ISARIC Stakeholders' Meeting: Collaboration and partnerships for global outbreak research preparedness and response

30 November – 1 December 2015
Wellcome Trust, London, UK

Meeting Report

Table of Contents

Executive Summary

One of the key lessons learnt from the 2014-15 Ebola outbreak research response effort in West Africa is that it is critical to establish excellent working relations and collaborations in the inter-epidemic period in order to improve the response to future outbreaks.

The International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) convened this meeting to bring together key global stakeholders (including representatives for clinical research networks, clinicians, research funders, public health bodies, industry, and non-governmental organisations) in order to improve the prospects for a rapid and coordinated clinical research response to the next outbreak or pandemic.

Word Cloud for the meeting proceedings

Apart from facilitating a discussion on collaboration, the meeting identified pathways for strengthened capacity building for research preparedness, particularly in low-and-middle-income countries, and discussed setting up a global rapid response task force within the clinical research community. Participants also explored the barriers and bottlenecks to rapid research responses and identified solutions.

The meeting brought forth the following actions that need to be addressed as part of ISARIC's Strategic Objectives:

- The establishment of Regional Hubs in regions where platforms such as the Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE (FP7)) do not exist. The hubs should be run by research networks in the regions, and address diseases, bottlenecks, and barriers specific to the region, while also enabling regional capacity building.
- The development and establishment of a global data management platform that is CDISC (Clinical Data Interchange Standards Consortium) compatible and that will enable harmonised data collection and global data sharing.
- The need for the clinical research community to engage more closely with humanitarian organisations and other partners ahead of infectious disease outbreaks.
- The establishment of a global rapid research response task force that will enable a rapid response to outbreaks in resource poor areas of the world where there are capacity and capability gaps for research.

This two-day meeting was well attended, with 18 countries represented (encompassing 8 low-and-middle-income countries, including Liberia and Sierra Leone, which experienced widespread and intense transmission during the recent Ebola outbreak). The meeting output will feed into the development of the World Health Organization (WHO) Research and Development Blueprint for preparedness for epidemics.

This report outlines the core output from the meeting under Meeting Proceedings, including summaries of each speaker presentation and Q&A session.

Meeting Proceedings

Day 1: Monday 30 November, 2015

Professor Mike Turner (Wellcome Trust (WT)) welcomed the group of 70 participants attending in person and those joining through webinar.

In his opening remarks, Professor Roberto Bruzzone (Institut Pasteur & ISARIC Vice Chair) highlighted the need for ISARIC to take stock and find ways to strengthen collaborations, with the added goals of planning ahead and capacity building.

The keynote address was delivered by Dr Robin Robinson (Biomedical Advanced Research & Development Authority (BARDA)), who focused on the resilience chain and BARDA's role in bridging the "valley of death", the term given to the inverted pyramid which illustrates the expensive, risky and lengthy process involved in vaccine and drug development, where only 1 in 50 candidates succeed (for reasons of cost rather than efficacy). The paradigm of normal preparedness versus emergency research and development was put forward and highlighted the question of whether emergency R&D for emerging infectious diseases is going to become the new norm. BARDA key successes were noted to include creating a robust and innovative medical countermeasure development pipeline, establishing and nurturing partnerships, establishing robust manufacturing capacity and helping medical countermeasure developers for preparedness & response. The meeting was invited to consider the question of further global bio preparedness uncertainty and will bioterrorism fatigue, disbelief & denial persist? Robin Robinson raised the key question of who is steering the ship as a number of groups are trying to fill the space and where are we going?

Ana Maria Henao-Restrepo (WHO) presented an overview of the WHO Blueprint for Research and Development. The Blueprint aims to reduce the time lag between the declaration of an international public health emergency and the availability of effective medical technologies that can be used to save lives and avert crises. To do that, the Blueprint will promote research to better understand the human-pathogen interface and to generate safety data from Phase 1 studies in man for the most promising experimental products for priority infectious diseases before the outset of an outbreak. It was acknowledged that R&D can and must be accelerated and research gaps must be anticipated.

The rest of Day 1 and all of Day 2 of the meeting was divided into six speaker sessions, each followed by a Q&A session that has been summarised following each session. The presentations delivered during the sessions have, where permission has been granted, been included through the hyperlinks via the name of the speaker concerned. Any difficulty accessing the links should be reported to sarah.moore@ndm.ox.ac.uk.

Zika virus – Fernando Bozza (National Institute of Infectious Disease, Oswaldo Cruz Foundation (Fiocruz); Brazilian Research in Intensive Care Network (BRICNet))
The meeting took the opportunity to break from the agenda to include a presentation by Fernando Bozza on the Zika virus outbreak in Brazil and a significant increase in observed congenital microcephaly, which raises serious questions about a direct association between the two. ISARIC agreed to set up a teleconference call and adapt existing CRFs and protocols which might be of use in the study of microcephaly.

Speaker Sessions: Day 1

Session I: Rapid Research Response task force

Trudie Lang (The Global Health Network (TGHN) & ISARIC): *Rapid Response Task Force*

- Aim to deliver clinical trials on infectious diseases in challenging settings in a thorough, rapid and versatile fashion
- Clinical trials require excellent staff who understand the protocol and can apply it to the specific setting
- Advance in trial efficiency is required: Ebola pre-clinical research began in March 2014 but the trials did not start until January 2015
- Increase capacity in low-resource countries by establishing a system of readiness and rapid deployment
- On-going training and briefing activities online and at annual regional meetings

Nikki Shindo (WHO): *Role of clinical management and infection control in reducing emerging infectious diseases*

- Create a platform for information exchange to aid clinicians
- Identify experts in each disease, document this and other guidelines and publicise
- Public health and contingency plans in low-resource areas or 'hot spots'
- The clinician's role is increasing: ensure information is up to date, risk factors are accounted for and the care and cure are determined
- Challenge faced: front line staff are overwhelmed and have limited information available to them
- Offer tools to clinicians to improve healthcare of country by providing documents within 48 hours
- Make use of all networks and authorities to help control epidemics and pandemics
- Continue to update pre-approved standard guidance to different countries to achieve the best treatment

David Hui (Chinese University Hong Kong): *Experiences of responding to outbreaks investigation as part of a team*

- Personal experiences of epidemic deployment and response
- SARS HK in 2003
- In 2004 DH went to Vietnam, the Vietnamese MoH had asked for WHO's help with the H5N1 outbreak; no proven therapies or diagnostic tests were available, mass cull of chickens ended the outbreak
- Learned from infection control mistakes in HK where isolation rooms became available from 2005 only, hygiene and limited contact measures improved patient outcomes
- China was opening up to visiting clinicians during outbreaks, in 2005 DH visited Hunan where village homes were still shared with domestic animals
- Causes for super-spreading of the South Korean outbreak were poor infection control, patient movement within and between hospitals, poor ventilation, overcrowding, visitors, 'doctor-shopping' (= seeking care in multiple facilities) and contaminated environments
- Factors assisting access to outbreak sites; employer support for urgent leave, cover, remembering visa restrictions, collaboration with hosting countries
- Learning experience, helping to understand for future epidemics

Maria Van Kerkhove (Institut Pasteur): *Pasteur's Outbreak Investigation Task Force*

- Institut Pasteur works in co-operation with WHO, responding to global infection outbreaks, and assisting with local government response

- OITF (Outbreak Investigation Task Force) - roster of individual experts
- Primary aim is to stop an outbreak and offer support
- 33 institutes in 26 countries
- Aim is to be deployed to smaller outbreaks within 48 hours
- Findings from the H5N1 experience in Cambodia; investigations, surveillance and shared experiences between countries important
- For Ebola, IP offered assistance, working with GOARN (WHO) and setting up incident management structures
- Recruitment is in progress
- Preparedness; logistics etc. – typically takes 2-4 weeks
- Other considerations; security aspects, tackling ethical concerns, applying tools in the field
- Complementing with existing programmes, not duplicating

Discussion & Q&A
Panel: Chair: Mike Turner (WT) & Mauricio Ferri
Panellists: Trudie Lang (TGHN & ISARIC), Nikki Shindo (WHO), Maria Van Kerkhove (Institut Pasteur), David Hui (Chinese University of Hong Kong), Rob Fowler (Canadian Critical Care Trials Group (CCCTG) & ISARIC), Gail Carson (ISARIC)

***Q**: Is there infrastructure to coordinate all the Rapid Response Task Forces currently operating or is it being developed?*
A: It is essential that the infrastructure necessary is developed ahead of the next outbreak. In order to do so we need to step back and look at what happened during the Ebola response and align our capacity and infrastructure building efforts accordingly. There is a leadership and coordination role here for WHO, though ISARIC should be bringing people together and, through its membership and partners, set up the regional capacity and capability to initiate rapid responses.

