MEETING REPORT

WHO Global Invasive Bacterial Vaccine-Preventable Disease (IB-VPD) Surveillance Strategic Review

14th-15th November 2017

Hotel Royal
Geneva, Switzerland
Meeting Objectives

- Review the current status of the WHO coordinated Global IB-VPD network
- Discuss the objectives and needs of IB-VPD and specifically pneumococcal surveillance
- Discuss what we want the IB-VPD Network to look like in the future: short term (1-2 years) and long-term (up to 5 years)
- Discuss leveraging the network for surveillance of other diseases

Day 1, Session I: Objectives of the meeting, global highlights and needs of the global network

Presenters: Adam L. Cohen and Fatima Serhan, WHO HQ

Background

In 2008, at the genesis of the global network, surveillance objectives included documenting disease burden and circulating genotypes and serotypes, establishing a system of measuring post-vaccine impact, and monitoring antibiotic sensitivity in the pre-vaccine introduction era. Post-vaccine introduction surveillance objectives include assessing disease trends over time, monitoring immunization programs and changes in circulating genotypes and serotypes, and evaluating vaccine effectiveness and safety.

A strategic review of the Global Rotavirus and IB-VPD Surveillance Networks was conducted in 2014 and an informal technical advisory group (iTAG) did a systematic review of the data generated from the 2009 to 2014 from the Networks. Today, three years after the strategic review, WHO and partners reviewed the status of the IB-VPD network and to update the global surveillance objectives specifically pneumococcal surveillance, now that most of participating countries have introduced the PCV. The role of WHO has been the coordination and technical support provided to countries through global, regional and country level activities in collaboration with key partners and donors. The laboratory network plays a critical role in standardizing laboratory procedures, maintaining and quality assurance (QA)/ quality control (QC) programs such as global external quality assessment (EQA), and building and sustaining regional and national laboratory capacities.

The 2016 summary data were presented. There are regional differences in the number of children enrolled in meningitis and pneumonia/sepsis surveillance, the pathogens identified, and the laboratory tests used to confirm pathogens. Across all regions and for both meningitis and pneumonia surveillance, there is a high level of enrollment, sample collection, and sample testing, but a low positivity rate. The laboratories demonstrated a high level of competency through the 2016 EQA exercise: 94% (n=116) laboratories passed the EQA. QC for confirmatory testing also showed a high level of concordance between the global reference laboratory (GRL) and regional reference laboratories (RRLs). Laboratory assessments and regional trainings to increase molecular technique capacities were undertaken in 2016. If the IB-VPD network is to be leveraged to contribute to the monitoring of antimicrobial resistance (AMR) globally, increasing bacteriology capacity at the country level will be critical.

Day 1, Session II: Regional highlights including priorities, successes, and challenges
**AFRO**

*Presenter: Jason Mwenda, WHO AFRO*

Showing PCV impact is a strategic priority for AFR and progress has been made although this has been difficult in the region. Collaboration with partners such as U.S. Centers for Disease Control and Prevention (CDC) has been important in using surveillance data to show vaccine impact. Efforts are currently ongoing to coordinate the IB-VPD surveillance network and other meningitis surveillance systems through joint annual meetings and harmonization of laboratory and data systems. Results of these efforts include IB-VPD EQA expansion to include meningitis belt countries and enhanced outbreak response. Priorities include further integration of the 3 meningitis surveillance systems [pediatric bacterial meningitis surveillance (which is the AFR component of the IB-VPD surveillance network), enhanced meningitis surveillance, and case-based meningitis surveillance through MenAfriVac], evaluating PCV and MenAfriVac impact, and evaluating the cost of VPD surveillance to link to the immunization business case being developed in the Region.

