

## ISARIC Council Meeting

Summary of the proceedings,  
Page 3



*Official logo, presented at  
Council Meeting, Annecy*

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## ISARIC's vision is to

...**change** the approach to **global** collaborative patient-oriented **research** between and during epidemics of SARI and other **rapidly emerging public health threats** – in order to **generate new** knowledge, maximize the **availability** of clinical information, and thereby **save lives**.

## Message from the Chairman

Welcome to the second ISARIC Newsletter. With the Secretariat firmly established through the appointments of Gail Carson and Kajsa-Stina Magnusson, we aim to make this Newsletter a quarterly release. We appreciate just how important communication is in an organization as complex as ISARIC, and we would welcome ideas and suggestions on how to keep all ISARIC members engaged, without overwhelming your already overly full in-boxes!

The recent isolation of a novel coronavirus from a patient who had travelled from the Middle East to

Europe demonstrated the constant threat of emerging infections with potential public health importance. Incidents such as these, highlights the challenges faced by ISARIC to facilitate and ensure a clinical research response is integrated with the 'public health' and increasingly coordinated and impressive basic science response. The Secretariat has done a remarkable job in linking ISARIC with national and international public health authorities, and

keeping ISARIC's partners regularly updated.

These events are common. At the time of writing, there are on-going outbreaks - to name a few, of Ebola in the DRC, Hand Foot and Mouth Disease across South East Asia, Chikungunya in Cambodia, concerns of an increase in Hepatitis E cases in Europe and South Sudan, CCHF in Eastern Europe, and reports of West Nile Infections in the Balkans. None of these are novel infections, all cause intermittent epidemics and all share a common feature – we have no evidence on how best to treat a patient or knowledge of how any treatment

may impact on transmission, and hence, complement the public health response. The threat of the emergence and spread of a novel infection and our continued ignorance of how to treat patients affected, underline the critical importance of a global consortium dedicated to helping to provide evidence on how to treat patients through clinical research. ISARIC was established in response to our collective experience of SARS, H5N1, and pH1N1. It is clear, however, that the initial focus on respiratory infections will need to be expanded to include other diseases and syndromes in the

future.

The last three months have been incredibly busy in getting the Secretariat established and facilitating and helping prepare applications for funding for the research that is in the heart of ISARIC. More information about some of these activities is to be found in the rest of this Newsletter. We hope you find it enjoyable and informative, and we would very much welcome any other suggestions of things that we as a Secretariat can do to help you.

*Jeremy Farrar, ISARIC Chairman, Ho Chi Minh City, Viet Nam*

## ISARIC Updates

### ACTIVITIES Q2 & 3

#### April 2012

ISARIC's structure was finalized through the help of Dan Korbel and Fred Hayden, Wellcome Trust

Preparations for Council Meeting

#### May 2012

Kajsa installed at Centre for Tropical Medicine in Oxford

Regular meetings of the working groups and Executive

Setting up a website with Incuna and Global Health Network

#### June 2012

FP7 Call meeting in Amsterdam

WG3 submitting a full proposal

(IISIG) for a WT strategic award

The setting up of a teleconference (TC) facility through MeetingZone

TC with External Advisors

#### July 2012

Council Meeting in Annecy 2-4 July

Undertaking a membership inventory

Preparing a strategic plan

Meeting ECDC in Stockholm

#### August 2012

Holiday season standstill

FP7 Call meeting in Antwerp

Annual report for BMGF submitted

### ACTIVITIES PLANNED Q4

Submitting a proposal for – “Potentially new and re-emerging epidemics” (FP7 Health)

Submitting a proposal for the MRC/DFID/WT call for Global Health Trials

IISIG being interviewed for a WT Strategic Award

Website with document development facility

Delphi based study completed

ISARIC Tools developed through ICNARC and WHO Geneva

Completion of ISARIC/InFACT Capacities and Barriers Survey

F2F meeting, Lisbon

(Re-) formulation of governance documents

## Organisational update

### SECRETARIAT

The ISARIC Secretariat has been firmly established at the Centre for Tropical Medicine at the University of Oxford, following the appointment of a Project Manager – Kajsa-Stina Magnusson - in May and a **Clinical Lead – Gail Carson** - in August.

Gail, who has previously been the acting clinical lead for ISARIC, will join the Consortium full-time in November. A consultant in Infectious Diseases, Gail is currently based at the UK Health Protection Agency (HPA) two days a week while working for ISARIC Mondays through to Wednesdays. Apart from her experiences as a clinician, Gail brings several years of experience within public health organisations with a particular interest in emerging pathogens and research.

### OPERATIONS

ISARIC has launched a **website**, hosted by The Global Health Network. The website is meant to be a public and open portal where anyone will be able to download finished protocols and initiate discussions. A document development tool is being added, and should be available for ISARIC's working groups by the end of September. Only working group members will be able to see and use

the document development facility.

Following on from the Council Meeting in Annecy, the Secretariat is conducting a **Membership Inventory**, due to be completed by the end of September. All members and prospective members are asked to fill in membership forms, available for download under Resources on the ISARIC website.