***Q**: First issue is coordination and the potential for resistance. Could look at a model of regional and sub regional structures (e.g. WATER). These should become part of the platform and framework for ethical issues etc. Africans want to take ownership.*
A: It is important to consider the challenges faced by the countries themselves when they receive "help" from other countries, local leadership and involvement is necessary for coordination. However, 'seasonality' and lack of hospital/ICU infrastructure pose a challenge to surveillance let alone research in some settings. That said, WHO has implemented a programme of district hospital training for staff at all levels (not primary care), from security to triage staff that is supported by the MoHs. There is a mobile reporting system and the programme has sample collection and lab links. WHO is seeking to roll out the programme in all hotspot countries. Examples given concerning capacity building efforts were a *clinician* surveillance course that has started in Sierra Leone and that includes basic training and capacity building adapted to local conditions; the capacity building activities supported by the European and Developing Countries Clinical Trials Partnership EDCTP; and effort by TGHN and EDCTP to link up networks in the region.

Session II: Connecting with industry, funders and public health bodies

Carol Epstein (MediVector) via Webinar:
- MediVector is a smaller pharmaceutical company with a perspective on preparedness
- Favipiravir January 2014 - MediVector was managing an influenza program under HDTRA1-11-R-0019 (Advanced Development of New Antiviral Against Influenza Virus)

- Significant investment was required by MediVector for the B&P effort; $1.7M internal funding + $1.2M external = $2.9M; a complex process Utilised Earned Value Management System (EVMS); designed to help manage time and costs
- Cost of setting up and supporting EVMS is approximately $9.2M external + $2.9 internal = $12.1M for the life of the contract (these costs would be reimbursed under the contract)
- Ebola contract; Justification and Approval (J&A, sole source) approach was used to award this contract. Normal process would have been impossible
- Does not involve full and open competition as required by the Federal Acquisition Regulations (FAR)
- Possible because of: flu contract, broad spectrum data, animal work done (rodent and NHP) by USAMRIID
- Normal process would have been impossible
- Ongoing work with USAMRIID (NHP studies) continued
- Discussions with multiple branches of DoD regarding logistics and goals of Ebola project
- Phase 1/2 and Phase 2 placebo controlled studies
- Next programme; a solicitation package, development and delivery of a FDA licensed Biodefense therapeutic (Marburg, Ebola), due in January 2016

Richard Hatchett (BARDA):

- As a public health body and funder, for BARDA there are challenges in contracting processes, therefore partners are important
- For emerging infectious diseases the public expects results quickly
- Aim is to end an outbreak and have medical countermeasures available as necessary
- Public health intervention offers opportunities to develop medical countermeasures and for the development to have reached the late stages
- Ebola is not a typical emerging infectious disease; on the radar for an extensive period
- Can be a model for other threats; MERS medical countermeasures are being developed
- How to respond to novel threats? e.g. with broad-spectrum antivirals, rapid re-purposing, animal and human trials
- 'tech-watch' programme; representatives meet with companies informally (before white papers)
- Annual industry day allows for discussion on priorities, changes, Q&A
- Coordinating privileged relationships e.g. with DoD, FDA and other regulatory authorities
- Tasks: linking up with local resources, preparing toolkits, tailoring protocols for unpredictability, anticipate not having vaccine or drug
- Benefits: mapping pipelines, optimal attributes for medical technology diagnostic tools, approaches to leverage industries, mechanisms to improve global coordination, portfolio of promising expertise
- Procure and produce network familiarisation
- Research and development should be accelerated through addressing gaps, working with experts on the blueprint, toolkits and surveillance systems
- Community engagement: communication of blueprint, giving community empowerment

Pasi Penttinen (European Centre for Disease Prevention and Control (ECDC)): *Clinical research during outbreaks*

- Perspective from a public health agency
- Reflections on the translational medicine lessons from the 2009 pandemic
- In the EU, public health is a shared competence, and ECDC's role is primarily in surveillance and risk assessment
- Advisory role in risk management
- Providing guidance

- 2009 pandemic: ECDC was monitoring the fatalities by officially reported cases and through active social media and internet-based monitoring within Epidemic Intelligence activities
- Mortality is not the only indicator of severity and another way to look at it is to look at the proportional pyramid, or iceberg
- WHO commissioned the Review committee assessing the International Health Regulations also to look into the global response to the pandemic
- Concluded that WHO should develop and apply measures that can be used to assess the severity of every influenza epidemic
- Routine and ad hoc surveillance systems should form the bulk of the assessment but leading clinical practitioners and researchers need to improve the preparedness for rapid studies in the first affected countries to inform policy making
- Management of severe influenza; there is a paucity of high quality clinical research to inform clinical care
- MERS-CoV discovered via epidemic intelligence, surveillance, early detection, and with help from media
- MERS preparedness in Europe to include lab capabilities and External Quality Assessment (EQA), case studies, rapid risk assessments, scientific guidance
- More work to be done on hospital preparedness and on surge capacity for large-scale outbreaks
- What public health needs from clinical research; improving case detection and surveillance, studies to assess primary infections, studies to assess risk factors for nosocomial transmission, human serological studies, treatment options, vaccine
- Conclusions; during outbreaks organisations should network, using and linking surveillance and communication systems

Johan Van Hoof (Janssen Pharmaceuticals): *Industry perspective*

- Janssen's commitment to a filovirus vaccine; the fact that an adenovirus-based Ebola vaccine was already in the clinic is no coincidence
- Achieved complete proof-of-concept in highly stringent NHP model
- The announcement by WHO of the public health emergency forced a change of gear with the acceleration of Ebola Monovalent Vaccine Program
- WHO meeting on Ebola vaccines access and financing in October 2014; stakeholders were working shoulder to shoulder. The outcomes of the meeting were ambitious. Everyone was eager to overcome obstacles. Important to ensure that if the vaccines worked, they could be made available
- Need to develop multivalent vaccines
- Challenges specific to the Ebola outbreak; technology, field conditions, epidemic dynamics
- Janssen is involved in 4 projects relating to Ebola, 1 of which is how to ensure the communities are engaged (through local radio etc.). Additional support is provided by BARDA and NIH
- Lessons learned;
- positive: eagerness across all stakeholders to join forces, "Can do attitude", several successful Public Private Partnerships created
- challenges: as epidemic wanes, sense of urgency is less, interest in getting early solution is diminishing, several hurdles still not addressed, regulatory pathways still unclear, not sustainable model for industry
- path forward: design and implement sustainable model to ensure readiness for future biological threats
- GSK has recently launched the idea of a business preparedness organization. Janssen is interested in joining this type of thinking.

Finnian Hanrahan (European Commission (EC)): *The GloPID-R initiative - Global research collaboration for infectious disease preparedness*

- The only initiative of its kind to bring together research funders and coordinate their response to epidemics at a global level
- GloPID-R does not involve a financial commitment from members
- Goal: launch of an effective research response within 48 hours of an outbreak. This was initiated under the Ebola response. Importance of the exchange of information.
- Currently there are 14 members, with WHO as an observer. Wellcome Trust and the - African Academy of Sciences have recently joined
- On-going activities: readiness plan for funders in case of an outbreak, Scientific Advisory Board (SAB) being established, Work on barriers: surveys by the secretariat, data sharing in public health emergencies, MERS-CoV: mapping of related research activities

Discussion & Q&A

Panel: Chair: Roberto Bruzzone (Institut Pasteur) & Ilaria Capua (Istituto Zooprofilattico delle Venezie, Member of the Italian Parliament)
Panellists: Carol R. Epstein (MediVector), Richard Hatchett (BARDA), Pasi Pentinnen (ECDC), Johan Van Hoof (Janssen/Johnson & Johnson), Finnian Hanrahan (European Commission)

***Q**: What part do industry funders play in the inter-pandemic period?*
A: Supporting a trial designs platform. Context is important e.g. Ebola trial designs reflected the state of product developments. Adaptive trial designs are complex and capacity would need to improve simultaneously to be able to complete them in low-resource settings.

