CONSISE
CONSORTIUM FOR THE STANDARDIZATION OF INFLUENZA SEROEPIDEMIOLOGY

September 2016 CONSISE Newsletter

Dear CONSISE Members,

Hope that you all had a nice summer and found some time to relax with family and friends. Please find below our 4th newsletter for CONSISE. We would like to update you on some of our recent activities.

Standardized research protocols for Zika Virus (ZIKV) are available

As you know, the ZIKV outbreak in the Americas and the severe neurological conditions identified in adults (Guillain-Barré syndrome) and in the fetuses of infected pregnant women has led the World Health Organization to declare a Public Health Emergency of International Concern (1 Feb 2016). Given the large grographic scope of this outbreak, the use of standardized research tools to address key public health unknowns is crucial to ensure results of these studies can be compared across regions. Given this, CONSISE and the Institut Pasteur were asked to draft six standardized research protocols for ZIKV. Our expertise in rapidly drafting such technical documents, summoning and incorporating technical input have allowed us to support efforts to harmonize epidemiologic and clinical research for ZIKV.

The six protocols (listed below) were developed by Maria Van Kerkhove and colleagues at IP and WHO in April-July, and have undergone significant technical review by research and public health professionals working on ZIKV and other arboviruses. We worked closely with WHO, affected countries in the Americas and Caribbean and ISARIC to draft and finalize the protocols. A face-to-face meeting was convened by WHO/PAHO in Mexico City in June 2016 to discuss four of the six protocols (the two case-control studies and the two cohort studies) in great detail and agree on points where harmonization is needed.

The protocols currently available include:

- Case-control study to assess potential risk factors related to microcephaly caused by Zika virus infection
- Case-control study to assess potential risk factors related to Guillain-Barré Syndrome caused by Zika virus infection
- Prospective longitudinal cohort study of women and newborns exposed to ZIKV during pregnancy
- Prospective longitudinal cohort study of newborns and infants born to mothers exposed to Zika virus during pregnancy
- Cross-sectional seroprevalence study of Zika virus infection in the general population
- Prospective longitudinal cohort study of Zika-infected patients to measure the persistence of Zika virus in body fluids

The draft standardized protocols have already been shared with a number of affected countries in the Americas, Caribbean and with some African countries. All protocols are currently undergoing ethical review by WHO and will be posted online soon. For further information, please contact Maria (maria.van-kerkhove@pasteur.fr) directly.

For your information, a seventh protocol (called the *Clinical Characterization Protocol for Zika Virus Infection in the Context of Co-circulating Arboviruses*) to better understand the natural history of ZIKV infection has been drafted by WHO and ISARIC. This protocol will also be available on the WHO website soon.

CONSISE statement on the Reporting of Seroepidemiologic Studies for Influenza (ROSES-I statement): an extension of the STROBE statement

Several members from CONSISE have recently published a statement on the reporting practices for Seroepidemiology studies. The paper entitled *CONSISE statement on the Reporting of Seroepidemiologic Studies for Influenza (ROSES-I statement): an extension of the STROBE statement* is now available from the journal Influenza and Other Respiratory Viruses.

The ROSES-I Statement is an extension of the STROBE Statement and includes a 42 item checklist of information that should be included in the publications of seroepidemiologic studies. Thank you to all of the authors of this paper, especially Peter Horby, and to funding from Institut Pasteur to make this article open access.

CONSISE Epidemiology Working Group Meeting

A 1-day international meeting of CONSISE's Epidemiology Working Group members was held at Institut Pasteur, Paris, on 20 January 2016. Twenty-six participants from 14 countries participated in the meeting.

At this CONSISE meeting, members and invited speakers presented the updates of the development and application of CONSISE tools. Prof. Benjamin Cowling investigated factors associated with transmission using household studies in Hong Kong based on protocols developed by CONSISE. Dr. Kaat Vandemaele from the World Health Organization recommended improved coordination among modelers and epidemiology-laboratory group, and further standardization of the influenza protocols. Several seroepidemiology protocol templates have been adapted for MERS-CoV by the World Health Organization. Drs. Elmoubasher Farag and Maria Van Kerkhove shared their experiences using CONSISE protocols in Qatar and Saudi Arabia, respectively.

Dr. Abha Sexen (World Health Organization) pointed out that comprehensive international ethics guidance is lacking for epidemic or outbreak situations and supports our view that ethical consideration is essential for the use of CONSISE tools. Dr. Peter Horby gave an overview of the statement on Reporting of Seroepidemiologic Studies for Influenza (ROSES-I), which is aimed to improve the quality of reporting of methodological details of influenza epidemiologic studies. Dr. Marcel Müller discussed the challenges in diagnostic testing in seroepidemiologic studies. Members were also actively engaged in the discussions on the development of a question bank for influenza seroepidemiologic studies. An online interface for users to create questionnaires is under development.