**AMRO/PAHO**

*Presenters: Lúcia Oliveira and Gloria Rey, PAHO/WHO AMRO*

There are 42 sentinel sites that are part of the AMRO Regional Sentinel Surveillance Network for Bacterial Pneumonia and Meningitis. Over the years, IB-VPD case-based and aggregated sentinel surveillance have shown a decrease in the number of probable bacterial pneumonia and meningitis cases. In 2017, two countries were using the web tool VINUVACasos and eight countries were trained on the tool, which is the web-based surveillance database for case-based surveillance. The web tool will be used by ten countries for the next reporting period beginning in January 2018. Supervisory visits occurred at all sentinel sites in 2017. Funding for supervision, national and regional meetings, and laboratory supplies has been limited. Other challenges include the large number of mandatory variables for reporting and the performance requirements for sentinel sites that have fewer cases after vaccine introduction.

**EMRO**

*Presenters: Kamal Fahmy and Amany Ghoneim, WHO EMRO*

The number of countries and the number of sites per country participating in the network have been decreasing over the years. Currently there are 3 sites in Pakistan, 1 site in Afghanistan, 4 sites in Yemen, and 3 sites in Sudan. This year, sentinel site assessment visits occurred in Pakistan and Afghanistan. Successes in the region include establishing PCR capacities in laboratories in Pakistan and Sudan, and the adoption of laboratory standards and use of standard operating procedures (SOPs) in Pakistan. Challenges included decreasing motivation of in-country staff, funding, the polio transition, low isolation rates, procurement of laboratory supplies, and security in participating countries.

**WPRO**

*Presenter: Varja Grabovac, WHO WPRO*

Successes include increased molecular capacity in the Philippines, Mongolia, Vietnam and Fiji. Challenges include lack of funding given the low number of Gavi eligible countries and procurement of supplies. Priorities include facilitating another regional training to expand PCR capacity to more national laboratories, integrating China into the network, and developing a diphtheria outbreak response plan by leveraging the IB-VPD network. Vietnam is the only country in WPR that has yet to introduce PCV. Papua New Guinea is a priority country for Gavi and may be able to benefit from health system strengthening (HSS) grants for surveillance.
Presenter: Danni Daniels, WHO EURO

The regional IB-VPD laboratory workshop on direct PCR training held in April 2017 increased PCR laboratory capacities and created a platform to strengthen coordination between national, regional, and global IB-VPD laboratories. By the end of 2017, all participating countries in the global IB-VPD network will have graduated from Gavi. This will have a direct impact on funding for provision of rapid diagnostic tests (RDTs) and specimen transportation. During this transition time, access by countries in the region to the CDC International Reagent Resource has the potential to be important. Other challenges include low isolation rates, high use of antibiotics, and difficulty monitoring trends over time. The feasibility of using secondary datasets to monitor the impact of PCV introduction will be explored in Armenia.

Discussion and recommendations

- The surveillance network or possibly only the laboratory network may be leveraged for priority pathogens identified by the WHO Global Antimicrobial Resistance Surveillance System (GLASS), including *Streptococcus pneumoniae* and *Salmonella* typhi. The network can contribute to enhance bacteriology capacities and maintain quality assurance systems.
- Maintaining surveillance will be important for countries, particularly in Asia, that have not yet introduced PCV.
- All AMR/PAHO countries included in global IB-VPD surveillance network have introduced PCV.
- Country ownership and increasing country level capacities will be critical for sustaining surveillance long-term.
- Draft the pneumococcal surveillance chapter as part of the WHO-recommended standards for surveillance of selected vaccine-preventable diseases that are being updated this year.
- Review and revise the NUVI surveillance objectives from 2008 given current global and regional needs and the current funding situation. This latter recommendation was added to the list of actions to complete during this strategic review.

Day 1, Session III: SAGE PCV Working Group recommendations, including data gaps & surveillance

Presenter: Katherine O’Brien, IVAC Johns Hopkins Bloomberg School of Public Health

For the October 2017 SAGE meeting, the PCV working group reviewed available effectiveness and impact evidence on disease and non-disease outcomes regarding dosing schedules, product choice, and catch-up vaccination. SAGE did not recommend one specific schedule for administering PCV or one particular product over the other. However, countries may want to consider PCV13 in settings with a high burden of serotypes 19A or 6C. SAGE recommended catch-up for under 5-year-olds in high transmission settings, with consideration of a narrower and younger age stratum for catch-up in low transmission settings, and consideration of catch-up in outbreaks and humanitarian emergencies. SAGE made several recommendations regarding on surveillance. These included recommendations for long-term, post-introduction, serotype-specific surveillance in a representative number of settings for meningitis, invasive pneumococcal disease, and pneumonia. This may include population based surveillance, sentinel site surveillance, and periodic carriage studies.