***Q**: Designs are complex even in well-resourced areas but there is no empowerment in the developing world. All actions are coming from the developed world. This inequality is not sustainable. What is the long term strategy for a more partnered approach with the developing world?*
A: Ethical steps are being taken in developing countries to improve the environment and platform in which research is done. Samples are also being retained in countries of origin and capacity is built around that.

***Q**: What attempts are being made to mobilise funds outside Europe, Canada and US to make research and political $$s available in LMICs?*
A: Africa is becoming more equally governed. As a result we are better placed to approach the issue through study templates and capacity building.

***Q**: Convince stakeholders that studies like convalescent plasma for influenza can be done in an inter-pandemic environment and could we then start pushing for repurposing to improve patient care in poor countries.*
A: Influenza is already being supported in this way but there is not enough money to implement a large scale intervention. Such an intervention would also mean government involvement. More emphasis should be placed on educating people to prevent influenza by handwashing and correct food preparation.

Session III: Barriers, bottlenecks & solutions

Abha Saxena (WHO): *Ethics Review – bottlenecks and pre-review; how to be more efficient?*

- Protocol needs to be complete, coherent, scientifically sound and ethically appropriate
- It needs to be understood and implemented in the same site throughout
- It should have an appropriate study design

- One of the biggest issues is the drug dose. These are basic factors but they create the barriers
- Frequently advised that the protocol has been approved by a scientific peer review group; true but all too often what has been approved is the proposal/concept note and this is where the tension lies – Ethics Committees review the protocols
- Most protocols do not provide responses that Ethics Committees want e.g. what will happen to the samples? If investigators consider what Ethics Committees really need, this would make a difference.
- WHO received Oct 14 - Dec 14 1400 research projects. Very often the Ethics Committee was frustrated.
- Research activity in the field. Was it or was it not research? If it is not research then the output from the analysis should be used to support the clinical management of the patient. The sample collection approach should be decided upfront. Investigators should think about how they will store the samples.
- Multiple ethics reviews creates a bottleneck, if it involves more than 2 or 3 countries. There is no communication between ethics committees. The view is that it adds value to have multiple reviews and local ownership. This raises several disadvantages; logistically cumbersome, Ethics Committees may have had no prior engagement, local and some international ethics committees are over-burdened during an emergency
- There is also a problem that the local ethics committees are challenged. Used to reviewing less than a dozen protocols in a year. In a 6 month period, one of the affected countries had 60 registered trials. Quality of review needs to be questioned
- Plan for discussion: When there is a sponsor or PI submitting to the ethics committees, WHO submit their responses to the central ethics committee, which takes responsibility for review. The central committee would review all comments from each committee and everyone would agree to the final set of recommendations
- Template protocols and consent forms: guidance required on what needs to be done. Difficult to pre-approve anything from an ethics perspective. The peer reviewed protocol will be standardized. Further thinking and guidance is needed.
- Community engagement – should begin in 'peacetime'. Researchers should engage with the communities
- Capacity strengthening – not only of committees but of their secretariats and researchers
- Capacity strengthening to go beyond clinical trials

Ilaria Capua (Istituto Zooprofilattico delle Venezie, Member of the Italian Parliament): *Gorillas in the mist: talking science to politicians*

- A different perspective; need to improve on communication. IC has had to develop a language to talk to politicians.
- Emerging or re-emerging infectious diseases encompass events that can be; predictable/rather predictable/unlikely/very surprising/surreal
- The international scientific community has the responsibility of generating sound scientific data, but is that enough?
- Need to descend to the general public and ensure that they are engaged
- Scientists are bad at talking to politicians. Why? funding /direction /strategy
- Politicians are not interested in the data but what the press says (not the article itself but the headline)
- Politicians are influenced by their constituency and fear not being re-elected
- If scientists are not capable of delivering the right messages, they cannot expect to put the view across to politicians

- From a European perspective (in US emerging disease research is linked to defence) need to be able to plug into European framework policies
- Awareness about inequality: united against terror. Terror groups thrive on poverty and despair. Hunger and disease are embedded in poverty
- Would it not make sense for one group in the fight against terrorism and against poverty to say "we need to fight for health"? Make the money available for a more sustainable health system for people and animals.
- We need to stop thinking that the scientific community does not need to interact with politicians - it is **our** problem

Brian McCloskey (Public Health England (PHE)): *Barriers to research in outbreaks*

- A substantial number of MERS CoV cases were reported in 2012 in various low-income countries
- Lack of funding and available information, as well as coordination and governmental issues appear to be the main obstacles in helping these patients. Ownership for these problems needs to be taken. The blueprint will help with this
- What we have learnt from Ebola needs to be taken forward
- A commitment to sharing information, data and samples needs to be made. In doing so, care should be taken for this to be done fairly so that poor countries are not disadvantaged
- Factors preventing sharing, such as lack of patient consent or fear of losing intellectual property, should be resolved. For instance, it should be agreed that sharing for public health purposes will not prevent papers covering this information, from being accepted for publication

Laura Merson (WorldWide Antimalarial Resistance Network (WWARN) & ISARIC):

- Data collection forms contain a number of common outcome measures for creating a data sharing platform
- Although everybody completes the same information, certain text can be interpreted in different ways, e.g. 'severe' can be measured at different levels
- The second stage after form completion is the recording of this data. The variety of ways in which people record this information can also pose a problem
- Data sets need to formatted and responsible data sharing should be implemented
- The Ebola clinical trial lab data should be collated
- Framework should be standardised and sent to the contributor, curator and collaborators
- WHO support required to publish new treatment guidelines and policy

Discussion & Q&A

Panel: Chair: Fernando Bozza (Brazilian Research in Intensive Care Network (BRICNet) & ISARIC) & John Amuasi (Kumasi Center for Collaborative Research in Tropical Medicine (KCCR) & West African Task Force for the Control of Emerging & Reemerging Infections (WATER))

Panellists: Abha Saxena (WHO), Ilaria Capua (Istituto Zooprofilattico delle Venezie, Member of the Italian Parliament), Brian McCloskey (PHE), Laura Merson (WWARN & ISARIC)

The Chairs suggested that the Discussion session should particularly focus on the failure of clinical research and educational aspects, how to involve LMICs in research better, ethical questions, and information sharing.

***Q**: Are data collection forms used well in MERS (e.g. in Saudi Arabia)?*

A: When Ebola progressed in August 2014 there was no ethical guidance, this was prepared as issues came up. For other outbreaks there have been established frameworks in place. In May 2015 a WHO public health response for epidemics meeting took place. Operational guidance is lacking in the field. A WHO working

group will be set up, any guidance to that is welcome. During the Ebola outbreak the community structure helped to obtain a successful study, every participant was invited to contribute. MERS is different. A lot depends on the science and context.

***Q**: Regarding the WHO ethics protocol submission; can you give examples where errors have occurred?*
A: Investigations are often conducted in a hurry, one template (copy & paste) is being used for all. Should be careful with this, also not to pass a research project to an inexperienced person or group. We need to recognise that scientists hate filling in forms.

***Q**: How can ethics committees help with collection and storage of data and samples?*
A: Templates exist and should be used. During a research study, planning negotiations on data sharing agreements are time-consuming and are often done when studies are started, but ideally they would be conducted before an agreement is reached with a committee and before the study is started. An ECDC framework for sample and benefit sharing to all parties is in place. The WHO Blueprint is providing guidance on data sharing (e.g. MTAs). Sample sharing protocols are in place between countries.