The full agenda and speaker presentations can be found here.

CONSISE Presentation at Options IX

The International Society for Influenza and Other Respiratory Virus Diseases (ISIRV) organized the Options IX for the Control of Influenza Conference in Chicago, Illinois, from 24-28 August 2016. At the Options meeting, we presented our ongoing work and current findings for the Laboratory Working Group and Epidemiology Working Group (please see attached ppt).

Update from the CONSISE Laboratory Working Group

The Laboratory Working Group has conducted a CONSISE microneutralisation (MN) assay and Haemagglutination Inhibiton (HI) assay comparison study. The study has several aims, including the assessment of inter-laboratory variability when using in-house assay protocols and when using the CONSISE consensus protocols, analysis of correlation between the two MN assay formats and HI as well as assessment of the potential benefit of using standards. For the latter, various materials, such as purified IVIG, ferret antiserum and plasma from immunised trans-chromosomal bovines, were included as candidate standards. 30 laboratories participated in the comparison study and returned data; statistical analysis is now being conducted at NIBSC. Once the data analysis is complete, we hope to generate a manuscript for publication to disseminate the findings of this study to the wider scientific community

CONSISE Steering Committee

As you all know, the primary responsibility of the Steering Committee is to advise working group leads on the focus, direction and plans of CONSISE activities, to attend steering committee and general CONSISE conference calls and meetings, and serve as the liaison between CONSISE and the organizations they represent.

Our current list of Steering Committee Members are listed below. Each has agreed to serve for a term of 3 years from 1 September 2016 to 31 August 2019. We thank you for your dedication and support of CONSISE.

Steering Committee Members (in alphabetical order)

- Eeva Broberg: European Centres for Disease Control
- Benjamin Cowling: The University of Hong Kong, School of Public Health, Hong Kong
- Maryna Eichelberger: US Food and Drug Administration, USA
- Othmar Engelhardt: NIBSC, Medicines and Healthcare Products Regulatory Agency, UK
- Peter Horby: Centre for Tropical Medicine and Global Health, University of Oxford, UK
- Katja Hoschler: Public Health England, London, UK

- Olav Hungnes: Norwegian Institute of Public Health, Norway
- Karen Laurie: WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia
- Min Levine: US Centres for Disease Control and Prevention, Atlanta, United States
- Anthony Mounts: US Centres for Disease Control and Prevention, Atlanta, United States
- Richard Pebody: Public Health England, London, UK
- Malik Peiris: The University of Hong Kong, School of Public Health, Hong Kong
- Steven Riley: MRC Centre for Outbreak Analysis and Modelling, Imperial College London, UK
- Amanda Shane: Public Health Agency Canada
- Tim Uyeki: US Centres for Disease Control and Prevention, Atlanta, United States
- Marianne van der Sande: National Institute for Public Health and the Environment (RIVM), the Netherlands
- Maria Van Kerkhove: Center for Global Health, Institut Pasteur, Paris, France
- Kaat Vandemaele: World Health Organization
- John Wood: NIBSC, UK, retired
- Wenqing Zhang: World Health Organization

The CONSISE website has been updated under "What's new!" and "Protocols" to reflect these changes.

CONSISE Member Highlight

John Wood Ph.D., National Institute for Biological Standards and Control, United Kingdom, retired.

Can you tell us a little about yourself?

I have recently been researching my family history and although I have always thought of myself as the son of a long line of UK Yorkshire coal miners, I was surprised to find out that my ancestors' trades included stonemason, shoe repairer, agricultural labourer (there were a lot of them!), school teacher and both an inmate and head of a workhouse. Not a scientist in sight! My interest in science was kindled at secondary school (equivalent to high school in US) and it was there that I had my first experience of the devastating impact of a flu pandemic. 'Asian flu' (H2N2) swept through my school in 1957/8 and even got a mention in the school magazine. If you have seen the flu history posters prepared by Public Health England, you will have seen this magazine article alongside a photo of an eleven year old schoolboy who may be familiar to you.

