vice-Chairs and the Coordinating Centre. Members of the Executive Committee must inform the rest of the Executive Committee of any conflict of interest arising from competitive bids for funding and other research ventures.

Where an individual fills a vacancy for Chair or Vice-Chair, if less than one year is served this will not count as a term, but if more than one year is served, this will count as a term. An individual who has served for two consecutive terms as Vice-Chair remains eligible to become Chair of the Executive Committee.

2.4.4 Responsibilities of the Chair and Vice-chairs

The Chair's responsibilities are to preside over Council and Executive Committee meetings; to conduct the elections; to advise and work closely with the Coordinating Centre; and to report to the Stakeholder Advisory Board on a semi-annual basis, and when called upon to do so. The Vice-Chairs assist the Chair with these responsibilities.

In the absence of the Chair, the Vice-Chairs preside over meetings, conduct elections, and report to the Stakeholder Advisory Board.

2.4.5 Meetings of the Executive Committee

The Executive Committee meets in person at the annual meeting of the Council, and on a monthly to bi-monthly basis via teleconference. The number of teleconferences

may change when needed, and will be determined by the Executive Committee and the Coordinating Centre. Additional meetings (in person or via teleconference) will be scheduled as required. Minutes of each meeting of the Executive Committee are kept by the Coordinating Centre and are submitted to Council members and External Advisors once they have been ratified by the Executive Committee.

2.4.6 Proposal review committee

All study protocols, projects, publications and other documentation seeking ISARIC branding and endorsement on ISARIC's behalf must be presented for review to the Review Committee. The members of the Review Committee are chosen on the discretion of the Chair and Vice-Chair based on their professional and academic expertise in subject areas related to the documents sent for review. Final approval of such documents as ISARIC-labelled rests with the Executive Committee. (sub paragraphs or reference to publication strategy: how the process works)

2.5 Stakeholder Advisory Board

2.5.1 Role of the Stakeholder Advisory Board

The Stakeholder Advisory Board helps to develop the strategic vision of the Consortium, provides advice to the Executive Committee and identifies funding opportunities, and ensures that progress is in accordance with the mission and objectives of the Consortium.

2.5.2 Composition of the Stakeholder Advisory board

The Stakeholder Advisory Board will be formed of six to eight members, including a representative from the institution where the Coordinating Centre is located (currently the University of Oxford), and representatives from the funding organisations providing direct support to the Consortium (maximum of six).

The Chair of the Stakeholder Advisory Board is nominated on a rotational basis from among its members and at a two-year interval. Funding organisations that provide financial or in-kind support to the Consortium exceeding £50K can each name one representative.

Governmental agencies and not-for-profit organisations that fund specific protocols of the Consortium are eligible. Pharmaceutical industry groups that might provide funding or materials for study are not eligible for membership in the Stakeholder Advisory Board.

The tenure of the representative from funding organisations is at the discretion of the individual organisation.

In the future, if more than eight organisations provide support and nominate representatives, the Stakeholder Advisory Board will establish a suitable process of rotating membership every two years.

The Chair of the Executive Committee may sit in on Stakeholder Advisory Board meetings as an observer. If appropriate, further members of the Council or the Coordinating Centre can be invited by the Stakeholder Advisory Board to attend its meetings as observers.

2.5.3 Voting rights

Each member of the Stakeholder Advisory Board has one vote. Representatives of funding organisations are expected to recuse themselves and abstain from voting on matters that concern activities in which they have potential conflicts of interest (e.g., involvement as investigators). Any real or potential conflict of interest should be declared at the outset of any meetings.

2.5.4 Meetings of the Stakeholder Advisory Board

The Stakeholder Advisory Board convenes in person at the annual meeting of the Council and, via teleconference as required.

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3. Operational structure

ISARIC's operational arm includes the Regional representatives/hubs, the Working Groups, and the Coordinating Centre. The operational structure is also supported by the Independent Data Access Committee.

3.1 Regional representatives/hubs

3.1.1 Role of the regional representatives/hubs

Regional representatives/hubs are critical components of ISARIC. It is their role to strengthen the Consortium's global approach to collaborative research by ensuring that all parts of the world and member networks of each region are represented adequately on the Council, Executive Committee, and the Working Groups by facilitating regular communication between networks in the various regions through close interactions with the Coordinating Centre; and by integrating activities of the Working Groups and their project teams at the regional level.

3.1.2 Regional representative/hub status

Regional representatives/hubs are identified by the member networks of each region and voted in regionally and endorsed by the Council. The Council can formally assign Regional representative/hub status to the existing operations or communications centres of a member networks that represent certain regions. If it

serves the best interest of the Consortium, Regional representative/hub status can be revoked by a majority vote of the Council. Member networks may relinquish their Regional representative/hub status at any time by giving notice in writing to the Chair of ISARIC and the Coordinating Centre.

