UK/PHE approach to RSV surveillance pilot and reference laboratory activities – what can countries expect as learning points and support?

Maria Zambon & Joanna Ellis
Respiratory Virus Unit, National Influenza Centre
National Infection Service, Public Health England
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WHO RSV Reference Laboratory
Respiratory Virus Unit, Public Health England

- WHO National Influenza Centre, 20-25 staff
- Virus isolation, PCR detection respiratory viruses, antigenic typing, whole genome sequencing, phenotypic/genotypic antiviral susceptibility, seroepidemiology (HAI, MN, NAI)
- PHE respiratory virus reference lab (RSV/PIV/hMPV/adeno etc)
- Annual molecular EQA panel for UK influenza network laboratories
- Currently have Clinical Pathology accreditation & ISO15189

- Member laboratory of European Reference Laboratory Network for Human Influenza (ERLI-Net)

- WHO SARS & MERS CoV Reference Laboratory – 2013
- Invited as WHO RSV Reference Laboratory in 2015
- Invited as a participating country for European region in the pilot in 2017
Terms of Reference:
Respiratory Syncytial Virus Reference Laboratories

1. Work under the coordination of the WHO Global Influenza Programme (GIP);
2. Fulfil the terms of reference using financial support provided only by governmental and/or other non-commercial sources;
3. Assume full responsibility for complying with their respective national biosecurity and biosafety regulations on the understanding that such regulations and rules shall, at a minimum, meet the relevant and current WHO standards;
4. Appropriately acknowledge in presentations and publications, the contributions of collaborators, including RSV Laboratories and countries participating in the WHO RSV Surveillance Pilot.

General activities:
Respiratory Syncytial Virus Reference Laboratories:

1. Serve as a technical resource to WHO and RSV Pilot Laboratories as time and resources permit;
2. Monitor RSV Pilot Laboratories in Quality Assessments of their assays;
3. Prepare and distribute RSV diagnostic reagents as agreed with WHO and as time and resources permit;
4. Analyse performance of RSV Pilot Laboratories on EQA panels and submit timely feedback and reports to RSV Pilot Laboratories and WHO;
5. Provide training and laboratory support to RSV Pilot Laboratories on laboratory techniques as time and resources permit;
6. Maintain and strengthen active communication and collaboration with RSV Pilot Laboratories and WHO to ensure that up-to-date information is exchanged.
Current PHE RSV PCR detection

- Real-time multiplex 2-step PCR assay on Qiagen Rotorgene platform
- Real-time Platinum qPCR superMix-UDG (ThermoFisher)
- Targets RSV A, RSVB (N gene) hMPVA, hMPVB (N gene) IC (soil borne cereal mosaic virus)
- Positive Controls RSVA Long & RSVB 9320 RNA transcripts hMPVA/hMPVB/IC)
RSV virologic surveillance

- Need for structured RSV strain surveillance, including sequence deposition
- As for influenza detection, RSV primer/probe sequences need to be regularly checked against sequences from circulating strains
- Issue identified in 2016 in PHE and Kilifi, Kenya\(^1\) with detection of some RSVB strains using in-house PCR assays based on a published protocol\(^2\) which was modified from a previously published assay\(^3\)
- Investigation (confirmatory PCR testing with different assays, N gene sequencing) revealed false negative RSVB results with these in-house assays due to genetic variation in RSVB probe region
- EQA schemes – inclusion of contemporary strains is needed
- Elderly and adult protocols may need attention

\(^1\)Kamau et al; Recent sequence variation in probe binding site affected detection of respiratory syncytial virus group B by real-time RT-PCR. J Clin Virol. 2017 Mar;88:21-25.

\(^2\)Gunson et al. 2005 JCV (33) 341-344
Conclusions so far

- Necessity for advocacy: Build case with WHO for financial support to strengthened laboratory capacity & capability
- Define minimum datasets for regions/countries to support segmented vaccination campaigns......GOAL of surveillance
- Understand existing activities...Gap analysis
- How to leverage information already in system