

Message from the Chairman

ISARIC was formally launched at the American Society of Tropical Medicine Meeting in December 2011, and a great deal of work has gone on behind the scenes to establish a functional Secretariat and meet the goals stated in our initial Letter of Intent. To date this has been accomplished primarily via a series of regular teleconferences and several meetings arranged by the Chairs and Co-Chairs of the Working Groups. In addition to the activities of the Working Groups, the Executive Committee has been formed and held several teleconferences and the leads for four Regional Hubs designated. The current members of these various groups are listed below, and an outline of recent activities and of plans for second quarter of 2012 is also provided.

With the appointment of Kajsa Magnusson as Programme Manager and Dr Gail Thompson as Interim Secretariat Director we hope to have a fully functional ISARIC Secretariat in place by May 2012. The Secretariat will then be available to facilitate and support the work of ISARIC and any of its members and partners.

By Q1 2012 more than seventy networks and consortia had expressed an interest in the work of ISARIC. Close to a hundred individuals from these groups have joined meetings and teleconferences and come from over 30 countries across six continents.

We are extremely grateful to the support from Dan Korbel and Fred Hayden from the Wellcome Trust who have continued to support us through the setting up of the Consortium and in establishing the infrastructure needed to help coordinate the planned activities. Dan has moved to a new post at the Wellcome Trust and on behalf of everyone involved in ISARIC we wish him well in his new position.

Jeremy Farrar, Ho Chi Minh City, April 2012

Updates

Activities Q4-2011/Q1-2012

12/2011

- Formal launch of ISARIC at the American Society of Tropical Medicine Meeting, Philadelphia, Pennsylvania
- Meeting on Design of Clinical Trials, Hosted by Prof. Derek Angus, University of Pittsburgh, Pittsburgh, Pennsylvania

01/2012

- Finalisation of the ISARIC Chair and Co-Chairs of the Working Groups and Regional Hubs
- Start of monthly teleconferences for Working Groups 1-4

02/2012

- Nominations and voting by Chairs/Co-Chairs for the ISARIC Advisory Group
- Meeting of the ISARIC European Hub to discuss and plan for the forthcoming FP7 European Union Call for "A Network focused on Clinical management of patients in severe epidemics."

03/2012

- Presentations and Meeting at the 32nd International Symposium on Intensive Care and Emergency Medicine, Brussels
- Appointment of Kajsa Magnusson as Project Manager and Dr Gail Thompson as Interim Secretariat Director
- ISARIC overview for the British Medical Journal

Activities planned for Q2-2012

- Finalise the structure, organisation and policies of ISARIC
- Development of communication strategies within ISARIC and externally
- Prepare for the FP7 EU Grant and Wellcome Trust Strategic Award (led by WG3) and explore others opportunities
- Working Group activities
- Finalise the website with dedicated workspaces etc.
- Appoint permanent Secretariat Director
- Draft a manuscript describing the aims and mission of ISARIC
- Preparation for the first Council meeting in Annecy in July

Executive Committee

Jeremy Farrar (Chairman of ISARIC)
 Roberto Bruzzone
 Abdullah Brooks
 Xavier de Lamballerie
 Guillermo Ruiz-Palacios
 John Marshall (InFACT representative)
 Gail Thompson (Secretariat Director)

Regional Hubs**Americas**

Guillermo Ruiz-Palacios

Europe

Gernot Rohde and Jordi Rello

Africa

Kath Maitland and Dean Everett

Asia and Australasia

Zhancheng Gao

Working Groups**WG1 – Clinical Studies**

Chair Menno de Jong
 Co-Chairs John Marshall & Robert Read

WG2 – Existing Data Bases, Minimal Data Sets

Chair Kathy Rowan
 Co-Chairs Calum Semple & Tim Uyeki

WG3 – Genetics, Pathophysiology and Pharmacology

Chair Ken Baillie
 Co-Chairs Sylvie van der Werf & Peter Openshaw

WG4 – Changing clinical research paradigms for rapidly emerging public health threats

Chair Steve Webb
 Co-Chairs Lewis Rubinson & Fernando Bozza

External Advisors

The Chairs and Co-Chairs of the Working Groups, the Executive Committee and the Regional Hubs nominated individuals for the ISARIC External Advisory Group and then voted on the nominees. All will be attending the first ISARIC Council Meeting in Annecy July 2012.

We are delighted to announce that the following people have agreed to be External Advisors to ISARIC. We are also awaiting replies from two other nominees.