Discussion and recommendations

- The case-to-carrier ratio is important data to collect for modeling and to interpret surveillance and nasopharyngeal carriage data.
- There is concern regarding manufacturer marketing given the recommendation for preference of PCV13 in settings with substantial burden from serotypes 19A and 6C.
The WHO should periodically and systematically review surveillance data and identify specific evidence gaps to be addressed.

**Day 1, Session IV: Workgroup discussion of evolving IB-VPD surveillance objectives to meet current global, regional and country needs and identify data gaps**

Three workgroups discussed what the current objectives for IB-VPD surveillance should be, what the surveillance, laboratory and data needs are to achieve these objectives, and how the network may be leveraged for other public health surveillance goals such as AMR. (Workgroup discussion topics are listed at the end.) The revised IB-VPD surveillance objectives identified by the workgroups and the types of surveillance that can meet these objectives are as follows:

<table>
<thead>
<tr>
<th>Pneumococcal Surveillance Objectives</th>
<th>Type of Surveillance Necessary to Meet Objectives</th>
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<tbody>
<tr>
<td></td>
<td>Sentinel Surveillance</td>
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<tr>
<td>1. To quantify disease burden and document the presence of disease</td>
<td>YES</td>
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<td>2. To describe serotype distribution and serotype replacement</td>
<td>YES (distribution)</td>
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<tr>
<td>3. To quantify vaccine impact to drive vaccine program optimization including dosing schedule and product choice</td>
<td>YES (in some places if sufficient number of cases)</td>
</tr>
<tr>
<td>4. To monitor AMR to improve patient care through informing bacterial VPD treatment recommendations</td>
<td>YES (in some places if sufficient number of cases)</td>
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<tr>
<td>5. To identify pneumococcal and meningococcal outbreaks</td>
<td>NO</td>
</tr>
<tr>
<td>6. To reveal immunization program implementation gaps</td>
<td>YES (in some places if sufficient number of cases)</td>
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The capacities needed to meet the objectives include the following: Laboratory EQA/QC, Data Management, Data Analysis, Laboratory consumables, Laboratory training support, National laboratory capacity, Predictable sustained funding, and Country level resources.

Stakeholders include the following: Countries/Ministries of Health, Funders, Industry, WHO, SAGE.
Recommendations

- The countries in the Global IB-VPD Surveillance Network are providing high quality data that are contributing to documenting the disease burden and serotype distribution.
- Sentinel site surveillance, however, is not sufficient in all countries to meet all of the above objectives and other surveillance or research methods might be needed.
- The Global IB-VPD Surveillance Network can be leveraged to monitor other VPDs and non-VPDs such as typhoid, diphtheria, and pertussis and can contribute to enhancing bacteriology capacity globally especially in a time where AMR is a high public health priority.
- Moving Forward, WHO should ensure that the pneumococcal and IB-VPD surveillance in countries is adequately sized and focuses on high quality sites that can contribute to meeting all of the above objectives.

Day 2, Session I: Future directions for IBD surveillance and the global and regional networks

Plenary Discussion

- Data generated by the Global IB-VPD Surveillance Network has been valuable at both the regional and global level. The surveillance data have been and will continue to be important for driving vaccine introduction. The network has led to huge increases in laboratory capacities and technical operational skills such as data management and analysis. This “collateral benefit” of capacity building is not specific to IB-VPD surveillance and is difficult to quantify.
- Surveillance may not be able to inform some policy questions given comparisons across different geographical and epidemiological settings provide limited evidence. SAGE identified head-to-head studies of different formulations and schedules as a research priority.