3.1.3 Regional representative/hub representatives

The networks in each designated region (currently the Americas, Asia, Africa, Europe) nominates two representatives to the Council and the Executive Committee who are responsible for maintaining effective communication between the Council, Executive Committee and member networks in their region. At least one representative for each region is expected to participate in Council and Executive Committee meetings.

3.2 Working Groups

3.2.1 Role of Working Groups

ISARIC Working Groups are investigator-led and represent the constituent units of the Consortium. They generate ideas, concepts, study protocols and related documents, including applications for funding for specific projects.

In the first instance, the Consortium is expected to include the following four Working Groups:

Working Group 1: “Inter-pandemic clinical trials"
Working Group 2: “Global data collection and collation”
Working Group 3: “Genomics, pathogenesis and pharmacology”
Working Group 4: “Changing clinical research paradigms for rapidly emerging public health threats”

The scope of planned activities for these four Working Groups is outlined in Appendix II. Within a Working Group, individual project teams (also known as sub-groups) are responsible for the delivery of these activities, including the development of specific protocols to be submitted to funding agencies. The number and topic focus of Working Groups is expected to change as the Consortium evolves.

3.2.2 Composition of the Working Groups

Each of the Working Groups includes ordinary members, a Chair and two Vice-Chairs, and project team leads. The size of the Working Groups and their project teams will be at the discretion of the Working Group members.

3.2.2.1 Ordinary members

Working Groups are composed of both representatives of member networks and of individual members of ISARIC. Observers may be members of working groups but do

not have voting rights and cannot be elected as Working Group Chairs. ISARIC members wanting to join working groups need to contact the Coordinating Centre and Working Group Chair directly.

Unless otherwise decided by the Council, Working Group membership will remain open and individuals will be able to join or leave Working Groups at any stage. All members have the freedom to carry out other research projects, and ISARIC membership does not limit any other activity outside of the Consortium.

3.2.2.2 Working Group Chair and Vice-chairs

Each Working Group has a Chair and two Vice-Chairs who are elected by a majority vote of the Group and are accountable to the Executive Committee.

The Chair leads the Working Group, organises and runs its meetings, and assigns and coordinates activities within the Group. The Vice-Chairs will perform these activities in the absence of the Chair or as requested by the Chair. The term of office for the position of Chair and Vice-Chair is for two years in the first instance and renewable once.

The Chair or Vice-Chairs may resign from office at any time by giving notice in writing to the Working Group and the Coordinating Centre. If it serves the best interest of the Consortium, the Chair or Vice-Chairs may be removed by a majority vote of the Working Group.

3.2.2.3 Project Team leads

Project team leads are responsible for leading individual project team or sub-group activities within a Working Group. They are accountable to and appointed by the Working Group based on their specific expertise and contributions to developing individual projects and protocols. The tenure of project team lead is determined by the project requirements and is not time-limited.

Project team leads may resign at any time by giving notice in writing to the Working Group. If it serves the best interest of the Consortium, the project team lead may be removed by a majority vote of the Working Group.

3.2.3 Representatives to the Executive Committee and Council

Each Working Group has a voting representative on the Executive Committee and Council who is elected by a majority vote of the Group. The representative is, unless otherwise decided by the Working Group, the Chair of the Working Group, who is replaced by one of the Vice-Chairs or another Working Group member if unable to attend. The representative liaises with the rest of the Working Group to maintain an overview of the activities within the Group, provides regular progress reports to the Executive Committee and Council, and represents the interests of the Group at meetings of the Executive Committee and Council.

The term of office for the position of representative to the Executive Committee and Council is for two years in the first instance.

The representative may resign from office at any time by giving notice in writing to the Working Group and the Coordinating Centre. If it serves the best interest of the Consortium or the Working Group, the representative may be removed by a majority vote of the Working Group.

3.2.4 Conduct of Business and Accountability

Each Working Group project team establishes its own rules for conduct of business and work plan (including goals, objectives, timelines, critical milestones, monitoring and evaluation plans).

In the absence of a contrary provision by the Executive Committee, a majority (i.e. > 50%) of all members of each Working Group present (in person, telephonically, or electronically) at a Working Group meeting constitutes a quorum for the transaction of a business, should the Working Group consider a quorum necessary.