Lucille Blumberg

Deputy Director of the National Institute for Communicable Diseases, South Africa

Iliaria Capua

Director of Virology at the FAO/OIE Collaborating Centre for Diseases at the Human-Animal Interface, IZSV, Italy

David Heymann

Chairman of the Board of the UK Health Protection Agency

Raul Istúriz

Director of the Adult Vaccination Service and Senior Consultant in Internal Medicine and Infectious Diseases at the Centro Médico de Caracas, Venezuela

Keith Klugman

William H. Foege Chair of Global Health Rollins School of Public Health, Emory University, United States of America

Nick White

Professor of Medicine, Mahidol University, Bangkok, Thailand

Council meeting – 2-4 July

The first Scientific Council meeting of ISARIC will be hosted in Annecy, France courtesy of Fondation Mérieux. Each WG Chair has been asked to identify a total of 4-5 people from their WG to attend. If you have any questions regarding this, please email Jeremy Farrar (jfarrar@oucru.org).

There will be an opportunity for WGs to work face to face or with other WGs on the Monday afternoon. Each WG will be asked to present to the Council an update of their activities.

Secretariat

The ISARIC Secretariat will be hosted at the University of Oxford. We will let you know about contact email addresses which will portably have **isaric.org** as a backbone (e.g. info@isaric.org). Meanwhile please contact Gail Thomson at gail.thomson@hpa.org.uk.

Interim Secretariat Director – Gail Thomson. Dr Gail Thomson of the UK Health Protection Agency is temporarily acting up as Interim Secretariat Director. Gail will be seconded to ISARIC on a part-time basis from May. Gail will, however, be unavailable from April 11th – 30th as she is getting married! A permanent position will be advertised in April 2012.

Project Manager appointed – Kajsa Magnusson. An experienced project manager, Kajsa is joining ISARIC as Project Manager having previously managed an EC-funded science communication network at University College London. Kajsa has several years of international experience and, in the late stages of a part-time PhD in science policy and science communication, she has a very good understanding for the context in which ISARIC is operating. Kajsa will take up her position on 14 May. She can be contacted at k.magnusson@ucl.ac.uk or via Skype (Kajsa-Stina Magnusson).



Operational updates

Website

We have a domain <http://www.isaric.org> which will be functional in May 2012. This will be the public face of ISARIC and will give us access to Shared Workspaces etc. Kajsa and Gail will meet with the IT team working on the Global Health Network (GHN) website (<http://tghn.org/>) at the beginning of May as they will also assist ISARIC with the web needs.

The Oxford leads for the site are Dr Trudie Lang; trudie.lang@ndm.ox.ac.uk and Tamzin Furtado; tamzin.furtado@ndm.ox.ac.uk. Trudie and Tamzin sit in the same building as the ISARIC secretariat. The Global Health Network shares the same ethos as ISARIC where sharing and openness surrounding research is concerned. Jeremy Farrar was involved with the setting up of the Global Health Network and is on the GHN Founding Steering Committee.

Access to the ISARIC WG workspaces/share points will also be available through the Global Health Network's Epidemic Research site (<http://globalepidemicresearch.tghn.org/>) as well as directly via <http://www.isaric.org>.

Many of you have already joined this site and started to utilise it. We realise that there are a few changes to make for ISARIC but would encourage you to familiarise yourself with the site and check out the useful resources and think about how we can add to it.

What the current workspaces available on the GHN site can do:

It is possible to immediately set up a workspace for each of the working groups. In a workspace, members will be able to hold multiple discussions – for example, one in which they can put references, one in which they discuss a protocol, etc. Each workspace will be invite only, so although members of the public will be able to see that the workspace exists, they will not be able to see the content. Members of the group will be able to upload and download documents, discuss amendments and so on. The current functionality for the group will allow members to be emailed each time there is a new message on a discussion, but will not tell them what the new discussion is about (rather it will just direct them to the website itself). The current workspaces are accessible through the GHN's Epidemic Research site and will soon be accessible through our <http://www.isaric.org> website.

Membership, Organisation and Other Policies

These are being drafted and will be available for the Executive Committee to review in May.

ISARIC Emails

INCUNA, the IT consultants, will set up email addresses for the Secretariat, Executive Committee, Working Groups and Regional Hubs as required. This will be the same as having any extra email address (e.g. having a Hotmail address and a work address) – so it will allow you to email people from info@isaric.org, for example.