***Q**: Pre-approval and pre-positioning can work when Public Health England (PHE) supported, how ethical work approval is done, GloPID-R, data sharing platform and other frameworks are crucial, funding and political will are essential - with support for change. Therefore, how do we engage politicians? How do we get MoHs on our side, and a PH response?*
A: During the Ghana Ebola trial discussions politicians and public were closely involved. Politicians should be approached at the right time and keep them informed – however do not give them unlimited power.
The UK has a good Chief Scientific Advisor. Scientists need to 'sell a story' to the politicians, have a good communications strategy in place, create interaction and engender trust with them. Insufficient communication has implications for the countries, communication should be a part of the research agenda. ISARIC needs a story to sell. More effort needs to be devoted to creating a good communication strategy, using not only social media, but other avenues. The countries should be the top priority of funders. Crucial to talk to politicians of poorer countries, not necessarily our own. Working backwards is happening now, instead a data platform should be ready for the government. During Ebola, the community engagement was poor, the three countries had weak health care systems and these factors amongst others created a poor patient outcome. 'Lessons learned' exercise should be done. Preparedness plan should be independent from politicians.

***Q**: There is little enforcement capacity, should the IHR be changed?*
A: Changes to the IHR will be released in January 2016. Trying to remove them a bit from politics.

***Q**: What about regulatory approvals, and legal/ethical approvals at a community-consent level?*
A: Ethical and regulatory approvals don't mean there is community approval. How to ensure that there is community buy-in, in addition to national approval. There needs to be a public framework in place for communication, legal/liability issues, and political/access to product issues, before the trial starts. The final approval comes from the patient taking part in a trial.

Day 2 commenced with a summary by John Marshall (Canadian Critical Care Trials Group (CCCTG), International Forum for Acute Care Trialists (InFACT) & ISARIC Vice-Chair) of the **key themes** from Day 1, which were:

1. Creating and promoting common research infrastructure
2. Establishing a capacity for rapid and effective outbreak responsiveness
3. Inter-pandemic preparedness and global capacity building
4. Understanding the interface between research and clinical care

For each theme, participants were invited to consider 3 questions, which would form the basis of networking break-out sessions later in the day:

a. What resources/organisational structures are needed?
b. What activities can ISARIC initiate in the next year?
c. Who will be our key partners?

Speaker Sessions: Day 2

Session IV: Humanitarian collaboration

Mary Van Lieshout (GOAL)*: Strengthening Research Collaborations During Humanitarian Crises*

- GOAL is new in the field of research; the organisation sees the responsibility and potential to be involved in research
- Survivor studies - looking at a research and learning strategy.
- Evidence building. Barriers – knowledge of what is out there (operational). Identifying research potential
- Sufficient Development 'Orientation' of Health researchers
- Competing time pressures
- Access to populations, resources, competing organizational culture

Annick Antierens (Médecins Sans Frontières (MSF)): *Humanitarian collaboration*

- MSF's collaboration with NGOs depends on the context and situation on the ground
- For MSF it may not be possible or appropriate to conduct research, especially clinical research
- Local population may not welcome MSF at times, their involvement may be misunderstood
- MSF has done research studies and observational studies in the past - but not clinical trials
- Drugs for Neglected Diseases Initiative (DNDi) confirms that e.g. data sharing platform is important
- The aims are to reduce mortality, improve access and not to harm the patient, family or staff
- What are the relevance, objectives and agenda of research?
- What are the feasibility and ethics of research? Informed consent is required. More people should not be put in danger (e.g. PPE in Ebola)
- Ethics include different designs, acceptability, and depend on how the epidemics will evolve
- Getting intermediate results during epidemics is difficult, if the sample size is reached the trial will be more successful
- Who does what and who is in charge? Who deals with logistical needs, handling delays etc?
- Challenges in standard of care and intervention, where are research and diagnostic samples going? (Why out of the country, who is in charge?)
- Is there an ethical review board in the country with high-level ethicists?
- At times SOPs cannot be followed and recruitment of patients can become difficult

- Issues should be anticipated and built into protocols
- Despite good intentions, access to sites and medical care can be restricted
- What to do with data, how is post-trial access to an intervention arranged
- How to prepare MOUs, roles and responsibilities, IP, biobank, data sharing and trial agreements?
- MSF can help with the coordination, and would like to be involved in affected communities - Data sharing remains important

Michael von Bertele (Save the Children Fund (SCF)): *Should NGOS be undertaking research?*

- Save the Children Fund is a humanitarian and development organisation (merged with Merlin to develop a better health capability)
- With 32 member countries it is a service organisation providing multi sector project support and large-scale logistics
- SCF was asked to run a treatment centre although Ebola was considered more of a public health problem rather than a clinical one
- Research has not been very high on the agenda of SCF for some years
- SCF does have staff on the ground and logistics, to support research teams and data collection
- Low-level research that was useful to SCF was conducted e.g. retrospective data analysis, case fatality rate, outcome by stage
- SCF undertook other studies, treatments, protocols, different trial types
- SCF had to go to a national research committee in each country
- Donors retained an interest (e.g. DfID), together with general interest at the international level, also from universities
- SCF can provide governance support and a security 'wrapper', but the academics must do what SCF say in terms of security and domestic support

Discussion & Q&A
Panel: Chair: Dean Everett (Malawi-Liverpool-Wellcome Clinical Research Programme, University of Liverpool (MLW) & ISARIC) & Pasi Penttinen (ECDC)
Panellists: Cathy Roth (WHO), Annick Antierens (MSF), Mary Van Lieshout (GOAL), Michael von Bertele (SCF), Peter Horby (ERGO & ISARIC)

***Q**: Capacity building in low-income country healthcare systems should not be any different from any other trial, yet challenges such as hostile environments and priority of clinical work over research exist. Local people hold a negative view of research and we need to educate people, including clinicians, and bring about a cultural change in order to alter this view. There needs to be a firm belief that we are working with NGOs and not against them.*
A: Trust, communication, preventing harm to vulnerable populations, community involvement and a common understanding can all help in overcoming this issue. Collaboration and planning will help us to build a relationship and establish what is available in the country.

***Q**: Getting informed consent is very difficult in emergency care. A cultural shift needs to come about to move away from individual consent and towards community consent, with the ethical review at the population level. How can this be achieved?*
A: An emergency reform to the clinical management system is needed. NGOs should be trained and assigned to take care of Ebola and non-Ebola patients and to handle infection control. Bringing in certain standards of care will improve the survival rate. Rapid response to early warning signs is crucial.

***Q**: Can the mechanism work and be improved on?*

A: The advisory committee for Ebola and a priority list of interventions would assist. Coordination of a research agenda for central leadership should also be produced. WHO would be responsible for this but would not own all parts. Setting the ground rules is done through our research approach, adding on our care provision rather than taking parts away. We should decide on our roles and responsibilities in doing so, interlinking research and care.

***Q**: How do we manage community involvement, informed consent and horizon scanning?*
A: To answer those questions we need to evaluate standard of care by assessing how we do this. Alongside current processes, the lessons we have learnt from the past can help us plan for the future. Better approaches in products, behavioural and other research and surveillance can also help. Refugee populations and missing data are other factors to be considered.

***Q**: Will there be an ethics committee for NGOs amid high levels of competition between them?*
A: The advisory board will advise instead of an ethics committee

Two important areas of research in the future
- Evaluating the Standard of Care, and value of components of treatment
- Research on increasing care in refugee populations – there is danger here because there is no way to adequately evaluate the situation – no infrastructure to do this

***Q**: Was there competition between NGOs for research trials?*
A: Meta-Ethics: multiple trials competing for the same patients. There should be a larger ethics body to manage many trials. Received lots of support from other NGOs – no competition. Had no capacity to set up ERBs within the organization, so relied on academic and individual site ERBs. Donors and stakeholders (e.g. DfID, USAID, CDC) should decide on expectations, under the guidance of WHO. There was competition between trials and institutes, but not NGOs. There was huge political pressure on them. There may have been competition between countries.