The Secretariat is also currently working on the policy and strategy documents discussed during the Council Meeting, supporting the FP7 application and any other funding proposals, and working for the integration between the Working Groups.

*"...together we will change the paradigm for clinical research to ensure that we, as a community, can answer the key clinical questions during outbreaks".*

Jeremy Farrar, Chairman  
addressing the Council in  
Annecy

## ISARIC Council Meeting, Annecy

### ISARIC held its first Council

**Meeting in Annecy in July 2012.** The objective of the meeting was to agree on ISARIC's priorities, strategy, and outline and agree on the activities that underpin the scientific agenda for 2012-2014.

Recognising the importance of integration between clinicians, laboratories, and epidemiology and public health for an efficient outbreak response; the meeting gathered more than 60 clinicians, researchers, and representatives for national and international public health organisations.

The meeting gave ISARIC's working groups an opportunity to meet face-to-face for the first time to plan ongoing and future activities (see page 4), and it brought together paediatricians, some of whom established the Mother Child Partnership.

The full meeting summary, and all documents presented, discussed and developed during and following the meeting the meeting are available for download on ISARIC's website:

[www.isaric.org](http://www.isaric.org)

ISARIC is very thankful to Fondation Merieux for the use of Les Pensieres Conference Centre to host the meeting.



## Working group updates

### **WG1** - *Inter-pandemic clinical trials*

The critical milestone for WG1 is to finalise three protocols on therapeutic randomized controlled trials. A trial letter of intent has been sent in to the Wellcome Trust for a Cluster RCT for testing bundled care for adult intensive care units in middle income countries, targeting pneumonia prevention and hygiene. Another proposal for the study of oxygen therapy in severely ill children has been submitted to the MRC. WG1 is aiming to take the previous GACT-SARI document (InFACT and ISARIC) further to funders, and it will play an integral role in the FP7 bid. In terms of WG-interactions, WG1 will provide a study framework for the other WGs, and will utilise tools and lessons learned by the other WGs.

### **WG2** - *Global data collection and collation*

WG2 is developing an on-the-shelf, rapid-response protocol for outbreaks and emerging threats – ISARIC Tools,

which will contain standard definitions and flexible data sets to cover different resource settings. Elements of data that are collected and similar will be assigned and specified, maximizing our ability to pool data across studies for potentially completely different purposes – and gathered into a protocol or a ‘recipe’ with the data included as its ‘ingredients’. WG2 is working with the Global Health Network that will provide a platform through which to run ISARIC Tools. Additionally, ICNARC and WHO Geneva will work together to write a Natural History Protocol, which will benefit the development of ISARIC Tools. WG2 is also performing a Delphi based study to agree on common outcomes for ISARIC run studies. WG2 is, effectively, providing the other working groups with the building blocks through which their activities are shaped and determined.

### **WG3** - *Genomics, Pathogenesis and Pharmacology*

The group is writing a protocol on host

genetic studies in severe influenza, and also developing sample collection modules for pathogenesis and pharmacology studies to be added to the inter-pandemic and rapid response protocols. A full application was sent into the Wellcome Trust in June and an interview is scheduled for October, the project (IISIG) was also well received when presented to the Council Meeting in Annecy. A study of biomarkers is also under way. The group interacts with WG1 as it seeks to provide its collection modules for pathogenesis and pharmacology as components of studies carried out by WG1. WG2 provides building blocks to WG3, while the barriers and solutions identified by WG4 influence WG3.

### **WG4** - *Changing clinical research paradigms for rapidly emerging public health threats*

WG4 aims to publish a review of ethical and legal constraints to developing a rapid clinical research

(continued)



response, convene two workshops to address issues related to ethical challenges, develop an open access module, and work towards pre-approved protocols. The group is also trying to find a more efficient way to prioritise which interventions to study and to get stakeholders to participate in RCTs. The activities of WG4 are gathered around four work packages, whereof the first relates to the network's capabilities and capacity, which is the subject for a consortium-wide survey. The second work package relates to the needs analysis for stakeholders, while the third package looks into specific ethical and regulatory barriers. The last work package concerns an operational plan for what ISARIC will do more specifically in the event of a pandemic. WG4 interacts with all other working groups by identifying the ethical and legal barriers affecting their activities, and by suggesting solutions to them.

Would you like to join a working group? Please contact the Secretariat for more details.

## Mother and Child Research Partnership

*By Calum Semple (FLU-CIN, UK) and Tim Uyeki (USA)*

**Stimulated by discussions in Annecy, a group of ISARIC members active in paediatric clinical research came together to form a paediatric SARIC clinical research network.**

*The ISARIC Mother and Child Research Partnership*, which includes researchers and clinicians based in North America, Europe, Africa and Asia, raised concerns about there being comparatively fewer global clinical research networks focusing on SARI in children than in adults.

Additionally, paediatric intensive care units do not exist in some middle-income and low resource settings, despite the high mortality rates for acute respiratory infection in children aged 5 and younger worldwide.

