CONSISE Activities Overview and Update
Laboratory Working Group

John Wood and Othmar Engelhardt
CONSISE 4th International Meeting, Cape Town South Africa
3-4 September 2013
Background:

1st International Influenza Seroprevalence Meeting, Ottawa, Canada, February 9-10 2011

- *Influenza serological studies to inform public health action: best practices to optimise timing, quality and reporting*

- Several conclusions and actions agreed
  - Formed the basis for subsequent discussions
- Meeting report
  
  *Laurie et al. (2012) Influenza and Other Respiratory Viruses*

**One of conclusions**
Co-ordinate and standardise the international laboratory response

- develop an international network of laboratories for conducting serological studies and ensuring a common approach to generating comparable sero-epidemiological data
- establish commitment for production of international antibody standard and control panels
- establish collaboration/coordination between laboratory, clinical and epidemiological partners to access serum and virological samples rapidly in outbreak
Common assays for influenza serological studies

Haemagglutination Inhibition Assay

- Agglutination
- No agglutination

Microneutralization Assay

- Infection
- No infection

MN assay read-out:
- 7 day assay CPE on monolayer
- 3 day HA detection
- 2 day ELISA detection (WHO protocol)

In collaborative studies HI/MN assay variability between laboratories can be substantial. How can they be standardized?
MN assay comparison

Background

• Karen Laurie (WHO CC, AUS) coordinated comparison of 2d ELISA WHO and 3d HA protocols – consensus protocols developed

• Laboratory comparison exercise for H1N1 pdm09 assays began 4 October 2012

  • Comparison of two methods where labs used their own serum samples
  • Results from 11 labs submitted to NIBSC (UK) for analysis
  • Ratio of titres between 3-day and 2-day assay similar in most labs
  • Therefore, there were no underlying reasons that the two assays could not be comparable
  • As conclusions were based on only one subtype, plans were made to extend study with data for seasonal H3N2 and H5N1
MN assay comparison

Plan for Cape Town meeting

- Examine whether data from H1N1pdm09 study may have been biased due to factors such as:
  - Inexperienced with one assay format
  - Age group(s) of serum samples
  - Use of wild-type vs reassortant virus
  - Titre ($\text{TCID}_{50}$) of virus stocks
- Karen Laurie and Othmar Engelhardt to present preliminary analysis of MN H3N2/H5N1 extension study
- Discuss results and plan next steps
Background

• Group is strongly in favour of keeping HI as the primary serology assay, but will assess how it can be better standardized.

• HI assay variability between labs can be substantial and in collaborative studies no clear relationship between protocol used and inter-lab variability has been seen.

• Karen Laurie and John Wood coordinated comparison of HI protocols and tried to develop consensus assay
  – Starting point: WHO protocol

Plan for Cape Town meeting

• Discuss whether a consensus HI assay protocol is feasible
MN and HI assay standardization

Plan for Cape Town meeting

- A new collaborative study using panels of sera will be designed for implementation after Cape Town meeting
  - Laboratory comparison between consensus and local HI and MN methods
  - Evaluation of animal sera and Mab as antibody standards
International antibody standards

Background
• Previous collaborative studies have shown that use of antibody standards can significantly reduce variability between laboratories

Plan for Cape Town meeting
• John Wood to discuss pathway to developing antibody standards
• Othmar Engelhardt to discuss resources needed to prepare International Standards including presentation from Nick Martin (NMRC)
Quality assessment

Background

• A small group from CONSISE met with Dr Vivienne James from UK NEQAS
• Value of EQA is understood and appreciated by CONSISE Lab WG
• Consensus that formal EQA would be premature at the moment
  – CONSISE still exploring variables
• More emphasis currently on developing consensus protocols and standardisation
• Use of shared serum panels as a more realistic option at this point
NI assays

Background

• Some labs have begun evaluation of sera from influenza vaccine trials using ELLA assays with encouraging results. Some of the difficulties related to the source of NA

• All CONSISE labs have been encouraged to evaluate the ELLA assay.

Plan for Cape Town meeting

• Update on NI assays from Maryna Eichelberger (FDA) and Kim Westgeest (Erasmus University)

• Share experience on use of NI assays including those of Ralf Wagner (PEI)

• Discuss the next steps
New serology assays

Background

• At Hong Kong meeting CONSISE members indicated that new MN serology assays using virus pseudotypes were being evaluated
• It was agreed that the CONSISE group should review the new serology assay being used

Plan for Cape Town meeting

- Presentations by Ralf Wagner (PEI), Emanuele Montomoli (U of Siena), Jackie Katz (CDC) on new serology assays followed by discussion
- Group to review the new serology assays
CONSISE involvement with influenza A (H7N9) and MERS-CoV serology assays

H7N9

• CONSISE TC in May 2013 led to posting of H7N9 HI/MN assay protocols from China CDC on CONSISE website
• A further CONSISE TC in July 2013 led to posting of CDC H7N9 modified HI assay protocol using horse erythrocytes on CONSISE website

MERS-CoV

• WHO TC in June to assess MERS-CoV laboratory diagnoses included serology assays – CONSISE represented
• A variety of serology assays - need for serum panels
Thank you

CONSISE Steering Committee – Laboratory Working Group

Eeva Broberg, Katja Hoschler, Olav Hungnes, Jackie Katz, Karen Laurie, Malik Peiris, Wenqing Zhang

Also

Maria Van Kerkhove, Angus Nicoll from the epi working group