I graduated from the University of Salford with a BSc in Applied Biology and my first job was as a management trainee in a nationwide baking company. I was a baker! After 3 months, I realised that working in the real world was not for me and I thought about ways to go back to university. Eventually I secured a post graduate placement at the University of Glasgow, Scotland and my PhD research was on host range growth restrictions of vaccinia virus. I was fortunate to have as my mentor, Hugh Pennington who later went on to accept the Chair in Bacteriology at Aberdeen University and headed UK government enquiries into food borne bacterial outbreaks. At Glasgow I became immersed in vaccinia and herpes virus research and took little interest in flu until we had a visiting lecture from Graham Laver. Graham gave a fascinating talk about the possible avian origins of pandemic flu and his last slide was of a sunset over the barrier reef, where he had been sampling birds with Rob Webster. I was hooked and the rest is history.

After graduating from Glasgow in 1974, I left for a research post at the UK NIBSC (then located in Hampstead north London) with the task of improving the control and standardization of flu vaccines. Thirty six years later, I retired from NIBSC still with the same task! Soon after arriving at NIBSC, I was dispatched to nearby Mill Hill to watch and learn from Geoffrey Schild who was the Director of the WHO World Influenza Centre as it was then called. He had invented a new immunological technique that might have some use in testing flu vaccines. It was the Single Radial Immunodiffusion (SRID) assay and it transformed the control and standardization of flu vaccines, being still the gold standard assay today. Geoffrey soon joined me at NIBSC as head of Virology and had an immediate impact in building up and strengthening the flu group at NIBSC. I worked closely with Geoffrey to improve and validate the SRID assay and even branched out into the agricultural world to develop assays for equine, avian and swine flu vaccines.

In 1983 I was fortunate in spending my sabbatical year at the laboratory of Rob Webster in Memphis, USA. Rob's laboratory was buzzing with different projects and it was very exciting to be involved. During my stay, there was a devastating H5N2 bird flu outbreak in poultry in Pennsylvania and nearby States and I was thrust into the thick of the action trying to find out the extent of the disease in wild birds. Little did I know that bird flu would play such an important part in my life later on. Back at NIBSC I was the resident bird flu expert for a few weeks before settling down to human flu vaccines once more.

As well as developing assays for flu vaccines, I also started looking at the serological assays that were being used to assess vaccine immunogenicity. We had an idea that there was not much agreement in serology results from different laboratories, but didn't know the scale of the problem. One of the benefits of working at NIBSC is the amazing support given for inter-laboratory collaborative studies and I made use of this. As expected the Haemagglutination-Inhibition assay was extremely variable from laboratory to laboratory so we embarked on trying to improve it and to show how effective antibody standards can be.

In the late 1900s and early 2000s, when H5N1 bird flu began infecting humans, there was a new twist to my work. Apart from one or two labs in the world, we were at that time ill-equipped to work with such dangerous viruses; to prepare safe and effective vaccines and to standardize and control such vaccines. My remaining years at NIBSC were devoted to these new tasks and thanks to some excellent collaboration coordinated by the WHO, I am happy to say that as a flu community, we are much better equipped nowadays.

What is your involvement in CONSISE?

I became involved with CONSISE shortly after its formation in 2011, when I was asked to chair the Laboratory Working Group. I agreed to do this only if my successor at NIBSC, Othmar Engelhardt could be my co-chair. I was very impressed with the hopes and aspirations of CONSISE and with the already extensive number of collaborating partners in CONSISE. Othmar and I set out to form a core Steering Committee and began to prioritise our work for the next few years. We hold periodic progress and planning conference calls and have recruited a really impressive number of key seroepidemiology laboratories throughout the world in our Laboratory Working Group. I hope that my experience from NIBSC will help to steer the laboratory activities of CONSISE.

How do you see CONSISE adding to the standardization of serologic assays for influenza?

It was frustrating to leave NIBSC, without having a reliable and reproducible serological assay for flu vaccine immunogenicity. We had demonstrated how un-reliable the assays were and had opened the door to better standardization by showing how effective antibody standards could be, but there was little prospect of a long lasting solution. At NIBSC, I had little or no involvement with seroepidemiology, but I am very familiar with the laboratory problems as they are the same as those in vaccine serology. CONSISE has an amazing number of enthusiastic laboratories ready and able to evaluate different serology assays and methods for better standardization. Our strategy has been to first compare laboratory assay protocols and to develop a consensus protocol. The consensus assay protocol is then evaluated in an inter-laboratory study along with candidate antibody standards. We hope that by working together towards effective solutions we will have better and long lasting agreement between laboratories. An additional benefit of such collaboration is that we now have an excellent laboratory network to quickly evaluate new serology assays as they come along.

With best wishes,

Maria Van Kerkhove, Othmar Engelhardt and John Wood for the CONSISE Steering Committee