Financial update

	Year 1 Budget	Year 1 Expenditure (03/ 2012)
TOTAL	£ 208,885	£ 11,837

Updates from the Working Groups**Working Group 1 – Clinical Studies**

The focus of this Working Group is to develop clinical studies, including randomized clinical intervention trials, that can be implemented across the Consortium. Originating from discussions at a joint InFACT/ISARIC meeting in Pittsburgh in December 2011, the possibilities of developing a global adaptive randomized clinical trial program for this purpose are currently explored in WG1. Adaptive trial design is based on Bayesian statistics, generates estimates of effect as the trial is progressing which allows for preferential assignment of patients to arms that appear most likely to work, and it provides flexibility to add and drop trial arms over time, including in the event of an emerging outbreak. Once established, this adaptive program would provide an infrastructure where, beside trial execution, collection of samples and data are standardized which benefits the overall aims of ISARIC, including those represented in other ISARIC Working Groups. Last but not least, this approach would provide optimal guarantee for the generation of timely RCT evidence of treatment effectiveness as well as important impact and pathogenesis data during global outbreaks. Emanating from the Pittsburgh meeting, a planning document has been compiled by a group of InFACT and ISARIC representatives which addresses the essential developmental steps to launch this ambitious program (and acquire funding for it). Specifically, six objectives have been identified:

- (1) to formalize the intervention selection process (to prioritize intervention to be tested in the program),
- (2) to conduct observational studies (to provide input for simulation and design of the program),
- (3) to conduct simulation studies of proposed study designs (to finalize design of the adaptive trial),
- (4) to determine within-trial logistics,
- (5) to develop and implement international ethical oversight, and
- (6) to ensure overall oversight, coordination and implementation of the program.

These objectives will be addressed by specific task forces drawn from ISARIC and InFACT, which are currently being composed. Beside from WG1, these task forces will naturally also require engagement from members of other Working Groups.

While an adaptive trial program may be relatively straightforward in ICU settings, one (of many) challenge will be to expand this to non-ICU settings, especially in resource-limited regions of the world. In addition, development of the above adaptive trial program may require quite some time (and funding). For this reason, possibilities of developing a fairly simple clinical trial are also explored, which would also serve to 'kick-start' the infrastructure of ISARIC. For this, as for the adaptive trial program (objective 1), intervention selection is a current main priority of WG1.

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 evolution and virus/host interactions, and pharmacokinetic-pharmacodynamic relationships in treated patients.

Aims and deliverables:

(1) Assessment of existing evidence from studies in patients with SARI due to pandemic 2009 H1N1. We are conducting a systematic review of biomarkers in influenza, led by Dat Tran (Toronto).

(2) Survey of existing resources

Led by WG4 (Fernando Bozza). We are contributing specific questions relating to essential laboratory services in order to find key research hubs, and to identify any requirements for specific investment (Sylvie van der Werf, Paris).

(3) Genomics

A proposal arising from within this working group is currently at the preliminary application stage for a Strategic Award from the Wellcome Trust. This study aims to identify and characterise host genomic loci conferring susceptibility to severe influenza. (Ken Baillie, Edinburgh)

(4) Develop new protocols that address key questions regarding disease pathogenesis, host susceptibility, viral determinants of virulence, and pharmacokinetic-pharmacodynamic relationships including prevention of drug resistance.

We are undertaking a systematic two-stage process to first identify important studies to be undertaken during future outbreaks, and then to stratify studies according to urgency and difficulty. In this way we aim to produce a pragmatic, hypothesis-driven plan for the research response to emerging pathogens, in preparation for anticipated funding opportunities. (All participants).

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

WG4 is meeting regularly and working to provide support to Working Groups 1, 2, and 3. The theme for WG4 is to identify and overcome barriers to achieving the mission and vision of ISARIC. Potential areas of interest include ethical and regulatory requirements, enhancement and creation of network and site level research capacity and infrastructure, understanding the information that is required by clinicians and public health authorities during an outbreak of an emerging infectious disease, and understanding the logistics requirements for work involving multiple networks.

The first activity initiated by the group are a web-based survey of existing network capacity (with the intention of seeking one response per member network) which will be followed by interviews with each network about barriers to coordinated research during an outbreak. The intention is that the results of the survey, and possibility the interviews about barriers, will be presented at the Annecy meeting. The group is also supporting an activity initiated by Gail Thomson to identify the major questions asked by clinicians and public health authorities during a new outbreak so that this information can be used to guide decision being made by Working Group 2.