Working Groups are accountable to the Executive Committee and Council. They report to the Executive Committee and the Council through their representatives and to the rest of the Consortium during Council meetings, or through the quarterly Newsletter, the ISARIC website, or the ISARIC mailing list as required. Progress of Working Group activities is monitored by the Executive Committee and the Coordinating Centre.

3.2.5 Endorsement of Working Group outputs and outward-facing activities

In order to qualify for official endorsement as ISARIC output, protocols, documents for public posting, and manuscripts for publication generated by a Working Group need to be submitted to the Protocol Review Committee (see 2.4.6) and approved by the Executive Committee. All publications should be published in accordance with ISARIC's Publication Policy, and they should be made freely accessible through ISARIC's website with the Coordinating Centre's approval.

Any other outward-facing activities proposed by a Working Group (e.g. scientific colloquia, workshops) need to be approved by the Executive Committee in order to qualify for official endorsement as ISARIC activity, and should comply with ISARIC's Communication Strategy, if and when applicable.

All members are free to publish without official endorsement any documents that encompass their own data and are not in the name of ISARIC. Likewise, outward-facing activities not endorsed by the Consortium are not limited by ISARIC membership.

3.2.6 Authorship on Working Group publications

Ownership of samples and results remain with the individual investigators and networks. Group authorship is the preferred form of authorship for manuscripts submitted in the name of the Consortium, for example:
"The Inter-pandemic Trials Working Group on behalf of ISARIC" or
"Investigators of the IISIG study/project team", with contributions from individual ISARIC investigators and member networks acknowledged.

3.2.7 Meetings of the Working Groups

Working Groups and their project teams meet in person or via teleconference as required. It is the responsibility of the Chair of the Working Group or project team to arrange meetings. Minutes of each meeting of the Working Groups are kept and are submitted to the Executive Committee.

3.2.8 Setting up or disbanding Working groups

The Council or Executive Committee can propose the establishment of additional Working Groups. New Working Groups or major changes in their terms of reference have to be ratified by the Executive Committee before activities on behalf of ISARIC can commence. Working Groups can be disbanded by a majority vote (i.e. > 50%) of its members or by a majority vote (i.e. > 50% of all voting members) of the Council. In the latter case, Working Groups retain the right of appeal against this decision. The appeal should be addressed to the Executive Committee who will decide by a two-thirds majority vote.

3.3. Independent Data Access Committee

3.3.1 Role of the Independent Data Access Committee

When needed, ISARIC will set up an Independent Data Access Committee. Any external requests to access and use data generated by ISARIC investigators on behalf of the Consortium have to be submitted to the Coordinating Centre. For any requests in which an initial survey of involved investigators finds possible cause for not sharing data, the request will be referred to an Independent Data Access Committee for review. Decisions of the Committee are based on whether a request meets the criteria laid out in the ISARIC data access guidelines (see separate document – to be drafted) and on requirements of the local ethics committees where the relevant study was conducted.

Decisions made by the Independent Data Access Committee can be appealed by any member of the Consortium and can be overruled by a two-thirds majority vote of all members of the Council.

3.3.2 Composition of the Independent Data Access Committee

The Independent Data Access Committee will be composed of independent external experts selected to cover the full range of expertise including statistics and ethics required to critically evaluate requests and achieve ISARIC's data access objectives. These individuals may come from institutions outside or represented in the Consortium but they may not be investigators in Consortium-related studies or members of the Consortium's governance bodies. Members are nominated by the Council or Executive Committee and ratified by the Stakeholder Advisory Board.

3.3.3 Meetings of the Independent Data Access Committee

The Independent Data Access Committee meets via teleconference as required. If necessary and funds permitting, face-to-face meetings can be arranged by the Coordinating Centre. Minutes of each meeting of the Independent Data Access Committee are kept and are submitted to the Executive Committee and to the Stakeholder Advisory Board if requested.

3.4. Coordinating Centre

3.4.1 Role of the Coordinating Centre

The ISARIC Coordinating Centre has two key functions:

As a Secretariat for ISARIC: the Coordinating Centre carries out administrative (incl. financial) tasks and other daily activities necessary for the running of ISARIC, such as arranging and keeping records of meetings, maintaining the website and the teleconference facility, and keeping the records for the Consortium processes. The Coordinating Centre also offers support towards the activities of the Executive Committee, Working Groups and their project teams, Regional representatives/hubs, Funders, Independent External Advisory Board, and all other boards and committees within ISARIC. The Coordinating Centre is also actively seeking funding for Consortium activities, and for supporting ISARIC's infrastructure. The Coordinating Centre may also provide assistance in developing other funding proposals, and the development and drafting of protocols and supporting documentation related to research

In a coordinating capacity: the Coordinating Centre is charged with maintaining channels of Communication and is as a point of contact for internal and external networks, organisations, and partners. The Coordinating Centre will also help coordinating and supporting the expansion of the network. Depending on the nature of the projects, the Coordinating Centre may be involved with the global coordination of ISARIC-branded studies.