WHO activities on data sharing & biobanking update
Cathy Roth (WHO)*: Data sharing and biobanking Developing Global Norms for Public Health Emergencies*

- Flexible models of consent and clearer articulation of benefits
- Knowledge gaps. Background to the data and results sharing consultation
- Most important impact of not sharing is suffering and death
- Conclusions: data sharing must become the global norm in public health emergencies
- Just published a paper. Sharing of information of importance in a public health emergency will not impede the scientific evaluation. Need for a code of conduct to be developed
- Data sharing is the default option. Funders to encourage compliance of data sharing
- The standard is for all work to be published within 1 year, which is too long

Session V: Low and Middle Income Countries capacity building, collaboration and networking

Mauricio Ferri: *Capacity Strengthening – Real Life Example of "Simple" Intervention in a Complex System in Sierra Leone*

- Capacity strengthening for research and response together
- Rapid response versus capacity governing strength require balancing
- Training, mentoring, quality improvement and application of knowledge required at bedside
- Quality improvement and quality indicator guide over mentoring

- Training, behavioural change, mentoring/audit, and feedback lead to impact, improved clinical management and improved outcomes
- EVD screening, triage, feedback and monitoring steps
- Evidence and data collected by paper based forms and asking the Ministry of Health of Sierra Leone to approve a screening form
- The context is important: how much data is to be collected? And how successful will the collection be?
- Disease surveillance data collected by hospitals is included in a weekly WHO report for each district but currently, there is no central database for this information. No reports have been submitted since Ebola
- We have a 4-month endorsement to print forms and complete initiatives
- Ebola screening facilities in hospital entrances are to be introduced
- An interagency and international plan is underway to combat actions for the districts of Sierra Leone but this does not take into account the assets of the Ministry of Health
- A decision from the Ministry of Health regarding a case definition for Ebola changing and non-case definition changing, will soon be made. This will adapt across 3 months and will be the building blocks for the health system
- Does the emergency mind-set distort programming? How do we recognise this?
- The capacity of an individual, team, organisation or system are not free from boundaries or economic failure
- Knowledge to action changes behaviour and practice at the bedside

John Amuasi (KCCR & WATER): *Ebola Diagnostic Training in Ghana & Regional Collaboration to Address Emerging Infectious Diseases*

- With regard to diagnostics at the Kumasi Center in Ghana, the governments of Ghana and Germany need to have a more autonomous approach
- The KCCR grant has funded a new building and 30-40 new freezers to be housed in it. The grant does not allow the build of multiple upper floors but there is the possibility to build lower floors
- Help countries who have not suffered Ebola to prepare should they encounter it. The UK and Ghana are two of the highest risk countries due to increased travel
- Equipment and training material that teach about the virus and how to handle this pathogen should be available. The materials should include SOP's and e-SOP's
- Networking equals training opportunities and greater quality control. WATER (a West African partner) and others, could be part of this networking task force that is used to advise
- Greater quality control in the future may prevent the scale in which we are affected by diseases
- Important to not become bogged down with politics in order to achieve the desired effect
- Bio ethics is an evolving voice for engagement. How should the samples in the biobank be banked? And should there be an inventory? There is a biobank in at least one African country and we should look at how the samples in this bank have an influence on health care systems

Alistair Nichol (ICCTG): Global Adaptive Clinical Trial - Severe Acute Respiratory Infection (GACT-SARI))

- We need to establish the clinical research platforms before epidemics start and fast forward and integrate response during the early stages
- Measures such as regional hubs and trials at times of pandemics will aid us
- PREPARE-Europe holds €26M and PREPARE-Australia holds AUD$3M
- The ICU clinicians of SARI will take information from a trial to inform design and adapt the trial to the needs of 4,000 randomised patients (currently only adults, children to be included at a later stage).

They will also measure seasonal and pandemic surveillance of their system. This information could be linked into public health security systems
- Embed research in clinical response and capture information to improve external validity
- Armed and versatile infrastructure needed to improve quality of clinical care
- Staff, patients and approvals should already be in place before epidemics take hold

Peter Horby (PREPARE)*: Fast-forwarding clinical research during epidemics*
- Fast-forward clinical research via network sites and adapt to new trials during epidemics and include primary and secondary care groups
- TRACE and GRACE research consortia are linked to pre-clinical networks
- Clinical observational studies A. (MERMAIDS), B. (ALICE) and C. (ADSCAP) are ready to begin as part of PREPARE Europe
- A biobank and testing platform is required to establish if the second pandemic virus is compatible with other work packages such as the pathogenesis one (PATHOS).
- Outbreak preparation, mobilisation and response are key factors
- The central coordination unit is in Antwerp with different work packages led by different groups
- CRISP is the information platform. There is a centralised randomisation process and a centralised database
- Different trials have different eCRFs
- Each work package leader has their own clinical trials team which carries out monitoring
- Training includes investigator training and site visits with site training

John Marshall (CCCTG, InFACT, ISARIC)*: Capacity Building, Collaboration, & Networking: The Intensive Care Perspective*
- Every healthcare system has to care for sick patients but intensive care environments and capacities vary globally
- Popular view is that it is high-tech medicine with complex technology, yet clinicians' questions remain practical such as administering fluids, safe support, complication prevention
- Standardised standard of care doesn't exist and this has implications on outcomes
- Therapies and better applications certainly improve patient outcomes (e.g. with fluids and ventilation, without medications)
- CCCTG was formed in Sept 1989; it is a research collaboration of 20-25 intensivists in multi-centre clinical research in critical care
- Meetings take place three times a year, the members conduct reviews of 60 different research programmes, assist with publications
- Members are investigators, not academics, discussing protocols, studies etc. in order to gain confidence and knowledge – and providing a future model for interaction
- InFACT is one of the multiple groups globally
- Has influence of organisational model on study and practice
- Model can spread to global collaboration; mentoring emerging groups to understand infection is offered, and local expertise developed
- Also has a fellowship programme
- SPRINT-SARI is developing access maps for mapping global acute care capacity and crowd-sourced funding
- COMET initiative
- Conference "Building Global Collaboration in acute care research", Whistler Canada, on 28.2. – 2.3.2016 jointly with ISARIC, InFACT, CIHR, ICSR

Discussion & Q&A
Panel: Chair: Kath Maitland (KEMRI Wellcome Trust Programme & ISARIC) & Mandeep Chadha (Indian Council of Medical Research)
Panellists: Mauricio Ferri, Alistair Nichol (GACT SARI), Peter Horby (PREPARE), John Amuasi (KCCR & WATER), John Marshall (CCCTG, InFACT & ISARIC)

***Q**: How far have you got with the IC groups?*
A: There is lots of variability between the groups, some have done extensive research producing results and publications.

***Q**: How to integrate research into health care systems, and focus on quality and improvements? This should strengthen the health care systems.*
A: If the projects are narrow they are more manageable, but the piecemeal approach is difficult. In 10-15 years the health care systems will be different, investigators are more likely to get together and evidence-based systems become more popular. Institutions will establish quality improvement programmes. New opportunities will arise to conduct effective research, albeit expensive; from abstract science to delivery of health care. Continuing quality improvement is important, 'applied research' could be integrated into regular health care. In many countries the health care systems are weak or even non-existent. Sometimes starting from scratch is actually better or easier.

***Q**: Any estimations on patient preferences and cost effectiveness analysis?*
A: For clinical trials there are patient representatives on the committees, funders request this. Tools should help to conduct clinical trials cost effectively. All phases of research should be integrated, for the benefit of the end-user. Cost effectiveness factors are e.g. political intervention and funders. Costs should be clearly indicated and data shown to improve effectiveness.

***Q**: Lots of consortia at work in West African epidemics, how to rejuvenate Euro-African cooperation network and prepare West African countries for future epidemics? Infection control is an issue, many West African healthcare workers died in epidemics.*
A: There is no answer, SARS in Toronto affected healthcare workers in ICUs as well. Should epidemic case definitions be renewed, how to reconcile this?

***Q**: Would an Euro-African collaborative framework strengthen infrastructure?*
A: In 2016 there will be an inter-agency rapid response plan in place, committing to deliver different services internationally (WHO and UNRC).

***Q**: Are there plans for a hub in Africa for ISARIC to improve research readiness?*
A: We acknowledge and are very sorry for the loss of healthcare workers in Africa and beyond. Clinical and evidence-based research should go hand in hand. Infection control in outbreaks is not ISARIC's main focus. Networking is a necessity, a sign of the times. ISARIC member networks could tap into infection control, to support research initiatives. A proposal for PREPARE Africa is in the early stages. African Union CDC (US-backed) was not mentioned, the organisation is in discussions with the EU. It may help in giving direction to ISARIC for African-initiatives. In Africa there is a skills gap to be filled in the infection-control network.