Day 2, Session II: Funding status and opportunities

Plenary Discussion led by Adam L. Cohen and Fatima Serhan, WHO HQ

- Given likely reductions in funding, sentinel site surveillance may not be necessary to continue in sites that are not generating quality data and for which WHO is not able to provide enough technical support and other resources.
- For Gavi-eligible countries, funding for surveillance may come from individual country applications for Gavi HSS or targeted country assistance (TCA) grants. Gavi-graduating countries may receive some funding if surveillance is prioritized by the country in Gavi graduation grants. Support from the network is very important for Gavi-graduated countries and non-Gavi eligible middle-income countries. In the European Region, PCV introduction was higher in middle-income countries eligible for Gavi support compared to MICs that were not eligible for Gavi support.

Meeting Recommendations

- WHO will develop a strategic plan on the IB-VPD and pneumococcal surveillance and the future vision of how the network can be leveraged to contribute to other programs such as AMR.
- WHO and countries will document successes and value of the IB-VPD network and surveillance.
- WHO and partners will advocate for surveillance and encourage countries to add surveillance activities to the GAVI HSS and TCA grants, if Gavi-eligible.
- WHO will evaluate the performance of the participating sites and adapt the scope of surveillance to the surveillance needs; with decreased GAVI funding, the focus will target sites that are producing good quality data and have consistent surveillance.
- GAVI-graduating countries will look into funding opportunities and WHO to help in mapping the list of donors that might be interested in sustaining surveillance activities in specific regions.
**Working group I**

**Group Topic: Pneumococcal and non-pneumococcal VPDs**

1. Is the sentinel site surveillance meeting the initial objectives of the network (listed below) especially for pneumococcus disease?
2. Is the network best platform for meningococcal and Hib surveillance or should it focus on pneumococcus moving forward?
3. Can the network be platform to leverage surveillance for other VPD pathogens (e.g. Typhoid) and can it contribute to AMR surveillance? List potential VPDs.

Please include all components of surveillance in your discussions from epi to lab and data management. Thoughts to reflect global, regional and country level perspectives.

**Initial objectives of the network since its establishment in 2008:**

**During pre-vaccine introduction period**

- Document presence of disease, describe the disease epidemiology and provide data for estimating disease burden
- Establish system to measure impact after vaccine introduction
- Identify circulating genotypes and measure genotype distribution
- Monitor antibiotic sensitivity

**In the post-vaccine introduction period**

- Assess disease trends over time
- Monitor vaccination program impact
- Monitor changes in circulating strains/genotypes/serotypes
- Platform for effectiveness and safety evaluation

**Working group II**

**Group Topic: surveillance needs at global, regional and country level**

1. What are the capacities needed to sustain surveillance for IBD at global, regional and country level?
2. Should objectives of the IBD sentinel site surveillance be changed to meet those needs?
3. How should WHO ensure sustainability of surveillance in countries after PCV has been in use and in countries transitioning from GAVI?

Please include all components of surveillance in your discussions from epi to lab and data management. Thoughts to reflect global, regional and country level perspectives and status of vaccine introduction/use.
**Initial objectives of the network since its establishment in 2008:**

**During pre-vaccine introduction period**

- Document presence of disease, describe the disease epidemiology and provide data for estimating disease burden
- Establish system to measure impact after vaccine introduction
- Identify circulating genotypes and measure genotype distribution
- Monitor antibiotic sensitivity

**In the post-vaccine introduction period**

- Assess disease trends over time
- Monitor vaccination program impact
- Monitor changes in circulating strains/genotypes/serotypes
- Platform for effectiveness and safety evaluation

**Working group III**

**Group Topic: Data needs for IBD surveillance**

1. What type of surveillance do you think should the network adapt moving forward (e.g., sentinel, population-based, case-based, laboratory-based)?
2. What are the minimum clinical and lab data that needs to be generated (existing or new)?
3. What are minimum standards for surveillance (e.g., QA/QC) that are needed?