3.4.2 The Coordinating Centre staff

The Coordinating Centre is led by the Senior Clinical Coordinator and includes a Senior Programme Manager and other staff as required and depending on resources available.

The Senior Clinical Coordinator and the Senior Programme Manager, and any other staff, are recruited and employed by the academic institution that is hosting the Coordinating Centre. ISARIC's Executive Committee will have input into the terms of reference for both posts, and will be represented throughout the recruitment process. All Human Resource and staff-related guidelines and policies applicable to the host institution will also be applicable to Coordinating Centre staff.

All staff physically based at the Coordinating Centre is line-managed by the host institution, and reports to the Chair and the Executive Committee of ISARIC.

3.4.2.1 Senior Clinical Coordinator's key responsibilities

The key responsibilities of the Clinical Coordinator (also called Clinical Lead) is to lead, manage and develop the Consortium, ensuring its efficient and effective operation; and to aid in developing and implementing the Consortium's strategies.

3.4.2.2 Senior Programme Manager's key responsibilities

The key objectives of the Senior Programme Manager is to support the Clinical Coordinator in implementing the strategies of the Consortium, and; to effectively and efficiently manage and develop the Consortium's activities and operations.

3.4.2.3 Other Coordinating Centre staff

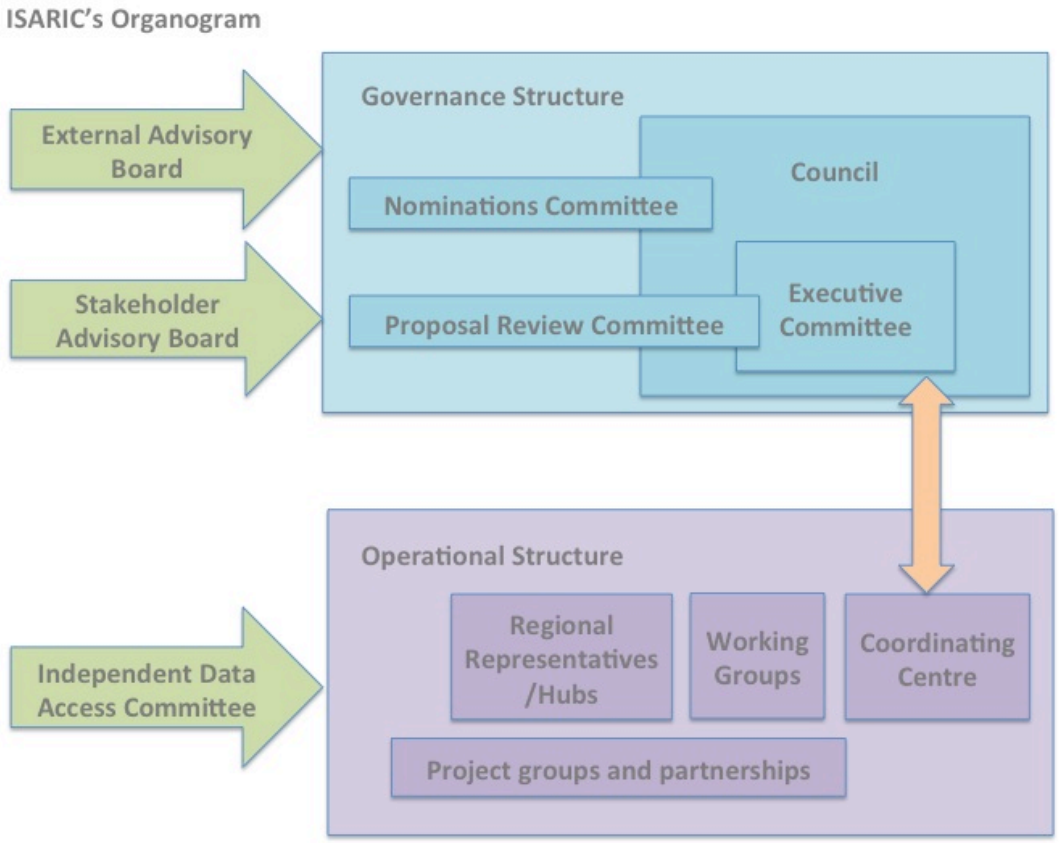
Additional post may be created at the host institution or elsewhere as ISARIC develops and expands.