We are in the midst of a fundamental shift in how research works. Becoming less abstract - tonnes of information available through admin data, researchers seeking to collaborate. This foundation is in place to

integrate research into routine clinical care. One of the next steps is how to integrate cost effectiveness into the routine collection of data and proposals and policy advocacy.

Session VI: Global studies and ongoing disease threats: addressing challenges and moving ahead

Rob Fowler (CCCTG): *Short PeRiod IncideNce sTudy of Severe Acute Respiratory Infection (SPRINT SARI)*

- SARI investigators across regions have predicted that an influenza pandemic will happen every 23 years
- Often activities combating these infections only start when pandemics emerge. The time spent at different study stages during an outbreak, like RCT and ICU surveillance, can be costly to lives
- Protocols and a 'shovel ready' foundation, built through activities, should be in place in advance
- Low infrastructure areas are evolving at different times. As such, the choices made in these areas, may affect the feasibility of their study data being deemed as a good contribution. Three tiers of data collection depending on site capacity and infrastructure
- Approval required over a number of years
- Patient and process focused
- Some networks represent hospitals. We should become engaged with these collaborators before the next cycle hits us

Annie Wilkinson (Institute of Development Studies (IDS)):

- The Anthropology Platform is a network which was set up to provide advice and insight into the social and cultural aspects of the Ebola epidemic – to national and international agencies, NGOs, etc. Currently in the process of looking at how to adapt this from Ebola to other emerging diseases
- Rumours have been rife and highlight both the research into, and the use of biomedical products, is fraught with negative perceptions and experiences of authority, health systems, governments and geopolitics
- Trust cannot be taken for granted. There is a need and a challenge to engage with local populations
- There are some big challenges concerning questions of viral sovereignty and as Ebola has shown there are some quite intractable relationships outside the control of research
- There is a lot of talk about community engagement but the term is often used in a way which is about making communities bend to our will, to accept the plans we've made for them, or that it is something you do on the periphery to make your intervention more palatable.
- Need to think in terms of mutual engagement, two-way learning, and about co-production of knowledge, research strategies and of epidemic control
- Systematic failures in the design and implementation of control interventions, were too slowly addressed - if at all.
- Early and meaningful involvement of local institutions who could have made positive contribution to the control effort by developing locally acceptable interventions and by building trust, was limited e.g. burials - a major source of transmission and persistent source of tension
- The importance of having ethical clearance and respecting national systems is not where ethics stops
- Flexible models of consent and clearer articulation of benefits are important
- 'negotiated methodologies' – local populations or beneficiary groups are not usually asked what they think of research tools - enable co-learning, which include different perspectives from the beginning. Even in very tightly controlled clinical research such as trials there is scope for involving people more even while keeping most of the design the same
- Demystify: These issues of trust are not unique to Africa, or Ebola; they are found throughout public health all over the world

Eric D'Ortenzio (Institut National de la Santé et de la Recherche Médicale (INSERM); REsearch and ACTion targeting emergING infectious disease (REACTing))*: An initiative for rapid research-response to epidemics of emerging infectious disease*

- Outbreaks: a constant repetition
- H1N1 2009 response: mixed results - Difficulties: Scientists with other commitments, Ethical and regulatory issues, Lack of emergency funding, Impediments to international collaboration, Communication gaps, Shortage of social scientists - A need to better organize and prepare for the next outbreaks
- Aim to optimize and coordinate the existing research capacities during emerging and re-emerging infection threats – Objectives: In Peacetime: improve research preparedness: governance, research tools and priorities, links between disciplines, regulatory issues, criteria of research emergency. Funding, During crisis: Timely initiation of research projects and funding - facilitate reactive, flexible and effective research in "times of crisis"
- Social Mobilisation and community engagement for the Ebola vaccine trial in Guinea and favipiravir trial were important

Discussion & Q&A
Panel: Chair: Mike Christian (CCCTG) and Richard Hatchett (BARDA)
Panellists: Alistair Nichol (GACT SARI, ISARIC), Rob Fowler (CCCTG & ISARIC), Annie Wilkinson (IDS), Peter Horby (ERGO & ISARIC), Eric D'Ortenzio (INSERM - REACTing)

***Q**: Role of network development for SPRINT-SARI?*
A: The biggest goal will be the benefit of developing relationships. A good example of something that can produce. Bulk of the data will be from adults.

***Q**: Rumours – what is your community engagement proposition for next time? Epidemiology was broad, as was the number of villages involved.*
A: Ideal would be to get in earlier. WHO has recommended; planning architectures and response structure and flexibility. Community engagement and anthropology should not be relegated to the field. Burials are a good example. Complaints about people of the wrong gender and wrong age burying their relatives' bodies. Logistical problems and resistance. Use the power of community.

***Q**: How are you planning to manage the SPRINT SARI CRF; assuming it is not possible to produce everything in English and not possible to have a single database for multiple languages?*
A: Created a translational database, in CDISC. Answers are created in code (MEDRA coding), which overcomes the language issue.

***Q**: Where do you think the focus lies?*
A: During the "holiday season" to effect mobilisation.

***Q**: Facing data protection issues if patient consent is not obtained?*
A: For SPRINT SARI patient consent is not obtained unless local ERB request it. Patient level consent will probably not be required because information collected will be mostly routine. Some jurisdictions may require it, especially those collecting more information, and some may require data to stay in national system. Data collection – provided there is a data agreement in place, most times this works. Some local storage options, which make this easier, for example, in Canada it is being housed on a Canadian server. A lot of the databases are being set up in country to overcome the issue. Feeding back information into communities is not a one off conversation. Need to understand the social dynamics of the community and

governments. With Ebola, a number of networks formed which transformed into pockets of expertise. Work is ongoing to continue those efforts. This is major topic with WHO (reducing risk to patients and HCWs). Separately, many countries can provide data going forward; consider also looking back. Open statement of interest to take advantage of a subset of data.

***Q**: Different kinds of events make it difficult to get a perspective on community engagement. Might communities consider scenario based best practices?*
A: Social, behaviour change interventions are critical to controlling infection.

***Q**: Does the curve show when the response is required?*
A: Emergency situations preapproved protocols? BARDA is unique – advanced research and development. Degree of international interest in the new partners. BARDA is substantially resourced but not to go it alone – seeking partners

Formulating next steps for a collaborative approach to research response

Chair: John Marshall (CCCTG, InFACT & ISARIC Vice-Chair)

Networking break-out session feedback:

1. <u>Creating and promoting common research infrastructure</u>
- Multidisciplinary approach, linking public health with communities
- Understanding constraints of the information
- Adaptable and accessible protocols – need to be publicized
- Data & sample sharing – ISARIC to create a code of conduct as part of the existing data sharing policy
- Activities – more promotion, engaging more with partners, scenario planning
- Expand membership and create a database of where the expertise lies (already exists)
- Further development of ISARIC protocols

2. <u>Establishing a capacity for rapid and effective outbreak responsiveness</u>

a. Activities:
- Define a set of core research data variables to be collected during outbreaks (clinical, epidemiological and anthropological data)
- Develop platforms for uploading, analysing, and sharing research data to better inform clinical management in real time during outbreaks
- Develop data sharing agreements between prospective players in advance
- Expand on the development of more detailed ready-to-go protocols for observational trials in known and unknown pathogen outbreaks. Pursue advanced ethical approval by the ethics committee of host nations where outbreaks are likely to occur (where possible this can also be done for drug/interventional trials)
- Develop a registry of researchers who can deploy at relatively short notice during an outbreak (ideally with the outbreak investigation teams) to help define the research context and potential questions early
- Build upon the existing mapping of lab capabilities and expansion potential in developed and developing countries
- Engage developing countries in research capacity building (developing and delivering training programs/tools, research opportunities and mentoring)

- Carry out education and outreach activities about ISARIC and its purpose with the wide range of target audiences (including NGOs, governments)
- Identify and attend mutually beneficial training sessions between ISARIC/partners and NGOs (humanitarian training, research training, psychological screening)
- Lobby funders

b. Key partners:

- WHO (national, regional, global), Governmental departments of health, NGOs, academic institutions in host nations, Laboratories, Pharma, research staff

c. Resources/organisational structures:

- People and money

General feedback:

- Don't try to do everything – it's a continuum.
- Brand as a response network, which brings together scientific expertise: Focus on science
- If there is a new disease don't underestimate what is required for a clinical trial
- Prospective high quality data collection to improve clinical care and thereby save lives. Foundation on which to build. This does not mean just in an outbreak setting (e.g. SPRINT-SARI is important to collect quality data in the inter-pandemic period)

3. <u>Inter-pandemic preparedness and global capacity building</u>

- Networking in LMICs
- Challenges for preparedness: networks are not joined up in these settings (lack of central coordination), fatigue/overload, speak to science at a local and regional level, not a one size fits all
- Teams from South East Asia (OUCRU) have large networks of ITUs – how could these be blended?
- Brazil network lacks central coordination
- Zika virus and coordinated elements – involve local and regional stakeholders.
- Approaching funders – need a concept note (a master), go back to HIROs for funding
- Zika virus could be used as a coordination point around CDC, GloPID-R?
- Use funding to set up regional hubs

4. <u>Understanding the interface between research and clinical care</u>

- Common core question: What affects clinical practice and how can we address this issue?
- Consider an outbreak-free perspective
- Generate and process evidence (data collection through ISARIC members)
- Tools to assess clinical practice and the effectiveness/impact of research results
- SPRINT-SARI and a new PREPARE (next year plan)
- WHO as strategic partner (Blueprint); holistic approach, beyond clinical care (behaviour, community, advocacy groups….)

Closing remarks and next steps

In closing, Roberto Bruzzone (Institut Pasteur & ISARIC Vice-Chair) noted that the meeting highlighted the need to focus on the main objectives of ISARIC. The network approach is fundamental to competing in the environment of rapid clinical research response. ISARIC needs to consider what will be the focus in the outbreak free period, with the reestablishment of regional hubs within the portfolio. ISARIC's Executive

Committee meeting (to be held on 2 December 2015) will seek to incorporate the outcomes of the Stakeholders' meeting into ISARIC's strategic objectives and ultimately feed into the WHO Blueprint.

APPENDIX A

The Agenda and List of Participants are provided below. Alternatively, please click the links to download a PDF of the Agenda and List of Participants

AGENDA

Monday 30 November	***Time***	***Topic***
	08:15-09:00	Registration/coffee & continental breakfast
	09:00–09:15	**Welcome/Opening remarks** *Speaker: Mike Turner, WT & Roberto Bruzzone, ISARIC Vice-Chair*
	09:15-09:45	**Keynote address/Introductory plenary**: Successful Collaboration and Preparedness in Global Governance *Guest speaker: Robin Robinson (BARDA)*
	09:45–10:15	**WHO blueprint for a research response** *Speaker: Ana Maria Henao-Restrepo (WHO)*
	10:15–10:30	Coffee break
	10:30–11:30	**Rapid Research Response task force** *Chair: Trudie Lang (TGHN & ISARIC) & Rob Fowler (CCCTG & ISARIC)* *Speakers:* - *Trudie Lang (TGHN & ISARIC)* - *Nikki Shindo (WHO)* - *Maria Van Kerkhove (Institut Pasteur)* - *David Hui (Chinese University of Hong Kong)*
	11:30-12:15	**Discussion and Q&A** *Chair: Mike Turner (WT) & Mauricio Ferri* Panellists: - *Trudie Lang (TGHN & ISARIC)* - *Nikki Shindo (WHO)* - *Maria Van Kerkhove (Institut Pasteur)* - *David Hui (Chinese University of Hong Kong)* - *Rob Fowler (CCCTG & ISARIC)* - *Gail Carson (ISARIC)*
	12:15–13:00	Buffet lunch
	13:00-14:15	**Connecting with industry, funders and public health bodies** *Chairs: Frederick G. Hayden (ISARIC) & Niteen Wairagkar (BMGF)* *Speakers:* - *Robin Robinson (BARDA)* - *Carol R. Epstein (MediVector)* - *Johan Van Hoof (Janssen/Johnson & Johnson)* - *Finnian Hanrahan (European Commission)*
	14:15-15:00	**Discussion and Q&A** *Chair: Roberto Bruzzone (Institut Pasteur) & Ilaria Capua (Istituto Zooprofilattico del Veneto, Member of the Italian Parliament)*

		Panellists: - *Robin Robinson (BARDA)* - *Carol R. Epstein (MediVector)* - *Johan Van Hoof (Janssen/Johnson & Johnson)* - *Bernadette Murgue (Aviesan/INSERM)* - *Finnian Hanrahan (European Commission)*
	15:00-15:15	Coffee break
	15:15-16:15	**Barriers, bottlenecks & solutions** *Chair: Alistair Nichol (University College Dublin & ISARIC) & Barbara Bannister (Royal Free Hospital)* *Speakers:* - *Abha Saxena (WHO)* - *Ilaria Capua (Istituto Zooprofilattico delle Venezie, Member of the Italian Parliament)* - *Brian McCloskey (PHE)* - *Laura Merson (WWARN & ISARIC)*
	16:15-17:00	**Discussion and Q&A** *Chair: Fernando Bozza (BRICNet & ISARIC) & John Amuasi (Kumasi Center for Collaborative Research in Tropical Medicine & WATER)* *Panellists:* - *Abha Saxena (WHO)* - *Ilaria Capua (Istituto Zooprofilattico delle Venezie, Member of the Italian Parliament)* - *Brian McCloskey (PHE)* - *Laura Merson (WWARN & ISARIC)*
	19:00-21:00	Dinner at Hotel Russell

	Time	***Topic***
Tuesday 1 December	08:30–09:00	Coffee/continental breakfast
	09:00-09:15	**Summary of Day 1** *Speaker: John Marshall (CCCTG, InFACT & ISARIC Vice-Chair)*
	09:15–10:00	**Humanitarian collaboration** *Chairs: Peter Horby (ERGO & ISARIC) & Annick Antierens (MSF)* *Speakers:* - *Mary Van Lieshout (GOAL)* - *Annick Antierens (MSF)* - *Michael von Bertele (Save the Children)*
	10:00–10:45	**Discussion and Q&A** *Chair: Dean Everett (MLW & ISARIC) & Pasi Penttinen (ECDC)* *Panellists:* - *Cathy Roth (WHO)* - *Annick Antierens (MSF)* - *Mary Van Lieshout (GOAL)* - *Michael von Bertele (Save the Children)* - *Peter Horby (ERGO & ISARIC)*
	10:45–11:00	Coffee break
	11:00-11:15	**WHO activities on data sharing & biobanking update** *Speaker: Cathy Roth (WHO)*
	11:15-12:30	**Network engagement breakout groups**

12:30–13:15	Buffet lunch
13:15-14:15	**Low and Middle Income Countries capacity building, collaboration and networking** *Chairs: Haja Ramatulai Wurie (COMAHS) & Cathy Roth (WHO)* *Speakers:* - *John Amuasi (Kumasi Center for Collaborative Research in Tropical Medicine & WATER)* - *Mauricio Ferri* - *John Marshall (CCCTG, InFACT & ISARIC)*
14:15-15:00	**Discussion and Q&A** *Chair: Kath Maitland (KEMRI Wellcome Trust Programme & ISARIC) & Mandeep Chadha (Indian Council of Medical Research)* *Panellists:* - *John Amuasi (Kumasi Center for Collaborative Research in Tropical Medicine & WATER)* - *Mauricio Ferri* - *John Marshall (CCCTG, InFACT & ISARIC)*
15:00-15:15	Coffee break
15:15-16:30	**Global studies and ongoing disease threats**: **addressing challenges and moving ahead** *Chairs: Ken Baillie (Roslin Institute, University of Edinburgh & ISARIC) and Bernadette Murgue (WHO)* *Speakers:* - *Alistair Nichol (GACT SARI)* - *Rob Fowler (SPRINT SARI)* - *Annie Wilkinson (IDS)* - *Peter Horby (ERGO ISARIC PREPARE)* - *Eric D'Ortenzio (INSERM – Aviesan REACTing)*
16:30–17:15	**Discussion and Q&A** *Chair: Mike Christian (CCCTG) and Robin Robinson (BARDA)* *Panellists:* - *Alistair Nichol (GACT SARI)* - *Rob Fowler (CCCTG & ISARIC)* - *Annie Wilkinson (IDS)* - *Peter Horby (ERGO ISARIC)* - *Eric D'Ortenzio (INSERM - REACTing)*
17:15-17:45	**Formulating next steps for a collaborative approach to research response** *Chair: John Marshall (CCCTG, InFACT & ISARIC Vice-Chair)*
17:45-18:15	**Closing remarks** *Chair: Roberto Bruzzone (Institut Pasteur & ISARIC Vice-Chair)*