Please include all components of surveillance in your discussions from epi to lab and data management. Thoughts to reflect global, regional and country level perspectives.
• Assess disease trends over time
• Monitor vaccination program impact
• Monitor changes in circulating strains/genotypes/serotypes
• Platform for effectiveness and safety evaluation
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4. Discuss leveraging the network for surveillance of other diseases

Tuesday, 14 November 2017
Day 1

Chair: Cynthia Whitney
Rapporteurs: Julia Bennett, Tomoka Nakamura, Stephanie Schwartz and Mahamoudou Ouattara

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
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<tbody>
<tr>
<td>8h30-9h00</td>
<td>Registration</td>
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<tr>
<td>9h00-9h30</td>
<td>Welcome, introduction, and objectives of the meeting</td>
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<tr>
<td>9h30-10h30</td>
<td>Global highlights and needs of the global network (30 min)</td>
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<td>o Current status of Global IB-VPD Surveillance Network</td>
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<td>o ST/GT pre-post vaccine introduction</td>
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<td><strong>Discussion question</strong>: What are the global objectives and needs of IBD surveillance? (30 min)</td>
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<td>9h30-10h30</td>
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<td>10h30-11h00</td>
<td>Coffee/tea break</td>
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<tr>
<td>11h00-12h30</td>
<td>Regional highlights including priorities, success, challenges</td>
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<td>o AFRO (will include integrated approach of meningococcal surveillance) (10 min)</td>
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<td>o PAHO (10 min)</td>
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<td>o EMRO (10 min)</td>
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<td>o Other WHO Regions inputs (10 min)</td>
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<td><strong>Discussion question</strong>: What are the regional objectives and needs of IBD surveillance? (50 min)</td>
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<td>12h30-13h30</td>
<td>Lunch break</td>
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<tr>
<td>13h30-14h00</td>
<td>SAGE PCV WG recommendations, including data gaps and surveillance (20 min presentation + 10 min discussion)</td>
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<tr>
<td>14h00-15h30</td>
<td>Workgroup discussions</td>
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<td>o Workgroup 1: Pneumococcal/non-pneumococcal VPDs</td>
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<td>o Workgroup 2: Country/Regional and global</td>
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<td>o Workgroup 3: Clinical/laboratory/data</td>
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<td><strong>Discussion questions</strong>: What are the current data needs in a post-PCV era? How should surveillance meet those needs?</td>
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<td>15h30-16h00</td>
<td>Coffee/tea break</td>
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<tr>
<td>16h00-17h30</td>
<td>Feedback from the three workgroups and group discussion</td>
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<td>Time</td>
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<tr>
<td>17h30-18h30</td>
<td>Reception</td>
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<td><strong>Wednesday, 15 November 2017</strong></td>
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<td><strong>Day 2</strong></td>
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<td><strong>Chair:</strong> Cynthia Whitney</td>
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<td><strong>Rapporteurs:</strong> Julia Bennett, Tomoka Nakamura, Stephanie Schwartz and Mahamoudou Ouattara</td>
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<tr>
<td>9h00-10h30</td>
<td><strong>Future directions for IBD surveillance and the global and regional networks</strong></td>
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<td>(Group Discussion)</td>
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<td>10h30-11h00</td>
<td><strong>Coffee/tea Break (group picture)</strong></td>
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<tr>
<td>11h00-12h00</td>
<td><strong>Funding status and opportunities</strong></td>
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<td>o Gavi eligible versus non Gavi eligible countries</td>
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<td>o Potential donors or opportunities</td>
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<td>(Adam Cohen, Fatima Serhan)</td>
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<td>12h00-12h30</td>
<td><strong>Closing of IB-VPD meeting</strong></td>
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<td>(Adam Cohen, Fatima Serhan)</td>
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<td>12h30-13h30</td>
<td><strong>Lunch break</strong></td>
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<tr>
<td>13h30-17h00</td>
<td><strong>Free time for participants to have side meetings and discussions</strong></td>
</tr>
</tbody>
</table>
List of Participants
Global Surveillance Network Meetings, 14-15 November 2017, Geneva

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