3.4.3 Location of the Coordinating Centre

In the first instance the Coordinating Centre will be based at the Centre for Tropical Medicine, Nuffield Department of Medicine, University of Oxford.

Administrative support is provided by the Nuffield Department of Medicine while the Coordinating Centre remains at the Centre for Tropical Medicine.

Appendix I: Organogram



Appendix II: Working Groups

Working Group 1 – Inter-pandemic clinical trials

Description: This Working Group will develop candidate cross-Consortium studies based on both novel and traditional clinical trial designs that can be implemented in the inter-pandemic period.

Activities: Lead development of a minimum of three clinical trials for implementation in children and adults including low and middle income countries. Possible topics include but are not limited to: large pragmatic trials of community acquired pneumonia, immunomodulatory therapy in SARI, anti-viral therapy for influenza.

Critical Milestones: Finalisation of at least two protocols on therapeutic randomised controlled trials in SARI/community-acquired pneumonia within 18 months. Success in at least one application to major funding organisations during the first 24 months including the WT/MRC/DFID Global Health Trials, European Union, US National Institutes of Health, or Bill and Melinda Gates Foundation.

Monitoring and Evaluation Plan: The representative of the Working Group will report at least quarterly to the Executive Committee. Key funding opportunities will be tracked by the Secretariat and Executive Committee. Funding applications will be endorsed by the Executive Committee of ISARIC.

Working Group 2 – Global data collection and collation

Description: This Working Group will complete a global inventory of existing databases related to SARI and pandemic H1N1 among ISARIC and InFACT networks, undertake standardisation and harmonisation of definitions, and develop on-the-shelf pandemic/novel threat response protocols.

Activities: All partners and networks of ISARIC have agreed to share existing databases and work towards harmonisation of definitions to facilitate meta-analyses. This will include development of standards for tiered and minimal data sets that will be used for developing outbreak/pandemic protocols.

Critical Milestones: Development of an on-the-shelf, rapid- response pandemic/novel SARI threat response protocol including standard definitions, tiered datasets, and data-sharing mechanisms within 12 months. Decision on creating a clinical database for patients with SARI due to 2009 H1N1 infection within 12 months.

Monitoring and Evaluation Plan: The representative of the Working Group will report at least quarterly to the Executive Committee. The Executive Committee and Stakeholder Advisory Board will monitor progress. Pandemic protocols will be endorsed by the Executive Committee and Council of ISARIC.

Working Group 3 – Genomics, Pathogenesis and Pharmacology

Description: This Working Group will develop pathogenesis studies aimed at understanding the dynamics of host responses, host genetic factors in susceptibility, virus/host interactions, and pharmacokinetic-pharmacodynamic relationships in treated patients.

Activities: Assess existing evidence from studies in patients with SARI due to pandemic 2009 H1N1 and develop new protocols that address key questions regarding disease pathogenesis, host susceptibility, and pharmacokinetic-pharmacodynamic relationships including prevention of drug resistance.

Critical Milestones: Submission within 18 months of a protocol on host genetic studies in severe influenza; develop sample collection modules for pathogenesis and pharmacology studies to be added to both inter-pandemic and rapid-response protocols.

Monitoring and Evaluation Plan: The representative of the Working Group will report at least quarterly to the Executive Committee. The Executive Committee and Stakeholder Advisory Board will monitor progress. Funding applications will be endorsed by the Executive Committee of ISARIC.

Working Group 4 – Changing clinical research paradigms for rapidly emerging public health threats

Description: This Working Group will drive the critical evaluation of the barriers and the ethical framework required to facilitate the development of clinical research in response to a rapidly emerging health threat.

Activities: Assessing the ethics of clinical research in the context of epidemics, developing an open access module that will be part of the "*E-Research Hub*" and work towards pre-approved protocols, documents and reporting forms, and address other challenges for undertaking clinical research studies in rapidly emerging health threats. Build research capacity by assisting in the development of new and established research groups that can contribute to ISARIC studies.

Critical Milestones: Publication within 18 months of a systematic review of ethical, legal, contractual, funding, information-sharing and publication constraints to developing a rapid clinical research response. There is confirmation of the Symposium at the American Society of Tropical Medicine meeting in December 2011 that will be the formal launch of ISAIRC and a linked Symposium at the same meeting on the "*E-Research Hub*" and Open Access**.** This Working Group will convene two international workshops to address issues on ethical challenges of clinical research in the context of rapidly emerging health threats and the practical barriers to the successful implementation of clinical research in such settings.

Monitoring and Evaluation Plan: The representative of the Working Group will report at least quarterly to the Executive Committee. The Executive Committee and Stakeholder Advisory Board will monitor progress.