List of Participants

First name	Family Name	Affiliation
John	**Amuasi**	Kumasi Center for Collaborative Research in Tropical Medicine/West African Task Force for the Control of Emerging & Reemerging Infections (WATER)
Annick	**Antierens**	MSF
Oumou Younoussa	**Bah-Sow**	Guinea Regulatory Agency – Hôpital Ignace Deen
Ken	**Baillie**	Roslin Institute, University of Edinburgh
Barbara	**Bannister**	Royal Free Hospital
Luke	**Bawo**	Ministry of Health, Liberia
Abdoul	**Beavogui**	Ministry of Health, Republic of Guinea
Fernando	**Bozza**	National Institute of Infectious Disease, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil; Brazilian Research in Intensive Care Network – BRICNet
Roberto	**Bruzzone**	HKU-Pasteur Research Pole
Ewen	**Callaway**	Nature
Ilaria	**Capua**	Istituto Zooprofilattico delle Venezie, Member of the Italian Parliament
Gail	**Carson**	ISARIC Coordinating Centre
Marco	**Cavaleri**	African Vaccine Regulatory Forum (AVAREF)
Mandeep	**Chadha**	Indian Council of Medical Research
Mike	**Christian**	CCCTG
Iza	**Ciglenecki**	MSF
Eric	**D'Ortenzio**	INSERM - REACTing
Menno	**de Jong**	PREPARE
Jake	**Dunning**	Public Health England
Carol	**Epstein**	MediVector, Inc.
Dean	**Everett**	Malawi-Liverpool-Wellcome Clinical Research Programme / University of Liverpool
David	**Fedson**	
Mauricio	**Ferri**	
Tom	**Fletcher**	HQ World Health Organisation, Wellcome Trust / MoD
Rob	**Fowler**	University of Toronto / World Health Organization
Arturo	**Galindo-Fraga**	La Red / Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán"
Ed	**Gibbs**	University of Oxford, CTMGH
Finnian	**Hanrahan**	European Commission
Richard	**Hatchett**	United States Department of Health and Human Services, the Office of the Assistant Secretary for Preparedness & Response Biomedical Advanced Research & Development Authority
Frederick	**Hayden**	University of Virginia School of Medicine
Ana Maria	**Henao Restrepo**	World Health Organization
Peter	**Horby**	University of Oxford, ERGO
David	**Hui**	The Chinese University of Hong Kong
Tuula	**Itkonen**	University of Oxford admin
Michael	**Jacobs**	NHS England

Sarah	**Jones**	University of Oxford admin
Stephen	**Kennedy**	Incident Management System (IMS), Liberia
Sandra	**Laney**	Paul G Allen Family Foundation
Trudie	**Lang**	The Global Health Network, University of Oxford
Kajsa-Stina	**Longuere**	ISARIC Coordinating Centre
Kath	**Maitland**	KEMRI Wellcome Trust Programme, Kilifi / Imperial College, London
John	**Marshall**	ISARIC/InFACT
Ignacio	**Martin-Loeches**	St James's Hospital, Trinity College Dublin
Line	**Matthiessen**	European Commission
Brian	**McCloskey**	Public Health England
Chelsea	**McMullen**	ISARIC Coordinating Centre
Laura	**Merson**	University of Oxford / WWARN
Catrin	**Moore**	University of Oxford, ERGO
Sarah	**Moore**	ISARIC Coordinating Centre
Bernadette	**Murgue**	World Health Organization
Jean-Jacques	**Muyembe-Tamfum**	Institut National de Recherche biomédicale-INRB
Binh	**Nguyen Cam**	
Alistair	**Nichol**	University College Dublin
Ian	**Norton**	World Health Organization
Raul	**Pardinaz-Solis**	ISARIC Coordinating Centre
Pasi	**Penttinen**	European Centre for Disease Prevention and Control (ECDC)
Fabien	**Quintard**	Fondation Mérieux
Morven	**Roberts**	MRC
Robin	**Robinson**	United States Department of Health and Human Services, the Office of the Assistant Secretary for Preparedness & Response, Biomedical Advanced Research & Development Authority
Cathy	**Roth**	World Health Organization
Alex	**Salam**	GOAL Global & King's College London
Abha	**Saxena**	World Health Organization
Peter	**Scott**	Parafinalé Research
Calum	**Semple**	University of Liverpool
Nikki	**Shindo**	World Health Organization
Prasanth	**Sukumar**	University College Dublin
Olga	**Tosas Auguet**	University of Oxford, OHSCAR
Mike	**Turner**	The Wellcome Trust
Timothy	**Uyeki**	CDC/OID/NCIRD
Rogier	**van Doorn**	University of Oxford, OUCRU
Johan	**Van Hoof**	Janssen Pharmaceutical Companies of Johnson & Johnson
Maria	**Van Kerkhove**	Institut Pasteur
Mary	**Van Lieshout**	GOAL
Richard	**Vaux**	Fondation Mérieux
Michael	**von Bertele**	Save the Children
Niteen	**Wairagkar**	Bill and Melinda Gates Foundation
Conall	**Watson**	London School of Hygiene & Tropical Medicine
Steve	**Webb**	InFACT/ANZICS

Charlie	**Weller**	The Wellcome Trust
Annie	**Wilkinson**	Institute of Development Studies
Haja Ramatulai	**Wurie**	College of Medicine and Allied Health Sciences, University of Sierra Leone

APPENDIX B

The ACRONYMS for participating organisations are listed below:

ACRONYMS	
ANZICS	Australia and New Zealand Intensive Care Society
AVAREF	African Vaccine Regulatory Forum
BMGF	Bill and Melinda Gates Foundation
BRICNet	National Institute of Infectious Disease, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil; Brazilian Research in Intensive Care Network
CCCTG	Canadian Critical Care Trials Group
CDC	Centers for Disease Control and Prevention
COMAHS	College of Medicine and Allied Health Sciences, University of Sierra Leone
CTMGH	Centre for Tropical Medicine and Global Health, University of Oxford
CUHK	The Chinese University of Hong Kong
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
ERGO	Epidemic Diseases Research Group Oxford, University of Oxford
FDA	Food and Drug Administration (USA)
FM	Fondation Mérieux
HSS, ASPR, BARDA	United States Department of Health and Human Services, the Office of the Assistant Secretary for Preparedness & Response, Biomedical Advanced Research & Development Authority
ICMR	Indian Council of Medical Research
IMS	Incident Management System
InFACT	International Forum for Acute Care Trialists
INRB	Institut National de Recherche Biomédicale (DRC)
INSERM	Institut National de la Santé et de la Recherche Médicale (France)
ISARIC	International Severe Acute Respiratory and Emerging Infection Consortium, University of Oxford
IZSVe	Istituto Zooprofilattico delle Venezie
KCCR	Kumasi Center for Collaborative Research in Tropical Medicine/West African Task Force for the Control of Emerging & Reemerging Infections (WATER)
KEMRI	The Kenya Medical Research Institute, Wellcome Trust Programme, University of Oxford
La Red	La Red / Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubiran"
LSHTM	London School of Hygiene & Tropical Medicine
MLW	Malawi-Liverpool-Wellcome Clinical Research Programme, University of Liverpool
MRC	Medical Research Council
MSF	Médecins Sans Frontières
NCIRD	National Center for Immunization and Respiratory Diseases (CDC)
NHS	National Health Service
OHSCAR	The Oxford Health Systems Collaboration, University of Oxford
OID	Office of Infectious Diseases (CDC)
OUCRU	Oxford University Clinical Research Unit, Vietnam
PHE	Public Health England
SCF	The Save the Children Fund
TGHN	The Global Health Network, University of Oxford
UCD	University College Dublin
WHO	World Health Organization
WT	The Wellcome Trust