The network aims to establish regional membership within ISARIC that can represent or recruit clinical research networks focused upon hospitalized children with SARI on general wards or requiring intensive care. The network will function under and enhance ISARIC to ensure good representation in observational studies and RCTs to improve clinical management of paediatric SARI patients.

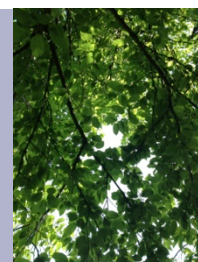
To date leading researchers such as Tex Kissoon (British Columbia's

Children's Hospital, and President of the World Federation of Paediatric Intensive and Critical Care Societies) and Stephen Stick (Lead of the Western Australia Respiratory Health Network) have agreed to join ISARIC, and Rosalind Smyth (Director of the UK NIHR Medicines for Children Research Network for the MCRN Clinical Studies Groups) have agreed to be involved.

Following its establishment, the network intends to widen participation in ISARIC by recruiting Maternal Health Research Networks. This should improve funding opportunities as bids are often invited by organisations that support "Mother and Child" health research.

*Calum Semple, Tim Uyeki, Dat Tran, Kathryn Maitland and Abdullah Brooks initiated the ISARIC Mother and Child Research Partnership.*

MCRP  
teleconference,  
under a tree...



## Children's Oxygen Administration Trial

*By Kathryn Maitland (KEMRI, Kenya)*

Addressing the poor outcome and mortality rates among children with respiratory distress and hypoxia in sub-Saharan Africa, COAST - a randomized controlled trial design, is aiming to provide evidence for the most clinically effective and cost-efficient targeted use of oxygen as a live-saving treatment.

In the developed world, high flow delivery of oxygen is used to provide substantial positive airway pressure in order to reduce the work of breathing, respiratory exhaustion, and the need for mechanical ventilation. This low-cost, easy-to-use technology has never been tested in a controlled trial in Africa.

At present, the in-hospital mortality rate for children in sub-Saharan Africa is 9-10% for those with oxygen saturation between 80% and 92% and 26-30 % for those with oxygen saturation below 80%, which indicates that current recommendations and/or management strategies are not working in practice.

COAST (Children's Oxygen Administration Trial), for which a funding application has been submitted to the MRC/DFID/WT Global Health Trials Call, will involve

4800 children, aged 2 to 12 years, from 4 sites in Uganda and Niger. The children will be enrolled at admission to hospital over 2 years, and followed for 28 days.

COAST will evaluate key elements of an integrated management strategy in African hospitals on the basis of clinical effectiveness and costs. Two related interventions to reduce shorter-term mortality at 48-hours and longer-term morbidity and mortality to 28 days in a fractional factorial design: (i) liberal oxygenation (recommended care) compared with a strategy that permits hypoxia to ( $\text{SaO}_2$ ) > or = 80% (routine care); and (ii) high flow compared with low flow delivery (routine care).

The trial has a pragmatic design to ensure that it includes a spectrum of high-risk children, who are identified largely by clinical criteria – guaranteeing that the results are applicable to the health services in Africa and their limited access to health technologies.

Although oxygen is a basic element of hospital care, poor implementation of current treatment recommendations – which are often based on weak evidence, is particularly visible in

low-income countries. Other reasons are related to the lack of availability of oxygen in many hospitals, or it cannot be used routinely due to unpredictable supply, faulty cylinders or limitations and interruptions of the electricity supply. This is resulting in a mismatch between supply and demand of oxygen in many rural hospitals in the developing world.

## Observational study

The ISARIC Executive endorsed the proposal that we should support ESICM in encouraging trial sites to take part in their international multi-centre, fourteen-day inception cohort study of severe acute respiratory infections on the ICU. ISARIC is very keen to learn from the challenges faced by ESICM in rolling out the study and the solutions found so far.

ISARIC needs to demonstrate collaboration between networks, and to set up a data management system and ISARIC tools. We will, in parallel, set up a non-ambitious observational study, which will involve ESICM.

Such a study could provide useful information that can be fed back into the activities of WG1, as they

**(continued)**

plan clinical trials. This would also provide feedback to WG2 regarding data variables, and WG4 would be able to use the study to build relationships with Ethics committees.

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## Membership

ISARIC offers two different types of memberships – Full and Individual. The Full membership is intended for networks while the Individual membership is there for individuals who are not yet eligible or otherwise not able to represent their networks. 'Networks' are very loosely defined in that they do not have to be very large or multi-national, but they do need to

meet the following pre-requisites:

- Independent, founded and led by academia (not industry)
- Scientifically active (scholarly contributions)
- Multi-centre (differing institutions involved)
- Access to patients for potential enrolment into studies
- Supportive of ISARIC's vision and mission
- Organised and structured in accordance to ISARIC's vision

Consideration will be given to organisations who are not networks but who are relevant to the mission of ISARIC.

To download a membership form and our membership policy please visit our website:  
[www.isaric.org](http://www.isaric.org)



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